IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CONTINUED EXAMINATION UNDER 37 C.F.R. § 1.114

This Request for Continued Examination under 37 C.F.R. § 1.114 is submitted in response to the Notice of Allowance dated January 20, 2016. A submission and fee in support of the Applicant's Request is enclosed.

Amendments to the claims are reflected in the listing of claims that begins on page 2.

Remarks begin on page 5.

EXELIXIS 2009
Azurity v. Exelixis
IPR2025-00210
PART 2 OF 2
1341 of 2169

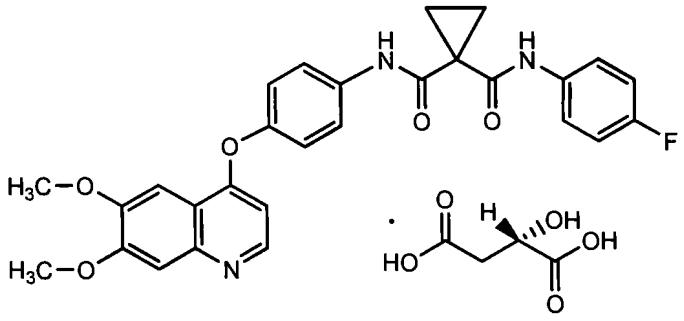
CLAIM AMENDMENTS

1-39. Cancelled.

40. (New) A capsule pharmaceutical composition:

Ingredient	$\frac{\textbf{mg/unit dose}}{\textbf{total fill weight}}$ **X 100**	**mg/unit dose**
Compound IB with 5 ppm or less of 6,7-dimethoxy-quinoline-4-ol (10 percent drug load formulation)	10	25
Silicified Microcrystalline Cellulose	78.7	196.75
Croscarmellose sodium	5	12.5
Sodium starch glycolate	5	12.5
Fumed Silica	0.3	0.75
Stearic acid	1	2.5
Total fill weight		250

wherein compound IB has the structure:



IB

41. (New) The capsule pharmaceutical composition of claim 40, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 25 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

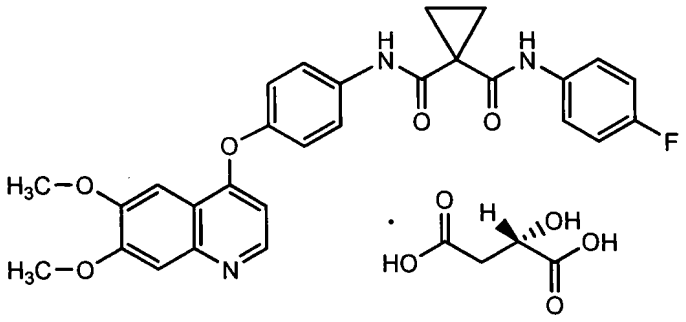
42. (New) The capsule pharmaceutical composition of claim 40, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 15 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

43. (New) The capsule pharmaceutical composition of claim 40, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 10 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

44. (New) A capsule pharmaceutical composition:

Ingredient	$\frac{\textbf{mg/unit dose}}{\textbf{total fill weight}}$ **X 100**	**mg/unit dose**
Compound IB with 5 ppm or less of 6,7-dimethoxy-quinoline-4-ol (50 percent drug load formulation)	50	100
Silicified Microcrystalline Cellulose	37.7	75.40
Croscarmellose sodium	5	10.00
Sodium starch glycolate	5	10.00
Fumed Silica	0.3	0.6
Stearic acid	2	4.0
Total fill weight		200

wherein compound IB has the structure:



IB ; and wherein the amount of carriers and excipients used in the capsule pharmaceutical composition can be varied proportionally according to the amount of Compound IB used.

45. (New) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 25 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

46. (New) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 15 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

47. (New) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 10 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

REMARKS

Claim Status

Claims 1-39 are cancelled.

Claims 40-47 are new and are supported by the specification, examples, and claims as originally filed.

Claim 40 is supported by allowed claim 23 and the "Pharmaceutical Composition" section of the specification beginning at page 22, paragraph 96 (which includes page 24, paragraph 116). Claims 41-43 are previously allowed claims 30-32.

Claims 44 is also supported by allowed claim 23 and the "Pharmaceutical Composition" section of the specification beginning at page 22, paragraph 96 (which includes page 24, paragraph 117). Claims 45-47 are previously allowed claims 30-32. No new matter has been added to new claims 40-47.

Thus, claims 40-47 are currently pending.

The claim amendments are made in the interest of expediting prosecution. The Applicant does not intend to surrender any range of equivalents to which the Applicant would otherwise be entitled in view of the prior art, nor does the Applicant agree with the Examiner's comments or arguments about the art cited in the Office Action. Further, by the present amendment, it does not follow that the amended claims have become so perfect in their description that no one could devise an equivalent. After amendment, as before, limitations in the ability to describe the present invention in language in the patent claims naturally prevent the Applicant from capturing every nuance of the invention or describing with complete precision the range of its novelty or every possible equivalent. *See* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 62 USPQ2d 1705 (2002). By amending the claims, the Applicant does not concede that patent coverage available to them would not extend as far as the original claim. The Applicant reserves the right to file divisional and/or continuation applications to pursue the breadth of the claims as filed. The Applicant respectfully requests the timely allowance of the amended claims.

REQUEST FOR CONTINUED EXAMINATION

It is believed that the Applicant's amendments to the claims and the arguments submitted herewith satisfy the requirement under § 1.114 for a submission accompanying a Request for Continued Examination. The fee set forth in 37 C.F.R. § 1.17(e)(2) is also submitted herewith.

INFORMATION DISCLOSURE STATEMENT

The Applicant notes that the filing of the enclosed Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement qualifies as prior art under 35 U.S.C. §§ 102 or 103, or is considered to be material to patentability as defined in 37 C.F.R § 1.56(b). The Applicant believes that the fee set forth in 37 C.F.R. § 1.17(p) is not required at this time pursuant to § 1.97(b)(4).

OTHER C-MET INHIBITOR CASES

The Applicant wishes to make the Examiner aware of the Applicant's other applications related to c-Met inhibitors and their use in the treatment of cancer. For the Examiner's convenience, the Applicant is providing a list of the Applicant's applications directed to the treatment of cancer using c-Met inhibitors. The Applicant understands the Examiner has electronic access to these applications and to the Office Actions that have issued in these applications, and has therefore not included copies with this Response. The Applicant will gladly provide the applications and Office Actions to the Examiner, however, upon request.

Application Number	Filing or 371 Date	Patent Number	Examiner	Status
10/573,336	09/18/2006		Koontz, Tammy J	Abandoned
11/571,140	12/21/2006	7,977,345	Moore, Susanna	Issued
11/586,751	10/26/2006	9,174,947	Ward, Paul V.	Issued
11/753,462	05/24/2007	8,178,532	Ward, Paul V.	Issued
11/753,503	05/24/2007	8,476,298	Ward, Paul V.	Issued
11/753,514	05/24/2007	8,067,436	Bernhardt, Emily A.	Issued
12/393,806	02/26/2009	7,579,473	Seaman, D. Margaret M.	Issued
12/911,442	10/25/2010		Ward, Paul, V.	Abandoned
13/087,094	04/14/2011		Chickos, Sarah, J.	Abandoned
13/129,183	05/13/2011		Seaman, D. Margaret M.	Abandoned
13/132,650	06/03/2011		Seaman, D. Margaret M.	Abandoned
13/145,054	10/20/2011	8,877,776	Carter, Kendra D	Issued
13/249,815	09/30/2011	8,497,284	Bernhardt, Emily A.	Issued
13/384,451	07/12/2012	8,673,912	Anderson, Rebecca L.	Issued
13/389,266	07/12/2012		Perreira, Melissa Jean	Abandoned
13/427,093	03/22/2012		Ward, Paul V.	Abandoned
13/438,964	04/04/2012		Brown-Pettigrew, Angela C.	Abandoned
13/634,275	09/12/2012		Anderson, Rebecca L.	Abandoned
13/753,031	01/29/2013		Pagonakis, Anna	Abandoned
13/753,146	01/29/2013		Pagonakis, Anna	Abandoned
13/810,537	08/26/2013		Pallay, Michael B.	Pending

Application Number	Filing or 371 Date	Patent Number	Examiner	Status
13/810,546	08/27/2013		Branson, Daniel L.	Pending
13/876,290	11/05/2013		Stone, Christopher R.	Abandoned
13/876,306	11/08/2013		Lee, Andrew P.	Abandoned
13/876,318	10/25/2013		Karol, Jody Lynn	Abandoned
13/888,592	05/07/2013		Ward, Paul V.	Abandoned
13/928,977	06/27/2013		Bernhardt, Emily A.	Abandoned
14/021,614	09/09/2013		Matos Negron, Taina Del Mar	Pending
14/115,236	02/28/2014		Anderson, James D.	Pending
14/166,545	01/28/2014		Not Yet Assigned	Abandoned
14/173,973	02/06/2014		Johannsen, Diana B.	Abandoned
14/340,871	07/25/2014		Carter, Kendra D.	Pending
14/346,570	03/21/2014		Calvillo, Y. Jeanmarie Z.	Pending
14/353,251	04/21/2014		Murray, Jeffrey H.	Pending
14/356,927	05/08/2014		Baek, Bong-sook	Pending
14/356,938	05/08/2014		Cerioni, Daniel Lee	Pending
14/398,188	10/31/2014		Henley III, Raymond J.	Pending
14/426,580	03/06/2015		Jean-Louis, Samira J.M.	Pending
14/518,733	10/20/2014		Chickos, Sarah J.	Pending
14/668,312	03/25/2015		Brown-Pettigrew, Angela C.	Pending
14/699,683	04/29/2015		Perreira, Melissa Jean	Pending
14/776,337	09/14/2015		Not Yet Assigned	Pending
14/782,493	10/05/2015		Not Yet Assigned	Pending
14/782,537	10/05/2015		Not Yet Assigned	Pending
14/843,480	09/02/2015		Not Yet Assigned	Pending
14/847,801	09/08/2015		Not Yet Assigned	Pending
14/933,801	11/05/2015		Brown-Pettigrew, Angela C.	Pending
15/066,872	03/10/2016		Not Yet Assigned	Pending

CONCLUSION

It is believed that due for this submission is the $850.00 fee set forth in 37 C.F.R. § 1.17(e)(2) for a small entity filing a second Request for Continued Examination under § 1.114. The Applicant authorizes the Office to charge this $850.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Respectfully submitted,

Date: April 20, 2016

Heidi M. Berven, Ph.D.
Reg. No. 48,951
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Ste. 300
Kalamazoo, MI 49007-3800
Direct (269) 337-7710
Fax (269) 337-7711

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/984,559	Filing Date 03/20/2014	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT **04/20/2016**

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 8	Minus	** 34	= 0	X $40 =	0
Independent (37 CFR 1.16(h))	* 2	Minus	***15	= 0	X $210 =	0
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	0

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/CORALIA BETANCOURT/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

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NOTICE OF ALLOWANCE AND FEE(S) DUE

91684 7590 01/20/2016

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 01/20/2016

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	04/20/2016

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 01/20/2016
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	04/20/2016

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29 — NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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United States Patent and Trademark Office
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91684 7590 01/20/2016

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 01/20/2016

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Examiner-Initiated Interview Summary	Application No.	Applicant(s)	
	13/984,559	WILSON ET AL.	
	Examiner	Art Unit	
	TIMOTHY R. ROZOF	1625	

All participants (applicant, applicant's representative, PTO personnel):

(1) *TIMOTHY R. ROZOF*. (3)_____.

(2) *HEIDI BERVEN, PH.D*. (4)_____.

Date of Interview: *31 December 2015*.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☒ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☒Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *23 and 30-32*.

Identification of prior art discussed: _____.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Discussed the allowability of the claimed subject matter. Requested that Applicant file a new ADS to show the addtion of the inventor Khalid Shah, to place the application in condition for allowance.

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/TIMOTHY R ROZOF/ Primary Examiner, Art Unit 1625	

Notice of Allowability	Application No. 13/984,559	Applicant(s) WILSON ET AL.	
	Examiner TIMOTHY R. ROZOF	Art Unit 1625	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *October 1, 2015, RCE, Amendment & Remarks*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *23 and 30-32*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☒ Interview Summary (PTO-413), Paper No./Mail Date *12.31.15* .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/TIMOTHY R ROZOF/
Primary Examiner, Art Unit 1625

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☐ Attachment

/TIMOTHY R ROZOF/ Primary Examiner, Art Unit 1625	

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

CPC							
Symbol						**Type**	**Version**
A61K		31	/	47		F	2013-01-01
C07D		215	/	233		I	2013-01-01
			/				
			/				
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CPC Combination Sets								
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 4	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625 (Primary Examiner)	01/07/2016 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
		A	6	1	K	31 / 47 (2006.0)						
CROSS REFERENCE(S)		C	0	7	D	215 / 233 (2006.01.01)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)											

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	4	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	01/07/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	23														
2	30														
3	31														
4	32														

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	4	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	01/07/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

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 NEWS 25  DEC 24  Additional Experimental Spectra Now Available in CAS REGISTRY
                  in STN
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 NEWS 28  JAN 26  Annual MEDLINE Reload on STN Features Enhanced Clinical Trial
                  Information and the 2015 MeSH Thesaurus
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 NEWS 30  APR 15  USPATFULL/USPAT2 Now Include Corporate Patent Applicant
                  Information
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 NEWS 38  DEC 17  Latest Release of New STN Enhances Search Functionality,
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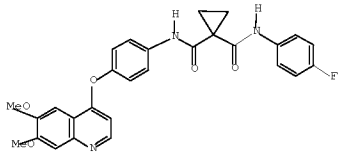
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L1      STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
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FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          159 TO      721
PROJECTED ANSWERS:               2 TO      124

L2            2 SEA SSS SAM L1

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REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Aug 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Sep 2014

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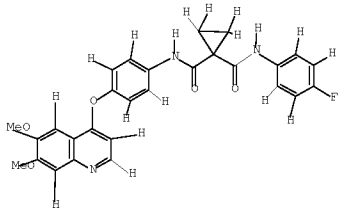
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or IB exact (10.4.14)

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L5 HAS NO ANSWERS
L5              STR
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SEARCH TIME: 00.00.01

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                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          159 TO      721
PROJECTED ANSWERS:               2 TO      124

L6            2 SEA SSS SAM L5

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100.0% PROCESSED      460 ITERATIONS                              31 ANSWERS
SEARCH TIME: 00.00.01

L7           31 SEA SSS FUL L5

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L8          340 L7

=> d ibib abs -340

L8   ANSWER 1 OF 340  CAPLUS  COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER:        2015:2059342  CAPLUS Full-text
TITLE:                   Methods and devices for treating posterior ocular
                         disorders
INVENTOR(S):             Noronha, Glenn; Brooks, Christopher John; Andino,
                         Rafael Victor; Patel, Samirkumar; White, Daniel
PATENT ASSIGNEE(S):      Clearside Biomedical, Inc., USA
SOURCE:                  PCT Int. Appl., 175pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:
     PATENT NO.          KIND  DATE        APPLICATION NO.         DATE
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     WO 2015195842        A1   20151223    WO 2015-US36299         20150617
         W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
             BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE,
             EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR,
             IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA,
             MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA,
             PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK,
             SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
             VC, VN, ZA, ZM, ZW
         RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR,
             HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS,
             SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM,
             ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,
             SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.:                   US 2014-62013209     P  20140617
                                         US 2014-62018148     P  20140627
                                         US 2014-62063792     P  20141014
                                         US 2015-61155367     P  20150430
                                         US 2015-62156802     P  20150504
AB   The present invention relates to a methods and devices for treating uveitis,
     macular edema associated with uveitis and macular edema associated with
     retinal vein occlusion in a human subject in need thereof.  In certain
     aspects, devices provided herein include a medicament container defining a
     lumen configured to contain a medicament, a distal end portion of the
     medicament container including a coupling portion configured to be removably
     coupled to a needle assembly, a proximal end portion of the medicament
     container including a flange and a longitudinal shoulder; a piston assembly
     including a distal end portion movably disposed within the lumen of the
     medicament container; and a handle coupled to a proximal end portion of the
     piston assembly.


L8   ANSWER 2 OF 340  CAPLUS  COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER:        2015:2015841  CAPLUS Full-text
TITLE:                   Anti-human Tumor endothelial marker TEM8 antibodies
                         and other molecularly targeted agent for combination
                         therapy of cancer
INVENTOR(S):             Saha, Saurabh; Zhang, Xiaoyan M.; Dimitrov, Dimiter;
                         Zhu, Zhongyu; St. Croix, Brad; Zudaire, Enrique
PATENT ASSIGNEE(S):      Biomed Valley Discoveries, Inc., USA; Untied States
                         Dept.of Health and Human Services
SOURCE:                  PCT Int. Appl., 121pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:
     PATENT NO.          KIND  DATE        APPLICATION NO.         DATE
     ----------          ----  --------    --------------------    --------
     WO 2015191610        A2   20151217    WO 2015-US34941         20150609
         W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
             BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE,
             EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR,
             IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA,
             MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA,
             PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK,
             SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
             VC, VN, ZA, ZM, ZW
         RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR,
             HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS,
             SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM,
             ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,
             SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.:                   US 2014-62009371     P  20140609
AB   The present invention provides, inter alia, methods for treating or
     ameliorating the effects of a disease, such as cancer, in a subject.  The
     methods include: administering to a subject in need thereof (a) a
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therapeutically effective amount of a molecularly targeted agent; and (b) a therapeutically effective amount of a monoclonal antibody or antigen binding fragment thereof, wherein the monoclonal antibody contains: (i) a heavy chain variable region (VH), which includes an amino acid sequence selected from SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, and SEQ ID NO:7; and (ii) a light chain variable region (VL), which includes an amino acid sequence selected from SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8. Compns., including pharmaceutical compns., and kits for treating diseases, such as cancer, are also provided herein.

L8 ANSWER 3 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1965343 CAPLUS Full-text
TITLE: Repurposing of anticancer drugs: in vitro and in vivo activities against Schistosoma mansoni
AUTHOR(S): Cowan, Noemi; Keiser, Jennifer
CORPORATE SOURCE: Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, CH-4002, Switz.
SOURCE: Parasites & Vectors (2015), 8, 1-9
CODEN: PVAEAK; ISSN: 1756-3305
DIGITAL OBJECT ID: 10.1186/s13071-015-1023-y
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Drug discovery for the neglected tropical disease schistosomiasis has a high priority. Anticancer drugs, especially protein kinase inhibitors, might serve as a starting point for drug discovery owing to the importance of protein kinases in helminth growth and development. Furthermore, the Schistosoma mansoni genome encodes several genes for targets of drugs marketed for human use, including several anticancer drugs. Methods: In this study, we screened the approved oncol. drug set of the National Cancer Institute's Developmental Therapeutic Program for antischistosomal activity. Drugs were tested in vitro against the larval and adult stage of S. mansoni. IC values and albumin binding were determined for active compds. Lead compds. were tested in the chronic S. mansoni mouse model. Results: Eleven of the 114 compds. tested revealed IC values ≤ 10 μM against both S. mansoni stages. Five of these lost activity against adult S. mansoni in the presence of serum albumin. Of 6 compds. studied in vivo, the highest activity was observed from two kinase inhibitors trametinib, and vandetanib, which reduced worm burden by 63.6 and 48.1 % resp., after a single oral dose of 400 mg/kg body weight Conclusion: Our study has confirmed that oncol. drugs possess antischistosomal activity. There is space for further investigation, including elucidation of the mechanisms of action of schistosome-active cancer drugs, application of different treatment courses, and structure-activity relationship studies for improving drug potency.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1892326 CAPLUS Full-text
DOCUMENT NUMBER: 163:709974
TITLE: Novel polymorphs of cabozantinib (S)-malate and cabozantinib free base
INVENTOR(S): Jetti, Ramakoteswara Rao; Indukuri, Anjaneyaraju; Punde, Dnyandeo; Bohra, Chandersingh; Gadakar, Mahesh
Kumar; Gore, Vinayak
PATENT ASSIGNEE(S): Mylan Laboratories Ltd., India
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015177758	A1	20151126	WO 2015-IB53765	20150522

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

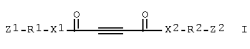
PRIORITY APPLN. INFO.: IN 2014-CH2561 A 20140523
AB The present disclosure provides novel cryst. forms of cabozantinib (S)-malate, designated as form-M1, M2, M3 and M4 and novel crystalline forms of cabozantinib free base, form-M1, M2 and M3 and methods of their production The present disclosure also provides processes for the preparation of crystalline cabozantinib (S)-malate form N-1. Formula (I).
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1818418 CAPLUS Full-text
TITLE: Advances in receptor tyrosine kinase inhibitors taking c-Met as anti-tumor target
AUTHOR(S): Zhang, Yuan; Cheng, Yulan; Zhou, Jinpei; Zhang, Huibin
CORPORATE SOURCE: Dept. of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2015), 46(1), 16-27
CODEN: ZHYXE9; ISSN: 1000-5048
DIGITAL OBJECT ID: 10.11665/j.issn.1000-5048.20150102
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 52 refs. on the c-Met signaling pathway and the resistance of kinase inhibitors caused by the cross-talk between c-Met and other membrane receptors and the progress of single-target and multi-target c-Met inhibitors.

L8 ANSWER 6 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1805828 CAPLUS Full-text
DOCUMENT NUMBER: 163:694481
TITLE: Acetylenedicarboxyl linkers and their uses in specific conjugation of a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: U.S. Pat. Appl. Publ., 80pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150322155	A1	20151112	US 2015-14799666	20150715

PRIORITY APPLN. INFO.: US 2015-14799666 20150715
OTHER SOURCE(S): MARPAT 163:694481
GI



AB Provided are novel acetylenedicarboxyl linkers used for the specific conjugation of compds./cytotoxic agents to a cell-binding mol., through bridge linking pairs of thiols on the cell-binding mol. Also provided are methods of making such linkers, and of using such linkers in making homogeneous conjugates, as well as of application of the conjugates in treatment of cancers, infections and autoimmune disorders. Particularly provided is a bridge linker compound of the Formula (I), wherein:The acetylenedicarboxyl group is capable of reacting with a pair of sulfur atoms of the cell-binding agent; Z1 and Z2 are the same or different a function group that enables to react with a cytotoxic drug; R1 and R2 are the same or different linear alkyl; X1 and X2 are independently selected from NH, N(R3), O, S or CH2; R3 is H, linear alkyl.

L8 ANSWER 7 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1783428 CAPLUS Full-text
DOCUMENT NUMBER: 163:681013
TITLE: Cabozantinib for the treatment of progressive metastatic medullary thyroid cancer
AUTHOR(S): Krajewska, Jolanta; Olczyk, Tomasz; Jarzab, Barbara
CORPORATE SOURCE: Nuclear Medicine and Endocrine Oncology Department, M.Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Pol.
SOURCE: Expert Review of Clinical Pharmacology (2016), 9(1), 69-79
CODEN: ERCPAG; ISSN: 1751-2433
DIGITAL OBJECT ID: 10.1586/17512433.2016.1102052
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (XL-184) is a potent inhibitor of MET, VEGFR 2/KDR, RET and other receptor tyrosine kinases, such as KIT, AXL and FLT3. Its efficacy against MTC has been demonstrated in a prospective, randomized, placebo-controlled study (EXAM). Cabozantinib comparing to placebo significantly prolonged progression free survival both in hereditary and sporadic MTC, 11.2 vs. 4.0 mo, resp. Final anal. showed no global differences in overall survival (OS) between cabozantinib and placebo. However, in a subgroup with RET M918T mutation the difference in OS was significant: 44.3 vs. 18.9 mo, resp. Among the most frequent cabozantinib-related adverse events (AEs), observed in >30% of patients were diarrhea, palmar-plantar erythrodysesthesia, decreased weight, decreased appetite, nausea, fatigue, dysgeusia, hair color changes and hypertension. Expert Commentary: Cabozantinib constitutes an effective treatment option with acceptable toxicity in MTC patients showing either germinal or sporadic tumor RET M918T mutation as the drug prolonged OS in these subjects.
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1726025 CAPLUS Full-text
DOCUMENT NUMBER: 163:628844
TITLE: Method of treating lung adenocarcinoma
INVENTOR(S): Aftab, Dana T.; Yu, Peiwen
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015164869	A1	20151029	WO 2015-US27800	20150427

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61984599 P 20140425
OTHER SOURCE(S): MARPAT 163:628844
AB This invention is directed to the treatment of cancer in a patient, particularly a patient with lung adenocarcinoma, and more particularly a patient with SLC34A2-ROS1, CD74-ROS1, or FIG-ROS1 fusion-pos. non-small cell lung cancer, with an inhibitor of MET, VEGFR2, and ROS1.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1723003 CAPLUS Full-text
DOCUMENT NUMBER: 163:632038
TITLE: Hepatocyte growth factor as marker of prognosis in small cell lung cancer (SCLC)
INVENTOR(S): Arriola Aperribay, Edurne; Canadas Castillo, Israel; Rovira Guerin, Ana; Albanell Mestres, Joan

PATENT ASSIGNEE(S): Fundacio Institut Mar d'Investigacions Mediques (IMIM), Spain
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015161885	A1	20151029	WO 2014-EP58375	20140424
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

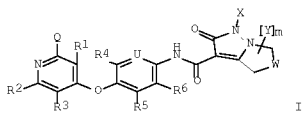
PRIORITY APPLN. INFO.: WO 2014-EP58375 20140424
AB The invention relates to a new marker, the hepatocyte growth factor (HGF) in serum or plasma for the prognosis of small-cell lung cancer (SCLC). The invention also provides methods for selecting subjects suffering from SCLC that are candidate to respond to certain substances inhibiting certain kinases expressed in the tumors. There are also encompassed the use of immunoassay and nucleic acid reagents for detecting HGF in serum or plasma, said reagents for carrying out the prognostic method.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1694942 CAPLUS Full-text
DOCUMENT NUMBER: 163:596944
TITLE: Methods for treating cancer using TOR kinase inhibitor combination therapy
INVENTOR(S): Fultz, Kimberly Elizabeth; Tran, Tam Minh; Xu, Shuichan; Xu, Weiming; Trowe, Torsten; Filvaroff, Ellen
PATENT ASSIGNEE(S): Signal Pharmaceuticals, LLC, USA
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

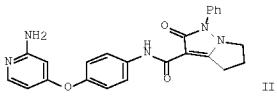
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015160868	A1	20151022	WO 2015-US25843	20150415
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2014-61982729 P 20140422
OTHER SOURCE(S): MARPAT 163:601731

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I



II

AB The title compds. I [Q = H, (un)substituted OH, NH2, etc.; U = CR7 or N; X = H, alkyl, cycloalkyl, etc.; Y = alkyl, cycloalkyl, aryl, etc.; m = 0-4; W = (CH2)n, (CH2)nO, (CH2)nNH, (CH2)nS (wherein n = 0-4); R1-R7 = H, F, Cl, Br, etc.; with the provisos], which are used to inhibit or modulate the activity of receptor tyrosine kinases, especially Axl, Mer, c-Met and Ron, were prepared E.g., a multi-step synthesis of II, starting from phenylhydrazine and 4-chlorobutanoyl chloride, was described. Exemplified compds. I were tested for their biol. activity (data given for representative compds. I). The invention also provides pharmaceutical compns. comprising the compound I, and a method of preventing, treating or lessening the severity of a proliferative disorder in a patient with the compds. I or the pharmaceutical compns. comprising I.

L8 ANSWER 12 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1654358 CAPLUS Full-text
DOCUMENT NUMBER: 163:601695
TITLE: 2,3-Disubstituted pyridine compounds as TGF-beta inhibitors and their preparation
INVENTOR(S): Singh, Rajinder; Bhamidipati, Somasekhar; Ding, Pingyu; Payan, Donald; Gelman, Marina; Kinsella, Todd
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 406pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015157093	A1	20151015	WO 2015-US24146	20150402
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150297590	A1	20151022	US 2015-14686872	20150415

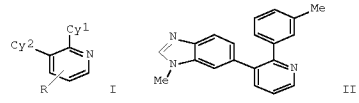
PRIORITY APPLN. INFO.: US 2014-61980124 P 20140416
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Provided are methods for treating or preventing cancer, comprising administering an effective amount of a 3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one TOR kinase inhibitor and an effective amount of a second active agent to a patient. Cancers treated by the method include solid tumors of the head, neck, breast, lung, ovaries, colon, rectum, stomach, prostate, urinary bladder, uterine, cervix, and other reproductive organs, wherein the tumors include relapsed, refractory or advanced solid tumors.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1694572 CAPLUS Full-text
DOCUMENT NUMBER: 163:601731
TITLE: Preparation of bicyclic pyrazolone compounds for inhibiting or modulating the activity of receptor tyrosine kinases
INVENTOR(S): Xi, Ning; Wu, Yanjun
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: U.S. Pat. Appl. Publ., 52pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150299219	A1	20151022	US 2015-14687992	20150416
WO 2015164161	A1	20151029	WO 2015-US26062	20150416
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2014-61982729 P 20140422
OTHER SOURCE(S): MARPAT 163:601731

IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2014-61976880 P 20140408
US 2014-62019577 P 20140701
OTHER SOURCE(S): MARPAT 163:601695
GI



I II

AB The invention described compds. of formula I and a method of treating cancer comprising administering to a subject having cancer one of the compds. in conjunction with another therapeutic treatment of cancer. The compds. I inhibit signaling by a member of the TGF-β superfamily such as nodal or activin. Compds. of formula I wherein Cyl is (un)substituted Ph, benzofuranyl, (un)substituted C1-3 alkyl, etc.; Cy2 is pyrazolo[1,5-a]pyrimidinyl, benzothiazolyl, imidazo[1,2-a]pyridinyl, (un)substituted phenylsulfonyl, etc.; R is (un)substituted Ph, (un)substituted heteroaryl and (un)substituted heterocycloalkyl; and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by cross-coupling of 2-chloro-2-(3-methylphenyl)pyridine with 1-methyl-1H-benzimidazole-6-boronic acids. The invention compds. were evaluated for their TGF-β inhibitory activity (some data given).
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1650548 CAPLUS Full-text
DOCUMENT NUMBER: 163:585951
TITLE: Preparation of bridge linkers used for specific conjugation of two or more cytotoxic agents to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin; Zhao, Robert
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 162pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

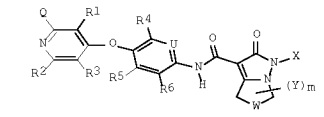
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015155753	A2	20151015	WO 2015-IB56083	20150810
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150284416	A1	20151008	US 2015-14740403	20150616
PRIORITY APPLN. INFO.:			US 2015-14740403	T0 20150616
OTHER SOURCE(S):	MARPAT 163:585951			

GI

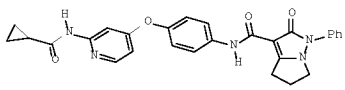
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to novel linkers contg. a 2,3-disubstituted succinic group, or 2-monosubstituted, or 2,3-disubstituted fumaric or maleic (trans (E)- or cis (Z)-butenedioic) group, e.g., (I), for conjugation of two or more compds./cytotoxic agents per linker to a cell-binding mol., through bridge linking pairs of thiols (reduced from the interchain disulfide bonds of the cell-binding agent by a reducing agent, such as dithiothreitol, dithioerythritol, L-glutathione and tris(2-carboxyethyl)phosphine (TCEP), or/and β-mercaptoethanol) on the cell-binding mol. specifically. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by treating reaction with drugs and to their use for cancers, infections and autoimmune disorders. Thus, linker I was prepared by cyclization of 2,3-dibromosuccinic acid in CH2Cl2 in the presence of P2O5. R1-COCHBrCHBrCO-R (II) was prepared in 3 steps from I and R1-H (preparation given) using R = H (preparation given). A herceptin antibody conjugate with II was prepared by reacting herceptin with and TCEP and II. The resulting conjugate was evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 889 and for SK-OV-3 cell was over 800. Five-week-old female BALB/c Nude mice inoculated s.c. in the area under the right shoulder with N-87 carcinoma cells treated with the conjugate had completely no tumor measurable at day 13 till day 60 (the end of experiment) in an in vivo antitumor activity study.

L8 ANSWER 14 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1646639 CAPLUS Full-text
DOCUMENT NUMBER: 163:612041



I



II

AB The invention provides bicyclopyrazolone compds. I [wherein Q = H, (un)substituted OH, NH2, etc.; U = (un)substituted CH or N; X = H, alkyl, alkenyl, alkynyl, etc.; Y = independently H, alkyl, alkenyl, etc.; W = (CH2)n, (CH2)nO, (CH2)nNH, or (cH2)nS; n = 0-4; R1-R6 = independently H, F, Cl, Br, CN, N3, etc.; m = 1-4; with provisos], stereoisomers, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts, or prodrugs thereof for suppressing the activity of receptor tyrosine kinase, especially Axl, Mer, c-Met and Ron kinases. The invention also provides pharmaceutical compns. comprising the title compds., and application of the title compds. and pharmaceutical compns. for preventing and treating proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 3 and 26 nM against Mer and c-Met tyrosine kinases, resp.

L8 ANSWER 16 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1635205 CAPLUS Full-text
TITLE: Selective targeting of CTNNB1-, KRAS- or MYC-driven cell growth by combinations of existing drugs
AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; Spijkers-Hagelstein, Jill A. P.; de Vetter, Judith R. F.; de Man, Jos; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE: Netherlands Translational Research Center B.V., Oss, Neth.
SOURCE: PLoS One (2015), 10(5), e0125021/1-e0125021/22
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0125021
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB The aim of combination drug treatment in cancer therapy is to improve response rate and to decrease the probability of the development of drug resistance. Preferably, drug combinations are synergistic rather than additive, and, ideally, drug combinations work synergistically only in cancer cells and not in non-malignant cells. We have developed a workflow to identify such targeted synergies, and applied this approach to selectively inhibit the proliferation of cell lines with mutations in genes that are difficult to modulate with small mols. The approach is based on curve shift anal., which we demonstrate is a more robust method of determining synergy than combination matrix screening with Bliss-scoring. We show that the MEK inhibitor trametinib is more synergistic in combination with the BRAF inhibitor dabrafenib than with vemurafenib, another BRAF inhibitor. In addition, we show that the combination of MEK and BRAF inhibitors is synergistic in BRAF-mutant melanoma cells, and additive or antagonistic in, resp., BRAF-wild type melanoma cells and non-malignant fibroblasts. This combination exemplifies that synergistic action of drugs can depend on cancer genotype. Next, we used curve shift anal. to identify new drug combinations that specifically inhibit cancer cell proliferation driven by difficult-to-drug cancer genes. Combination studies were performed with compds. that as single agents showed preference for inhibition of cancer cells with mutations in either the CTNNB1 gene (coding for β-catenin), KRAS, or cancer cells expressing increased copy nos. of MYC. We demonstrate that the Wnt-pathway inhibitor ICG-001 and trametinib acted synergistically in Wnt-pathway-mutant cell lines. The ERBB2 inhibitor TAK-165 was synergistic with trametinib in KRAS-mutant cell lines. The EGFR/ERBB2 inhibitor neratinib acted synergistically with the spindle poison docetaxel and with the Aurora kinase inhibitor GSK-1070916 in cell lines with MYC amplification. Our approach can therefore efficiently discover novel drug combinations that selectively target cancer genes.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1634096 CAPLUS Full-text
TITLE: Method for screening antitumor drug biomarkers, and application thereof
INVENTOR(S): Xiong, Lei
PATENT ASSIGNEE(S): HTS Biotechnology (Shanghai) Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 23pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104975063	A	20151014	CN 2014-10130154	20140401
PRIORITY APPLN. INFO.:			CN 2014-10130154	20140401

AB The invention discloses method for screening antitumor drug biomarkers, and application thereof. The method comprises the steps of: (1) providing tumor cells as starting cells, and tumor cells are from identical tumor tissue of the same object, (2) performing passage of the starting cells, establishing cell lines, and detecting genomic information of the cell lines so as to obtain at least 5 tumor cell lines that have genomic differences and are highly homologous, (3) performing antitumor drug sensitivity testing of the tumor cell lines, and typing the tumor cell lines based on the testing results, and (4) based on the typing results, analyzing the genomic information of the tumor cell lines to determine anti-tumor drug biomarkers. The method can maximally reduce background noise between different tumor cell lines, and can help to efficiently and accurately screen biomarkers of antitumor drugs.

L8 ANSWER 15 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1640328 CAPLUS Full-text
DOCUMENT NUMBER: 163:618028
TITLE: Preparation of bicyclopyrazolone compounds as tyrosine kinase inhibitors
INVENTOR(S): Xi, Ning; Wu, Yanjun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 81pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104974162	A	20151014	CN 2015-10167125	20150409
PRIORITY APPLN. INFO.:			CN 2014-10141156 A	20140409
OTHER SOURCE(S):	MARPAT 163:618028			

GI

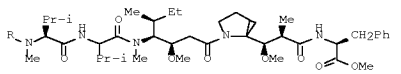
AB This study examd. whether oral administration of erlotinib to rats with cabozantinib led to any pharmacokinetic interactions or not. Twenty four rats were randomly divided into 3 groups, cabozantinib group (cabozantinib 30 mg/kg, n = 8), erlotinib group (erlotinib 25 mg/kg, n = 8) and co-administration group (erlotinib 25 mg/kg and cabozantinib 30 mg/kg, n = 8). The concentration of cabozantinib and erlotinib in rat plasma was determined by a sensitive and simple UPLC-MS/MS method. There was statistical pharmacokinetics difference for cabozantinib in the cabozantinib group and co-administration group, when co-oral administration cabozantinib with erlotinib, the AUC(0-t) and Cmax increased ($p < 0.01$). There was statistical pharmacokinetics difference for erlotinib in the erlotinib group and co-administration group, when co-oral administration erlotinib with cabozantinib, the AUC(0-t) increased and CL decreased ($p < 0.05$). These data indicate erlotinib could influence the pharmacokinetic

profile of cabozantinib in rats, and vice versa, which might cause drug-drug interactions when using cabozantinib with erlotinib.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

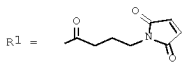
L8 ANSWER 18 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623830 CAPLUS Full-text
DOCUMENT NUMBER: 163:553993
TITLE: Preparation of cytotoxic auristatin analogs and their conjugates with cell-binding molecules
INVENTOR(S): Liang, Qingliang; Zhao, Robert Y.; Ye, Hangbo; Gai, Shun; Jia, Junxiang; Huang, Yuanyuan; Li, Xing; Guo, Huihui; Xie, Hongsheng; Li, Wenjun; Zhou, Xiaomai; Yang, Chengyu; Zhuo, Xiaotao; Zhao, Linyao; Cao, Minjun; Lin, Chen; Peng, Jie; Ye, Zhicang; Xu, Jun
PATENT ASSIGNEE(S): Hangzhou DAC Biotech Co, Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 127pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

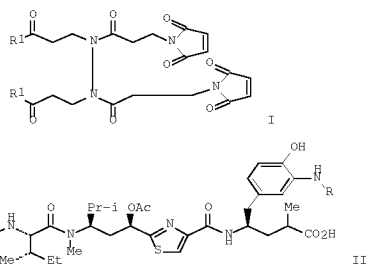
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151079	A2	20151008	WO 2015-IB54653	20150620
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			WO 2015-IB54653	20150620

OTHER SOURCE(S): MARPAT 163:553993
GI



I





II

AB The invention is related to the prepn. of novel linkers contg. a hydrazine unit, e.g., I, used for the specific conjugation in particular cytotoxic agents to a cell-binding mol., through bridge linking a pair of thiols on the cell-binding mol. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by reaction with drugs and to their use for treating especially cancer. Thus, the linker I [R1 = OH] was prepared by a multi-step synthesis starting from O-benzylhydroxylamine hydrochloride and tert-Bu acrylate using tert-Bu 3-aminopropanoate and 3-maleimidopropanoic acid. Reaction of I with oxalyl chloride, and treatment of the diacid dichloride with II [R = H] gave I [R1 = II wherein R is absent]. A herceptin antibody-I [R1 = II wherein R is absent] conjugate was prepared and evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 105 and for SK-OV-3 cell was over 3136.

L8 ANSWER 20 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623828 CAPLUS Full-text
DOCUMENT NUMBER: 163:585947
TITLE: Preparation of novel bridge linkers containing an acetylenedicarbonyl group for specific conjugation of a cytotoxic agent to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 113pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

AB The invention is related to the prepn. of cytotoxic auristatin analogs, e.g., I, in particular monomethyl auristatin F (MMAF) conjugates of such cytotoxic agents with a cell-binding agent, methods of using them to arrest or retard abnormal cell growth and /or proliferation and to their use for targeted treatment of cancer, autoimmune disease, and infectious diseases. Thus, I [R = H] was prepared and coupled to 4-maleimidobutyric acid to provide I [R = R1] linker drug conjugate. A herceptin antibody-I [R = R1] conjugate was prepared and evaluated for its in vitro potency against N-87 human gastric carcinoma cells.

L8 ANSWER 19 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623829 CAPLUS Full-text
DOCUMENT NUMBER: 163:553992
TITLE: Preparation of bridge linkers used for specific conjugation of a cytotoxic agent to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 112pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151081	A2	20151008	WO 2015-IB55264	20150712
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150314017	A1	20151105	US 2015-14799712	20150715
PRIORITY APPLN. INFO.:			WO 2015-IB55264	T0 20150712

OTHER SOURCE(S): MARPAT 163:553992
GI

WO 2015151080	A2	20151008	WO 2015-IB55051	20150704
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			WO 2015-IB55051	20150704

OTHER SOURCE(S): MARPAT 163:585947
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of novel bridge linkers contg. an acetylenedicarboxylic group, e.g., I, to link two drugs to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by reaction with drugs and to their use for treating especially cancer. Thus, I [R = 2,5-dioxopyrrolidin-1-yloxy] was prepared by reacting 13-amino-bis(4,7,10-trioxadodecanoic acid) (preparation given) with bis(2,5-dioxopyrrolidin-1-yl)but-2-ynedioate (preparation given) and treatment of the tetraacid with NHS. Amidation of I [R = 2,5-dioxopyrrolidin-1-yloxy] with tubulysin analog R1-H gave R1-I [R = absent] containing 4 tubulysins analog per bridge linker. A herceptin antibody-R1-I [R = absent] conjugate was prepared and evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 270 (IC50>10/IC50 = 0.037), and for SK-OV-3 cell was over 344.

L8 ANSWER 21 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623827 CAPLUS Full-text
DOCUMENT NUMBER: 163:553991
TITLE: Preparation of hydrophilic linkers for the conjugation of a cytotoxic agent or a chromophore to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151078	A2	20151008	WO 2015-IB54521	20150615

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2015-IB54521 20150615
OTHER SOURCE(S): MARPAT 163:553991
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of hydrophilic linkers contg. phosphamide, phosphinate, sulfonamide, sulfonyl, sulfonimide, and/or sulfoxide groups, e.g., I, to link drugs, in particular, cytotoxic agents or a chromophore mols. to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (e.g. cytotoxic agent) conjugates comprising either modification of the drugs with these hydrophilic linkers first, followed by reaction with cell-binding agents; or modification of cell-binding agents with these hydrophilic linkers first, followed by reaction with drugs. Thus, linker I was prepared from N-methylethane-1,2-diamine and succinic anhydride using POCl3, 3-(methylamino)propanoic acid and NHS. Conjugation of I with the tubulysin analog II [R = H] gave the drug-linker conjugate II [R = Rl]. An antiHer2-II [R= Rl] antibody conjugate of was prepared and evaluated for its in vitro cytotoxicity. The specificity of the conjugate for N87 cell was over 1315 (IC50> 50/IC50= 0.038), and for SK-OV-3 cell was over 1560.

L8 ANSWER 22 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1617130 CAPLUS Full-text
DOCUMENT NUMBER: 163:553989
TITLE: Preparation of hydrophilic linkers for the conjugation of a cytotoxic agent or a chromophore to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: U.S. Pat. Appl. Publ., 69pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015153514	A1	20151008	WO 2015-US23434	20150330

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20150307617	A1	20151029	US 2015-14673792	20150330

PRIORITY APPLN. INFO.:
US 2014-61973193 P 20140331
US 2014-61989448 P 20140506
US 2014-62073873 P 20141031
US 2014-62080171 P 20141114
US 2015-62113345 P 20150206
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose a cancer treatment method comprising the administering of an anti-angiogenesis agent and an OX40 binding agonist. In the one example, anti-VEGF antibody treatment resulted in reduced tumor growth, compared to anti-gp120 (control), in a syngeneic mouse colon carcinoma model. Anti-OX40 antibody treatment exhibited little activity alone. Anti-OX40 treatment in combination with anti-VEGF treatment demonstrated superior tumor growth inhibition when compared to single agent administration or anti-gp120 treatment.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1606231 CAPLUS Full-text
TITLE: Antitumor Effects and Mechanisms of AZD4547 on FGFR2-Deregulated Endometrial Cancer Cells
AUTHOR(S): Kwak, Yeonui; Cho, Hanna; Hur, Wooyoung; Sim, Taebo
CORPORATE SOURCE: KU-KIST Graduate School of Converging Science and Technology, Korea University, Seoul, S. Korea
SOURCE: Molecular Cancer Therapeutics (2015), 14(10), 2292-2302
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-15-0032
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Uncontrolled activation of FGFRs induces the progression of various cancers. It was recently reported that FGFR2-activating mutants are implicated in about 12% of endometrial carcinomas. AZD4547, a potent pan-FGFR inhibitor, is currently being evaluated in clin. trials for several FGFR-driven cancers. However, AZD4547 has not been examined yet against FGFR2 mutant-driven endometrial cancers. Thus, we evaluated the activity of AZD4547 against four different endometrial cancer cells, including AN3-CA, MFE296, MFE280, and HEC1A, where all but HEC1A cells express distinctive FGFR2 mutations.

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150284416	A1	20151008	US 2015-14740403	20150616
WO 2015155753	A2	20151015	WO 2015-IB56083	20150810

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-14740403 T0 20150616
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of hydrophilic linkers contg. phosphamide, phosphinate, sulfonamide, sulfonyl, sulfonimide, and/or sulfoxide groups, e.g., I, to link drugs, in particular, cytotoxic agents or a chromophore mols. to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (e.g. cytotoxic agent) conjugates comprising either modification of the drugs with these hydrophilic linkers first, followed by reaction with cell-binding agents; or modification of cell-binding agents with these hydrophilic linkers first, followed by reaction with drugs. Thus, linker I was prepared from N-methylethane-1,2-diamine and succinic anhydride using POCl3, 3-(methylamino)propanoic acid and NHS. Conjugation of I with the tubulysin analog II [R = H] gave the drug-linker conjugate II [R = Rl]. An antiHer2-II [R= Rl] antibody conjugate of was prepared and evaluated for its in vitro cytotoxicity. The specificity of the conjugate for N87 cell was over 1315 (IC50> 50/IC50= 0.038), and for SK-OV-3 cell was over 1560.

L8 ANSWER 23 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1617114 CAPLUS Full-text
DOCUMENT NUMBER: 163:551060
TITLE: Combination therapy comprising anti-angiogenesis agents and OX40 binding agonists
INVENTOR(S): Walsh, Kevin; De Almeida, Patricia; Du, Changchun; Kim, Jeong; Zhu, Jing; Bevers, Jack; Andya, James; Shen, Ye
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 166pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

We found that AZD4547 exhibits potent antiproliferative activity (EC50 = 31 nmol/L) against AN3-CA cells harboring FGFR2-K310R/N550K mutant. Anal. using a phospho-kinase array revealed that AZD4547 blocks FGFR2 downstream signaling, such as p38, ERK1/2, JNK, p70S6K, and PLCγ. Moreover, oral administration of AZD4547 (30 mg/kg, every day) remarkably delayed tumor growth in a mouse xenograft model of AN3-CA cells. Unbiased reporter gene assay showed that AZD4547 antagonizes the aFGF-induced activation of several transcription factors, including EGR1, ELK-1/SRF, AP-1, and NFκB. Genome-wide transcriptome anal. revealed that AZD4547 perturbs a number of transcriptions, and EGR1 was identified as one of the major targets of AZD4547. The significance of the FGFR2-EGR1 axis in endometrial cancer progression has not been reported. In addition, using kinome-wide inhibition profiling anal., we first identified potential new target kinases of AZD4547, including MAP4K3, MAP4K5, IRR, RET, and FLT3. Our study demonstrated that AZD4547 exhibits its therapeutic activity against endometrial cancer cells by perturbing various regulatory mechanisms related to FGFR signaling. Mol Cancer Ther; 14(10); 2292-302. ©2015 AACR.

L8 ANSWER 25 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1604658 CAPLUS Full-text
DOCUMENT NUMBER: 163:569777
TITLE: Preparation of

N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid salt and their crystal forms
INVENTOR(S): Chen, Minhua; Zhang, Yanfeng; Li, Jiaoyang; Zhang, Xiaoyu; Lu, Fei
PATENT ASSIGNEE(S): Crystal Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104961681	A	20151007	CN 2014-10641139	20141113

PRIORITY APPLN. INFO.: CN 2014-10641139 20141113
AB The title N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid salt has higher solubility than N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide malate, and plays important roles in improving the bioavailability, treatment effect, and safety of drug.

L8 ANSWER 26 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1604653 CAPLUS Full-text
DOCUMENT NUMBER: 163:569776
TITLE: Preparation of

N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms
INVENTOR(S): Chen, Minhua; Zhang, Yanfeng; Li, Jiaoyang; Zhang,

Xiaoyu; Lu, Fei
PATENT ASSIGNEE(S): Crystal Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104961680	A	20151007	CN 2014-10626255	20141107
PRIORITY APPLN. INFO.:			CN 2014-10626255	20141107

AB The title N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride has higher solubility than N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide malate, and plays important roles in improving the bioavailability, treatment effect, and safety of drug.

L8 ANSWER 27 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1602738 CAPLUS Full-text
TITLE: TAMing resistance to multi-targeted kinase inhibitors through Axl and Met inhibition
AUTHOR(S): Pinato, D. J.; Chowdhury, S.; Stebbing, J.
CORPORATE SOURCE: Department of Surgery and Cancer, Imperial College London, London, UK
SOURCE: Oncogene (2015) Ahead of Print
CODEN: ONCNES; ISSN: 0950-9232
DIGITAL OBJECT ID: 10.1038/onc.2015.374
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. TAM (Tyro3-Axl-Mer) receptor tyrosine kinases and Met are implicated in several hallmarks of cancer progression including sustained angiogenesis, enhanced motility, tissue invasion and acquisition of metastatic potential through the upregulation of epithelial-to-mesenchymal transition. Increasing evidence has confirmed Axl and Met as emerging central drivers of adaptive resistance to targeted therapies across a wide variety of cancers. In this issue of Oncogene, Zhou et al. describe the mechanisms linking Axl and Met activation to acquired resistance to sunitinib in renal cell carcinoma (RCC), providing a pre-clin. rationale for the development of Axl and Met inhibitors including cabozantinib in anti-angiogenic resistant RCC.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1593218 CAPLUS Full-text
DOCUMENT NUMBER: 163:673623
TITLE: Cabozantinib in Thyroid Cancer
AUTHOR(S): Fallahi, Poupak; Ferrari, Silvia M.; Di Bari, Flavia; Materazzi, Gabriele; Benvenga, Salvatore; Miccoli, Paolo; Antonelli, Alessandro
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56126, Italy
SOURCE: Recent Patents on Anti-Cancer Drug Discovery (2015), 10(3), 259-269

SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2014-61969706 P 20140324
US 2014-61985316 P 20140428
AB The present invention concerns cancer biomarkers. In particular, the invention concerns HGF as a biomarker for patient selection and patient prognosis in cancer, as well as methods of therapeutic treatment, articles of manufacture and methods for making them, diagnostic kits, methods of detection and methods of advertising related thereto. Cancer patients are treated with an anti-c-met antibody in combination with an anti-VEGF antibody.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1577497 CAPLUS Full-text
TITLE: Rapid modification of the bone microenvironment following short-term treatment with Cabozantinib in vivo
AUTHOR(S): Haider, Marie-Therese; Hunter, Keith D.; Robinson, Simon P.; Graham, Timothy J.; Corey, Eva; Dear, T. Neil; Hughes, Russell; Brown, Nicola J.; Holen, Ingunn
CORPORATE SOURCE: Department of Oncology, University of Sheffield, Sheffield, UK
SOURCE: Bone (New York, NY, United States) (2015), 81, 581-592
CODEN: BONEDL; ISSN: 1873-2763
DIGITAL OBJECT ID: 10.1016/j.bone.2015.08.003
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Bone metastasis remains incurable with treatment restricted to palliative care. Cabozantinib (CBZ) is targeted against multiple receptor tyrosine kinases involved in tumor pathobiol., including hepatocyte growth factor receptor (MET) and vascular endothelial growth factor receptor 2 (VEGFR-2). CBZ has demonstrated clin. activity in advanced prostate cancer with resolution of lesions visible on bone scans, implicating a potential role of the bone microenvironment as a mediator of CBZ effects. We characterised the effects of short-term administration of CBZ on bone in a range of in vivo models to determine how CBZ affects bone in the absence of tumor. Studies were performed in a variety of in vivo models including male and female BALB/c nude mice (age 6-17-wk). Animals received CBZ (30 mg/kg, 5 × weekly) or sterile H2O control for 5 or 10 days. Effects on bone integrity (μCT), bone cell activity (PINP, TRAP ELISA), osteoblast and osteoclast number/mm trabecular bone surface, area of epiphyseal growth plate cartilage, megakaryocyte nos. and bone marrow composition were assessed. Effects of longer-term treatment (15-day & 6-wk administration) were assessed in male NOD/SCID and beige SCID mice. CBZ treatment had significant effects on the bone microenvironment, including reduced osteoclast and increased osteoblast nos. compared to control. Trabecular bone structure was altered after 8 administrations. A significant elongation of the epiphyseal growth plate, in particular the hypertrophic chondrocyte zone, was observed in all CBZ treated animals irresp. of administration schedule. Both male and female BALB/c nude mice had increased megakaryocyte nos./mm2 tissue after 10-day CBZ treatment, in addition to vascular ectasia, reduced bone marrow cellularity and extravasation of red blood cells into the extra-vascular bone marrow. All CBZ-induced effects were transient and rapidly lost following cessation of treatment. Short-term administration of CBZ induces rapid, reversible effects on the bone microenvironment in vivo highlighting a potential role in mediating treatment responses.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 31 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1545892 CAPLUS Full-text
DOCUMENT NUMBER: 163:469529
TITLE: Target inhibition map system for combination antitumor therapy design and methods of using same
INVENTOR(S): Pal, Ranadip; Keller, Charles, III; Berlow, Noah E.; Seguin, Bernard
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 50pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150269307	A1	20150924	US 2015-14661918	20150318
PRIORITY APPLN. INFO.:			US 2014-61955068 P	20140318

AB Disclosed is a system and method for targeted therapy designs which model a cancer pathway for predicting the effectiveness of targeted anti-cancer drugs. The disclosed system and method includes utilization of a computer processor allowing for the selection of a set of drugs from available drugs using approximation algorithms utilizing cell viability data associated with a testable culture of a patient's tumor for generating a probabilistic target inhibition map (PTIM) from viability data for considering the selection of a set of drugs from available drugs, and further supports a wide variety of scenarios for personalized cancer therapy, related products and services.

L8 ANSWER 32 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1542977 CAPLUS Full-text
DOCUMENT NUMBER: 163:469542
TITLE: Dosing of cabozantinib formulations
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015142928	A1	20150924	WO 2015-US21072	20150317
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,			

CODEN: RPADDY; ISSN: 1574-8928
DIGITAL OBJECT ID: 10.2174/1574892810666150708110816
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib is an oral once-daily multitarget tyrosine kinase inhibitor of MET, VEGFR2, RET, acting against KIT, AXL, FLT3 and Tie-2. Cabozantinib has shown anti-cancer effects in preclin. and clin. models of cancers derived from both epithelial and mesenchymal origins [prostate cancer, non small lung cancer, medullary thyroid cancer (MTC) and differentiated thyroid cancer (DTC), renal cell carcinoma, etc.]. In a Phase III clin. study, cabozantinib improved PFS (11.2 mo vs. 4.0 mo in the placebo group) of patients with MTC (independently of age, bone metastases, RET status and prior treatment). Cabozantinib was approved in 2012 by FDA for metastatic MTC and in 2013 by EMA. Cabozantinib has been also evaluated in metastatic DTC patients, because they have activation on tyrosine kinases, including MET, VEGFR2 and RET, suggesting the possible use of cabozantinib in metastatic DTC. Actually, two Phase II trials of cabozantinib in DTC patients resistant to RAI are ongoing. To increase the antineoplastic effect of cabozantinib, and to overcome the occurrence of drug resistance, combination studies with other anticancer agents are ongoing. In conclusion, cabozantinib has shown to exert an important therapeutic effect in patients with MTC improving PFS. In DTC patients, cabozantinib has shown promising results.
REFERENCE COUNT: 152 THERE ARE 152 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1579900 CAPLUS Full-text
DOCUMENT NUMBER: 163:512733
TITLE: Cancer treatment with c-MET antagonists and correlation of the latter with HGF expression
INVENTOR(S): Yu, Wei; Shames, David; Koeppen, Hartmut; Phan, See; Rost, Sandra
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 178pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015148531	A1	20151001	WO 2015-US22282	20150324
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,			

VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2014-61954352 P 20140317
AB The invention relates to administration of various pharmaceutical formulations of N-(4-([6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1- dicarboxamide, (cabozantinib) a c-Met inhibitor, and its metabolites, to achieve desirable pharmacokinetic and pharmacodynamic effects.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 33 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1518424 CAPLUS Full-text
DOCUMENT NUMBER: 163:693610
TITLE: Cabozantinib for the treatment of non-small cell lung cancer with KIF5B-RET fusion. An example of swift repositioning
AUTHOR(S): Song, Minsoo; Kim, Seong-Heon; Yoon, Suk Kyoon
CORPORATE SOURCE: New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Taegu, 701-310, S. Korea
SOURCE: Archives of Pharmacal Research (2015), 38(12), 2120-2123
CODEN: APHRDQ; ISSN: 0253-6269
DIGITAL OBJECT ID: 10.1007/s12272-015-0660-1
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A new chimeric fusion transcript of KIF5B (the kinesin family 5B gene) and the RET (Rearranged during Transcription) oncogene, KIF5B-RET, was found in 1-2 % of lung adenocarcinomas (LADCs) in 2012. Several related clin. trials for non-small cell lung cancer (NSCLC) with KIF5B-RET rearrangements using existing RET inhibitors, such as cabozantinib, lenvatinib, vandetanib, sunitinib, ponatinib, and AUY922, have been swiftly initiated by the discovery of the KIF5B-RET fusion gene. Anti-RET activity and the status of clin. development of cabozantinib for KIF5B-RET fusion-pos. NSCLC are discussed.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 34 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1512965 CAPLUS Full-text
TITLE: Design, synthesis and pharmacological evaluation of novel 4-phenoxyquinoline derivatives as potential antitumor agents
AUTHOR(S): Hu, Hao; Jiang, Mingyan; Xie, Lijun; Hu, Gang; Zhang, Cuirong; Zhang, Lixia; Zhou, Shunguang; Zhang, Meihui; Gong, Ping
CORPORATE SOURCE: Key Laboratory of Structure-based Drug Design and Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Chemical Research in Chinese Universities (2015), 31(5), 746-755
CODEN: CRCUED; ISSN: 1005-9040
DIGITAL OBJECT ID: 10.1007/s40242-015-5166-3
PUBLISHER: Jilin University
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB A series of novel 4-phenoxyquinoline derivs. contg. 3-amino-2-cyano-acrylamide framework was designed and synthesized, and the in vitro cytotoxic activities of them against five cancer cell lines (HT-29, H460, A549, MKN-45, and U87MG) were evaluated. Most of the compds. exhibited moderate-to-significant cytotoxicity and high selectivity against one or more cell lines as compared with Foretinib. The studies of their preliminary structure-activity relationships (SARs) indicate that the compds. containing Me groups, especially Me groups at 4-position of the Ph ring (moiety B) are more effective. Among them, compound 36 shows the most potent antitumor activities with IC50 values of 0.04, 0.09, 0.67, 0.39 and 1.10 μmol/L against HT-29, H460, A549, MKN-45 and U87MG cell lines, resp.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 35 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1496569 CAPLUS Full-text
TITLE: Oral adverse events in cancer patients treated with VEGFR-directed multitargeted tyrosine kinase inhibitors
AUTHOR(S): Yuan, Anna; Kurtz, Sharyn L.; Barysauskas, Constance M.; Pilotte, Amy P.; Wagner, Andrew J.; Treister, Nathaniel S.
CORPORATE SOURCE: Division of Oral Medicine, Brigham and Women's Hospital, Boston, MA, 02115, USA
SOURCE: Oral Oncology (2015), 51(11), 1026-1033
CODEN: EJCCER; ISSN: 1368-8375
DIGITAL OBJECT ID: 10.1016/j.oraloncology.2015.09.003
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB This study characterized the incidence and clin. features of oral adverse events among cancer patients who received VEGFR-directed multitargeted tyrosine kinase inhibitor (VR-TKI) therapies. Electronic medical records of adult cancer patients treated with sunitinib, sorafenib, regorafenib, pazopanib, cabozantinib, imatinib, and bevacizumab therapy at Dana-Farber Cancer Institute from 2009 to 2012 were reviewed. Data collected included patient characteristics, oral and non-oral adverse events, and time to onset. Time oral adverse event-free was the primary outcome. A total of 747 patients with 806 individual courses of therapy were treated for a median of 3.9 mo with sunitinib (n = 161), sorafenib (n = 172), regorafenib (n = 15), pazopanib (n = 132), cabozantinib (n = 23), imatinib (n = 144), or bevacizumab (n = 159) for lung cancer (21%), gastrointestinal stromal tumor (15%), and metastatic renal cell carcinoma (13%). An oral adverse event was reported in 23.7% of patients at a median of 1.9 mo after starting therapy. The most commonly reported oral adverse event was oral mucosal sensitivity (dysesthesia), occurring in 12% of patients, typically without clin. findings. Multivariate models showed patients who received VR-TKI therapy were at greater risk of any oral adverse event compared with patients treated with imatinib or bevacizumab. Patients receiving VR-TKI therapy who developed an oral adverse event were also at increased risk for hand-foot skin reaction (15.9%). VR-TKI associated oral adverse events are characterized primarily by dysesthesia with lack of clin. signs. Oral dysesthesia is more commonly associated with VR-TKIs than with bevacizumab or imatinib. Management is largely empirical and requires further investigation.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 36 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1474667 CAPLUS Full-text
TITLE: Antioxidant and Anticoagulant Status Were Improved by Personalized Dietary Intervention Based on Biochemical and Clinical Parameters in Cancer Patients
AUTHOR(S): Lee, Ga-Yi; Lee, Jong Jyun; Lee, Seung-Min
CORPORATE SOURCE: Program of Clinical Nutrition, Yonsei Graduate School of Human Environmental Sciences, Seoul, S. Korea
SOURCE: Nutrition and Cancer (2015), 67(7), 1083-1092
CODEN: NUCADQ; ISSN: 0163-5581
DIGITAL OBJECT ID: 10.1080/01635581.2015.1073754
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB We investigated whether personalized dietary intervention could improve clin. measurements such as immune cell-mediated cytotoxicity, serum albumin, derivs. of reactive oxygen metabolites (D-ROMS), D-dimer, and fibrinogen. Cancer patients received either a treatment support diet (TD, for those with chemotherapy), or a remission support diet (RD; for those in remission) for at least 3 wk (21-61 days). Both diets were low glycemic, low fat, and high plant protein diets; the diet for the TD group contained an addnl. 0.5 servings of protein. Based on clin. values, addnl. amts. of garlic, onion, tomato, shiitake, rice bran, kale, blueberry, pineapples, and/or turmeric powder were provided in regular meals. Estimated daily intake of protein, plant fat, garlic, onion, allicin, and quercetin was greater in the TD compared to the RD. An increased intake of vitamin A, vitamin C, vitamin E and selenium and a reduction in D-dimer were noted compared to baseline diets in both groups. A decrease in D-ROMS in the RD and an increase in albumin and an increased tendency in cytotoxicity in the TD were observed In conclusion, personalized diets with supplemented functional ingredients improved antioxidant status and/or anticoagulant activity in cancer patients undergoing chemotherapy and in remission.
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 37 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1456151 CAPLUS Full-text
DOCUMENT NUMBER: 163:418831
TITLE: Structural insight into selectivity and resistance profiles of ROS1 tyrosine kinase inhibitors
AUTHOR(S): Davare, Monika A.; Vellore, Nadeem A.; Wagner, Jacob P.; Eide, Christopher A.; Goodman, James R.; Drilon, Alexander; Deininger, Michael W.; O'Hare, Thomas; Druker, Brian J.
CORPORATE SOURCE: Knight Cancer Institute, Oregon Health & Science University, Portland, OR, 97239, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2015), 112(39), E5381-E5390
CODEN: PNASA6; ISSN: 0027-8424
DIGITAL OBJECT ID: 10.1073/pnas.1515281112
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Oncogenic ROS1 fusion proteins are mol. drivers in multiple malignancies, including a subset of non-small cell lung cancer (NSCLC). The phylogenetic proximity of the ROS1 and anaplastic lymphoma kinase (ALK) catalytic domains led to the clin. repurposing of the Food and Drug Administration (FDA)-approved ALK inhibitor crizotinib as a ROS1 inhibitor. Despite the antitumor activity of crizotinib observed in both ROS1- and ALK-rearranged NSCLC patients, resistance due to acquisition of ROS1 or ALK kinase domain mutations has been observed clin., spurring the development of second-generation inhibitors. Here, we profile the sensitivity and selectivity of seven ROS1 and/or ALK inhibitors at various levels of clin. development. In contrast to crizotinib's dual ROS1/ALK activity, cabozantinib (XL-184) and its structural analog foretinib (XL-880) demonstrate a striking selectivity for ROS1 over ALK. Mol. dynamics simulation studies reveal structural features that distinguish the ROS1 and ALK kinase domains and contribute to differences in binding site and kinase selectivity of the inhibitors tested. Cell-based resistance profiling studies demonstrate that the ROS1-selective inhibitors retain efficacy against the recently reported CD74-ROS1G2032R mutant whereas the dual ROS1/ALK inhibitors are ineffective. Taken together, inhibitor profiling and stringent characterization of the structure-function differences between the ROS1 and ALK kinase domains will facilitate future rational drug design for ROS1- and ALK-driven NSCLC and other malignancies.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 38 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1433158 CAPLUS Full-text
TITLE: Altiratinib Inhibits Tumor Growth, Invasion, Angiogenesis, and Microenvironment-Mediated Drug Resistance via Balanced Inhibition of MET, TIE2, and VEGFR2
AUTHOR(S): Smith, Bryan D.; Kaufman, Michael D.; Leary, Cynthia B.; Turner, Benjamin A.; Wise, Scott C.; Ahn, Yu Mi; Booth, R. John; Caldwell, Timothy M.; Ensinger, Carol L.; Hood, Molly M.; Lu, Wei-Ping; Patt, Tristan W.; Patt, William C.; Rutkoski, Thomas J.; Samarakoon, Thiwanka; Telikepalli, Hanumaiah; Vogeti, Lakshminarayana; Vogeti, Subha; Yates, Karen M.; Chun, Lawrence; Stewart, Lance J.; Clare, Michael; Flynn, Daniel L.
CORPORATE SOURCE: Deciphera Pharmaceuticals, Lawrence, KS, USA
SOURCE: Molecular Cancer Therapeutics (2015), 14(9), 2023-2034
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-14-1105
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Altiratinib (DCC-2701) was designed based on the rationale of engineering a single therapeutic agent able to address multiple hallmarks of cancer (1). Specifically, altiratinib inhibits not only mechanisms of tumor initiation and progression, but also drug resistance mechanisms in the tumor and microenvironment through balanced inhibition of MET, TIE2 (TEK), and VEGFR2 (KDR) kinases. This profile was achieved by optimizing binding into the

switch control pocket of all three kinases, inducing type II inactive conformations. Altiratinib durably inhibits MET, both wild-type and mutated forms, in vitro and in vivo. Through its balanced inhibitory potency vs. MET, TIE2, and VEGFR2, altiratinib provides an agent that inhibits three major evasive (re)vascularization and resistance pathways (HGF, ANG, and VEGF) and blocks tumor invasion and metastasis. Altiratinib exhibits properties amenable to oral administration and exhibits substantial blood-brain barrier penetration, an attribute of significance for eventual treatment of brain cancers and brain metastases. Mol Cancer Ther; 14(9); 2023-34. ©2015 AACR.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 39 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1392691 CAPLUS Full-text
DOCUMENT NUMBER: 163:345656
TITLE: Use of ibrutinib to treat EGFR mutant cancer
INVENTOR(S): Fang, Bingliang; Roth, Jack A.; Wang, Michael; Wang, Li; Wu, Shuhong; Heymach, John V.; Swisher, Stephen G.; Hofstetter, Wayne L.
PATENT ASSIGNEE(S): The University of Texas System, USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015127234	A1	20150827	WO 2015-US16859	20150220

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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PRIORITY APPLN. INFO.: US 2014-61942255 P 20140220
AB Provided herein are methods of using irreversible BTK inhibitors, such as, for example, ibrutinib (PCI-32765), to treat EGFR mutant cancers, HER2 amplified cancers, and/or HER2 overexpressing cancers. In certain aspects, the method further comprises administering at least a second anticancer therapy to the subject.
OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 40 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1362724 CAPLUS Full-text
DOCUMENT NUMBER: 163:299275
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB C-MET is a receptor tyrosine kinase and potential oncol. target for cancer therapy. The activities of 1,2,3-triazolo[4,5-b]pyrazine series of c-MET inhibitors were analyzed according to the three-dimensional quant. structure-activity relationship and mol. docking methods. The results indicated that the hydrophobic and electrostatic fields play key roles in activity and QSAR model was reliable enough for activity prediction. Moreover, the docking results do validate the predicted 3D-QSAR scores, vital residues Asp1222, Asp1231, Met1160, Tyr1259 and Tyr1230 found in binding site. Four new c-MET inhibitor analogs designed in this Letter which are being currently synthesized by our labs.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

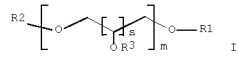
L8 ANSWER 42 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1315537 CAPLUS Full-text
DOCUMENT NUMBER: 163:323284
TITLE: Composition for vectorizing an anti-cancer agent
INVENTOR(S): Robic, Caroline; Mayer, Jean-Francois
PATENT ASSIGNEE(S): Guerbet, Fr.
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015118113	A1	20150813	WO 2015-EP52527	20150206

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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FR 3017295	A1	20150814	FR 2014-50972	20140207

PRIORITY APPLN. INFO.: FR 2014-50972 A 20140207
GI



I

TITLE: Preparation of crystalline solid forms of cabozantinib
INVENTOR(S): Aftab, Dana T.; Guz, Nathan; Lau, Stephen; Hamill, Noel; Walker, Tracy; Galbraith, Jana; Yau, Simon; Shah, Khalid
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015123639	A1	20150820	WO 2015-US16052	20150216

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61939985 P 20140214
AB The invention relates to novel cryst. solid forms of cabozantinib., and solvates thereof, including hydrates, that are useful for the treatment of cancer. Also disclosed are pharmaceutical compns. comprising the crystalline solid forms and processes for making the crystalline solid forms, as well as methods of using them for the treatment of cancer, particularly thyroid cancer, prostate cancer, hepatocellular cancer, renal cancer, and non-small cell lung carcinoma. The crystalline solid forms can be used to make the L-malate salt of cabozantinib.
OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 41 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1349511 CAPLUS Full-text
DOCUMENT NUMBER: 163:449411
TITLE: Identification of triazolo[4,5-b]pyrazine derivatives as hepatocyte growth factor receptor inhibitors through structure-activity relationships and molecular docking simulations
AUTHOR(S): Dong, Minghui; Ren, Yujie; Gao, Xiaodong
CORPORATE SOURCE: School of Chemical and Environmental Engineering, Shanghai Institute of Technology, Shanghai, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2015), 25(19), 4118-4126
CODEN: BMCLE8; ISSN: 0960-894X
DIGITAL OBJECT ID: 10.1016/j.bmcl.2015.08.025
PUBLISHER: Elsevier B.V.
AB The invention relates to a stable water-in-oil emulsion compn. contg.: 20% to 40% (volume/volume) aqueous phase in the form of droplets and containing an anti-cancer agent; and 60% to 80% (volume/volume) lipid phase containing an iodized oil and at least one surfactant, having formula I, in a proportion, of surfactant mass relative to the total volume of the composition, of 0.3% to 5%, formula II for said surfactant being the following in which: s has a value of 0 or 1; m is a whole number from 2 to 30; R1 is a formula I grouping wherein n is a whole number from 4 to 10, o is a whole number from 1 to 4, p is a whole number from 3 to 7; q is a whole number from 2 to 10, and r has a value of 0 or 1; R2 is a hydrogen atom or is identical to R1; and each R3 is, sep., a hydrogen atom or is identical to R1. The invention also relates to an emulsion obtained from said composition, to the preparing method thereof, and to the use thereof for treating cancer and the metastases thereof. An emulsion containing 50 mg doxorubicin, 1% PGPR in Lipidol, and 2.5 mL Xenetix 250 was prepared
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 43 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1289334 CAPLUS Full-text
DOCUMENT NUMBER: 163:438199
TITLE: Response to MET Inhibitors in Patients with Stage IV Lung Adenocarcinomas Harboring MET Mutations Causing Exon 14 Skipping
AUTHOR(S): Paik, Paul K.; Drilon, Alexander; Fan, Pang-Dian; Yu, Helena; Rekhtman, Natasha; Ginsberg, Michelle S.; Borsu, Laetitia; Schultz, Nikolaus; Berger, Michael F.; Rudin, Charles M.; Ladanyi, Marc
CORPORATE SOURCE: Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Cancer Discovery (2015), 5(8), 842-849
CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID: 10.1158/2159-8290.CD-14-1467
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutations in the MET exon 14 RNA splice acceptor and donor sites, which lead to exon skipping, deletion of the juxtamembrane domain containing the CBL E3-ubiquitin ligase-binding site, and decreased turnover of the resultant aberrant MET protein, were previously reported to be oncogenic in preclin. models. We now report responses to the MET inhibitors crizotinib and cabozantinib in four patients with stage IV lung adenocarcinomas harboring mutations leading to MET exon 14 skipping, highlighting a new therapeutic strategy for the 4% of lung adenocarcinoma patients whose tumors harbor this previously underappreciated genetic alteration. Significance: Oncogenic mutations in the MET exon 14 splice sites that cause exon 14 skipping occur in 4% of lung adenocarcinomas. We report responses to the MET inhibitors crizotinib and cabozantinib in patients with lung adenocarcinomas harboring MET exon 14 splice site mutations, identifying a new potential therapeutic target in this disease. Cancer Discov; 5(8); 842-9. ©2015 AACR. See related commentary by Ma, p. 802. See related article by Frampton et al., p. 850. This article is highlighted in the In This Issue feature, p. 783.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 44 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1288185 CAPLUS Full-text
TITLE: Pilot Trial of Selecting Molecularly Guided Therapy for Patients with Non-V600 BRAF-Mutant Metastatic Melanoma: Experience of the SU2C/MRA Melanoma Dream Team
AUTHOR(S): LoRusso, Patricia M.; Boerner, Scott A.; Pilat, Mary Jo; Forman, Karen M.; Zuccaro, Clarice Y.; Kiefer, Jeffrey A.; Liang, Winnie S.; Hunsberger, Sally; Redman, Bruce G.; Markovic, Svetomir N.; Sekulic, Aleksandar; Bryce, Alan H.; Joseph, Richard W.; Cowey, C. Lance; Fecher, Leslie Anne; Sosman, Jeffrey Alan; Chapman, Paul B.; Schwartz, Gary K.; Craig, David W.; Carpten, John D.; Trent, Jeffrey M.
CORPORATE SOURCE: Yale Cancer Center, New Haven, CT, USA
SOURCE: Molecular Cancer Therapeutics (2015), 14(8), 1962-1971
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-15-0153
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Targeted therapies and immunotherapies have led to significant improvements in the treatment of advanced cancers, including metastatic melanoma. However, new strategies are desperately needed to overcome therapeutic resistance to these agents, as well as to identify effective treatment approaches for cancer patients that fall outside major targetable mutational subtypes (e.g., non-V600 BRAF melanoma). One such strategy is to extend the paradigm of individually tailored, molecularly targeted therapy into a broader spectrum of melanoma patients, particularly those bearing tumors without commonly recognized therapeutic targets, as well as having failed or were ineligible for immunotherapy. In this nontreatment pilot study, next-generation sequencing (NGS) technologies were utilized, including whole genome and whole transcriptome sequencing, to identify mol. aberrations in patients with non-V600 BRAF metastatic melanoma. This information was then rationally matched to an appropriate clin. treatment from a defined pharmacopeia. Five patients with advanced non-V600 BRAF metastatic melanoma were enrolled. We demonstrated successful performance of the following during a clin. relevant time period: patient tumor biopsy, quality DNA/RNA extraction, DNA/RNA-based sequencing for gene expression anal., anal. utilizing a series of data integration methodologies, report generation, and tumor board review with formulated treatment plan. Streamlining measures were conducted based on the experiences of enrolling, collecting specimens, and analyzing the mol. signatures of patients. We demonstrated the feasibility of using NGS to identify mol. aberrations and generate an individualized treatment plan in this patient population. A randomized treatment study utilizing lessons learned from the conduct of this pilot study is currently underway. Mol Cancer Ther; 14(8); 1962-71. ©2015 AACR.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 45 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1265280 CAPLUS Full-text
TITLE: Pharmacokinetic (PK) drug interaction studies of cabozantinib: Effect of CYP3A inducer rifampin and inhibitor ketoconazole on cabozantinib plasma PK and effect of cabozantinib on CYP2C8 probe substrate rosiglitazone plasma PK
AUTHOR(S): Nguyen, Linh; Holland, Jaymes; Miles, Dale; Engel, Caroline; Benrimoh, Natacha; O'Reilly, Terry; Lacy, Steven
CORPORATE SOURCE: Exelixis, Inc., So. San Francisco, CA, USA
SOURCE: Journal of Clinical Pharmacology (2015), 55(9), 1012-1023
CODEN: JCPCBR; ISSN: 0091-2700
DIGITAL OBJECT ID: 10.1002/jcph.510
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is a small-mol. tyrosine kinase inhibitor that has been approved for the treatment of patients with progressive, metastatic medullary thyroid cancer. In vitro data indicate that (1) cytochrome P 450 (CYP) 3A4 is the primary CYP isoenzyme involved in the metabolism of cabozantinib, and (2) CYP2C8 is the CYP isoenzyme most potently inhibited by cabozantinib with potential for in vivo inhibition at clin. relevant plasma exposures. Pharmacokinetic (PK) drug-drug interactions (DDIs) were evaluated clin. between cabozantinib and (1) a CYP3A inducer (rifampin) in healthy volunteers, (2) a CYP3A inhibitor (ketoconazole) in healthy volunteers, and (3) a CYP2C8 substrate (rosiglitazone) in patients with solid tumors. Compared with cabozantinib given alone, coadministration with rifampin resulted in a 4.3-fold higher plasma clearance (CL/F) of cabozantinib and a 77% decrease in cabozantinib plasma AUC0-inf, whereas coadministration with ketoconazole decreased cabozantinib CL/F by 29% and increased cabozantinib AUC0-inf by 38%. Chronic coadministration with cabozantinib resulted in no significant effect on rosiglitazone plasma Cmax, AUC0-24, or AUC0-inf. In summary, chronic use of strong CYP3A inducers and inhibitors should be avoided when cabozantinib is administered, and cabozantinib at clin. relevant exposures is not anticipated to markedly affect the PK of concomitant medications via CYP enzyme inhibition.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 46 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1258933 CAPLUS Full-text
TITLE: Small-molecule kinase inhibitors: an analysis of FDA-approved drugs
AUTHOR(S): Wu, Peng; Nielsen, Thomas E.; Clausen, Mads H.
CORPORATE SOURCE: Department of Chemistry, Technical University of Denmark, Kgs. Lyngby, DK-2800, Den.
SOURCE: Drug Discovery Today (2015) Ahead of Print
CODEN: DDTOFS; ISSN: 1359-6446
DIGITAL OBJECT ID: 10.1016/j.drudis.2015.07.008
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Small-mol. kinase inhibitors (SMKIs), 28 of which are approved by the US Food and Drug Administration (FDA), have been actively pursued as promising targeted therapeutics. Here, we assess the key structural and physicochem. properties, target selectivity and mechanism of function, and therapeutic indications of these approved inhibitors. Our anal. showed that >30% of approved SMKIs have a mol. weight (MW) exceeding 500 and all have a total ring count of between three and five. The assumption that type II inhibitors tend to be more selective than type I inhibitors has been proved to be unreliable. Although previous SMKI research was concentrated on tyrosine kinase inhibitors for cancer treatment, recent progress indicates diversification of SMKI research in terms of new targets, mechanistic types, and therapeutic indications.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 47 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1256269 CAPLUS Full-text
TITLE: 2ME2 inhibits the activated hypoxia-inducible pathways by cabozantinib and enhances its efficacy against medullary thyroid carcinoma
AUTHOR(S): Lin, Han; Jiang, Xian; Zhu, Huaqiang; Jiang, Wenjing; Dong, Xuesong; Qiao, Haiquan; Sun, Xueying; Jiang, Hongchi
CORPORATE SOURCE: Key Laboratory of Hepatosplenic Surgery, Department of General Surgery, The First Affiliated Hospital of Harbin Medical University, Harbin, 150001, Peop. Rep. China
SOURCE: Tumor Biology (2015) Ahead of Print
CODEN: TUMBEA; ISSN: 1010-4283
DIGITAL OBJECT ID: 10.1007/s13277-015-3816-1
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cabozantinib is a multi-targeted tyrosine kinase inhibitor targeting vascular endothelial growth factor (VEGF) receptor (VEGFR)-2, MET (c-Met, also called hepatocyte growth factor (HGF) receptor), and other receptor tyrosine kinases. Cabozantinib has recently been approved for treating advanced medullary thyroid carcinoma (MTC), but its long-term benefit remains uncertain and dose-dependent adverse events are very common. The present study has demonstrated that 2-methoxyestradiol (2ME2), an inhibitor of hypoxia-inducible factors (HIFs) and a promising anticancer agent under investigation in clin. trials, strengthens anticancer activities of cabozantinib against MTC cells in vitro and in vivo. The activated hypoxia-inducible pathways, which are mainly regulated by HIF-1, contribute to the resistance of hypoxic MTC cells to cabozantinib. Cabozantinib upregulated HIF-1α expression at translational levels and increased the expression of the downstream factors including VEGF, lactate dehydrogenase A (LDHA), HGF, and MET. 2ME2 corrected the activated pathways by cabozantinib through downregulating HIF-1α expression and inhibiting its nuclear translocation in hypoxic MTC cells. Administration of 2ME2 enhanced the efficacy of cabozantinib in suppressing the growth of MTC cell line xenografts and patient-derived xenografts established in mice. Given that 2ME2 targets insensitive hypoxic cancer cells to cabozantinib and can inhibit the activated pathways by cabozantinib, the present results warrant further investigation of 2ME2, particularly in combination with cabozantinib, for the treatment of MTC.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 48 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1243654 CAPLUS Full-text
DOCUMENT NUMBER: 163:316612
TITLE: Biomarker TTF1 for predicting effect of c-met inhibitor
INVENTOR(S): Kim, Bo Gyou; Lee, Eunjin; Kim, Kyung Ah; Ahn, Tae Jin
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 92pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150212077	A1	20150730	US 2015-14604361	20150123
KR 2015088433	A	20150803	KR 2014-8733	20140124
PRIORITY APPLN. INFO.:			KR 2014-8733 A	20140124

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method of predicting an effect of a c-Met inhibitor and/or selecting a subject for application of a c-Met inhibitor using trefoil factor 1 (TFF1), a method of monitoring an effect of a c-Met inhibitor using TFF1, and a method of treating and/or preventing cancer including administering a c-Met inhibitor to the selected subject. Herein, the effect of a c-Met inhibitor may refer to the prevention, improvement, alleviation, and/or treatment of a c-Met related disease such as cancer.

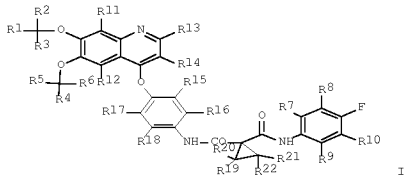
L8 ANSWER 49 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1226166 CAPLUS Full-text
TITLE: The study on synthetic technology of cabozantinib (S)-malate
AUTHOR(S): Qi, Baohui; He, Huan
CORPORATE SOURCE: Department of Bioengineering, Zhuhai Campus, Zunyi Medical College, Zhuhai, 519041, Peop. Rep. China
SOURCE: Guangdong Huagong (2014), 41(19), 22-23
CODEN: GHUAFI; ISSN: 1007-1865
PUBLISHER: Guangdong Huagong Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The cabozantinib(S)-malate, which was used for the treatment of locally advanced or metastatic progressive medullary thyroid cancer, was prepared from 3, 4-dimethoxyacetophenone by nitration, condensation, cyclization, chlorination and substitution, etc. In this synthetic route, raw materials were com. available, and reactive conditions were mild, and the operation was easy, and the yield was higher.

L8 ANSWER 50 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1213912 CAPLUS Full-text
DOCUMENT NUMBER: 163:271103
TITLE: Preparation of deuterated cabozantinib derivatives and their application as anticancer agents
INVENTOR(S): Chen, Xinghai; Peng, Wei; Parker, Omar; Zheng, Feiming; Fu, Yong
PATENT ASSIGNEE(S): Shanghai Shengkao Pharmaceutical Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 35pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent

LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104788372	A	20150722	CN 2014-10361351	20140725

PRIORITY APPLN. INFO.: CN 2014-10361351 20140725
OTHER SOURCE(S): MARPAT 163:271103
GI



I

AB The invention is related to the prepn. of deuterated cabozantinib derivs. I and their application as anticancer agents. The invention compound I, wherein R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, and R22 are H or D independently and contain at least one D and their pharmaceutically acceptable salts, crystalline hydrates, solvates, prodrugs, single crystal or polymorph are claimed. Compound I was prepared by multi-step procedure (procedure given). The deuterated cabozantinib derivs. have slow decomposition in vivo, thereby reducing adverse metabolism of drugs. The invention compds. were evaluated for their anticancer activity.

L8 ANSWER 51 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1181814 CAPLUS Full-text
TITLE: Population Pharmacokinetic Model of Cabozantinib in Patients with Medullary Thyroid Carcinoma and Its Application to an Exposure-Response Analysis
AUTHOR(S): Miles, Dale; Jumbe, Nelson L.; Lacy, Steven; Nguyen, Linh
CORPORATE SOURCE: Genentech (A member of the Roche Group), South San Francisco, CA, USA
SOURCE: Clinical Pharmacokinetics (2015) Ahead of Print
CODEN: CPKNDH; ISSN: 0312-5963
DIGITAL OBJECT ID: 10.1007/s40262-015-0295-x
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and Objectives: Cabozantinib is a tyrosine kinase inhibitor approved in the USA and EU for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC). The indicated cabozantinib dose is 140 mg/day, with dose modifications allowed for patients who develop adverse events (AEs). The anal. objective was to develop a population pharmacokinetic (PopPK) model in MTC patients and to use the model for exposure-response (ER) anal. of dose modifications. Methods: A PopPK model for cabozantinib was developed using data from three clin. trials (2079 evaluations from 289 patients), including a randomized, double-blind, placebo-controlled phase III study of patients with progressive, metastatic MTC. The PopPK model predictions [model-predicted steady-state area under the plasma concentration-time curve (AUCss,pred)] were used for an ER anal. of the time to first dose modification. Results: The final PopPK model was a one-compartment model with first-order absorption and first-order elimination. Estimated cabozantinib apparent oral clearance (CL/F) and apparent volume of distribution (Vc/F) were 106 L/day [±2.98 % relative standard error (RSE)] (males) and 349 L (±2.73 % RSE), resp. CL/F was reduced by 22 % (to 83 L/day) in females. Sex and body mass index (BMI) were significant covariates that combined contributed 15 % to the variability in cabozantinib CL/F, but did not warrant dose adjustment. Higher cabozantinib AUCss,pred was correlated to an increased risk of early dose modification and a lower average dose through to Day 85. Early cabozantinib dose modification was not associated with a reduction in progression-free survival (PFS). Conclusion: A PopPK model was developed for cabozantinib pharmacokinetics in MTC patients. Higher cabozantinib exposure was associated with earlier first dose modification and a lower average administered dose through to Day 85. Early first dose modification did not appear to impact PFS.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 52 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1173698 CAPLUS Full-text
DOCUMENT NUMBER: 163:302461
TITLE: Compositions and methods for the treatment of intraocular neovascularization and/or leakage using tyrosine kinase inhibitors
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 12pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150196649	A1	20150716	US 2015-14593704	20150109
WO 2015108787	A2	20150723	WO 2015-US10867	20150109
WO 2015108787	A3	20151112		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2014-61928061 P 20140116
US 2014-61969861 P 20140325
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention provides compns. and methods for the treatment of intraocular neovascularization and/or leakage including wet age-related macular degeneration. The compns. preferably use tyrosine kinase inhibitors with an IC50 for VEGFR2 of 20 nanomolar or less and an IC50 for c-MET of 20 nanomolar or less.

L8 ANSWER 53 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1169349 CAPLUS Full-text
DOCUMENT NUMBER: 163:218113
TITLE: Preparation of heterocyclic modulators of lipid synthesis for use against cancer and viral infections
INVENTOR(S): Wagman, Allan S.; Johnson, Russell J.; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.; Duke, Greg; Ohol, Yamini; Heuer, Timothy; O'Farrell, Marie
PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015105860	A1	20150716	WO 2015-US10459	20150107

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2014-61924520 P 20140107
OTHER SOURCE(S): CASREACT 163:218113; MARPAT 163:218113
GI

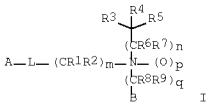
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [LAr = II-IV; Ar = V; R1 = H, CN, halo, etc.; R2 = H, halo, alkyl; R3 = H or F; R21 = H, halo, alkyl, etc.; R22 = H, halo, alkyl; R24 = alkoxy, O(alkylene)alkoxy, cycloalkoxy, etc.; R25 = H, halo, alkyl, etc.; with the provisos], useful for treating conditions characterized by dysregulation of a fatty acid synthase pathway, were prepared E.g., a multi-step synthesis of VI, starting from Me propanoate and Me formate, was described. Exemplified compds. I were evaluated for their FASN inhibition (data given for representative compds. I). Pharmaceutical composition comprising I was disclosed.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

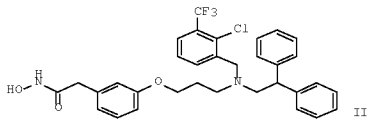
L8 ANSWER 54 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1169171 CAPLUS Full-text
DOCUMENT NUMBER: 163:217976
TITLE: Preparation of tertiary amines and amine oxides as LXR agonists
INVENTOR(S): Martinez, Eduardo J.; Kaiser, Bernd; Tavazoie, Sohail F.; Kurth, Isabel; Gonsalves, Foster Casimir; Darst, David M., Jr.; Tavazoie, Masoud Fakhr
PATENT ASSIGNEE(S): Rgenix, Inc., USA
SOURCE: PCT Int. Appl., 163pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015106164	A1	20150716	WO 2015-US10909	20150109

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2014-61926150 P 20140110
OTHER SOURCE(S): CASREACT 163:217976; MARPAT 163:217976
GI



I



II

AB This invention features compds. of formula I that modulate the activity of liver X receptors, pharmaceutical compns. including the compds. of the invention, and methods of utilizing those compns. for modulating the activity of liver X receptors in the treatment of cancer. Compds. of formula I wherein A is substituted Ph, (un)substituted azacyclyl, and (un)substituted oxobenzopyranyl; L is absent, O, S, amino and CR4R5; m is 2, 3, 4, 5, 6, 7 and 8;, n, p and q are independently 0 and 1; R1, R2, R6, R7, R8 and R9 are independently H, OH, halo, amino, thio, etc.; R3 is H, OH, amino, (un)substituted C1-6 alkyl, etc.; R4 and R6 are independently H, OH, halo, amino, thio, etc.; and pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by reductive amination of 2-chloro-3-trifluoromethylbenzaldehyde with 2,2-diphenethylamine followed by alkylation with 1,3-dibromopropane; the resulting (3-bromopropyl)([[2-chloro-3-(trifluoromethyl)phenyl]methyl])(2,2-diphenylethyl)amine underwent etherification with Me 3-hydroxyphenylacetate to give Me 2-{3-[3-([[2-chloro-3-(trifluoromethyl)phenyl]methyl]-(2,2-diphenylethyl)- amino)-propoxy]phenyl}acetate, which underwent amidation with hydroxylamine hydrochloride to give compound II. The invention compds. were evaluated for their LXR agonistic activity. From the assay it was determine that compound exhibited ApoE induction . 80% at 1 μM and > 40 % at 10 μM, and EC50 value of 1.0 μM.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 55 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1144766 CAPLUS Full-text
TITLE: Salvage systemic therapy for advanced urothelial carcinoma: on the cusp of a sea change?
AUTHOR(S): Sonpavde, Guru; Bellmunt, Joaquim
CORPORATE SOURCE: University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, AL, USA
SOURCE: Oncologist (2015), 20(5), 461-463
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2015-0077
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper studies about the salvage systemic therapy for advanced urothelial carcinoma.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 56 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1144752 CAPLUS Full-text
DOCUMENT NUMBER: 163:384755
TITLE: Prospective comprehensive genomic profiling of advanced gastric carcinoma cases reveals frequent clinically relevant genomic alterations and new routes for targeted therapies
AUTHOR(S): Ali, Siraj M.; Sanford, Eric M.; Klempner, Samuel J.; Rubinson, Douglas A.; Wang, Kai; Palma, Norma A.; Chmielecki, Juliann; Yelensky, Roman; Palmer, Gary A.; Morosini, Deborah; Lipson, Doron; Catenacci, Daniel V.; Braiteh, Fadi; Erlich, Rachel; Stephens, Philip J.; Ross, Jeffrey S.; Ou, Sai-Hong Ignatius; Miller, Vincent A.
CORPORATE SOURCE: Foundation Medicine Inc., Cambridge, MA, USA
SOURCE: Oncologist (2015), 20(5), 499-507
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2014-0378
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Gastric cancer (GC) is a major global cancer burden and the second most common cause of global cancer-related deaths. The addition of anti-ERBB2 (HER2) targeted therapy to chemotherapy improves survival for ERBB2-amplified advanced GC patients; however, the majority of GC patients do not harbor this alteration and thus cannot benefit from targeted therapy under current practice paradigms. Materials and Methods: Prospective comprehensive genomic profiling of 116 predominantly locally advanced or metastatic (90.0%) gastric cancer cases was performed to identify genomic alterations (GAs) associated with a potential response to targeted therapies approved by the U.S. Food and Drug Administration or targeted therapy-based clin. trials. Results: Overall, 78% of GC cases harbored one clin. relevant GA or more, with the most frequent alterations being found in TP53 (50%), ARID1A (24%), KRAS (16%), CDH1 (15%), CDKN2A (14%), CCND1 (9.5%), ERBB2 (8.5%), PIK3CA (8.6%), MLL2 (6.9%), FGFR2 (6.0%), and MET (6.0%). Receptor tyrosine kinase genomic alterations were detected in 20.6% of cases, primarily ERBB2, FGFR2, and MET amplification, with ERBB2 alterations evenly split between amplifications and base substitutions. Rare BRAF mutations (2.6%) were also observed One MET-amplified GC patient responded for 5 mo to crizotinib, a multitargeted ALK/ROS1/MET inhibitor. Conclusion: Comprehensive genomic profiling of GC identifies clin. relevant GAs that suggest benefit from targeted therapy including MET-amplified GC and ERBB2 base substitutions.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 57 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1128572 CAPLUS Full-text
TITLE: Metabolism and disposition of cabozantinib in healthy male volunteers and pharmacologic characterization of its major metabolites
AUTHOR(S): Lacy, Steven; Hsu, Bih; Miles, Dale; Aftab, Dana; Wang, Ronghua; Nguyen, Linh
CORPORATE SOURCE: Department of Non-Clinical Development, Exelixis, Inc., South San Francisco, CA, USA
SOURCE: Drug Metabolism & Disposition (2015), 43(8), 1190-1207
CODEN: DMDSAI; ISSN: 1521-009X
DIGITAL OBJECT ID: 10.1124/dmd.115.063610
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Metab. and excretion of cabozantinib, an oral inhibitor of receptor tyrosine kinases, was studied in 8 healthy male volunteers after a single oral dose of 175 mg cabozantinib l-malate containing 14C-cabozantinib (100 μCi/subject). Total mean radioactivity recovery within 48 days was 81.09%; radioactivity was eliminated in feces (53.79%) and urine (27.29%). Cabozantinib was extensively metabolized with 17 individual metabolites identified by liquid chromatog.-tandem mass spectrometry (LC-MS/MS) in plasma, urine, and feces. Relative plasma radioactivity exposures (analyte AUC0-t/total AUC0-t for cabozantinib + major metabolites) were 27.2, 25.2, 32.3, 7, and 6% for cabozantinib and major metabolites monohydroxy sulfate (EXEL-1646), 6-desmethyl amide cleavage product sulfate (EXEL-1644), N-oxide (EXEL-5162), and amide cleavage product (EXEL-5366), resp. Comparable relative plasma exposures determined by LC-MS/MS anal. were 32.4, 13.8, 45.9, 4.9, and 3.1%, resp. These major metabolites each possess in vitro inhibition potencies ≤1/10th of parent cabozantinib against the targeted kinases MET, RET, and VEGFR2/KDR. In an in vitro cytochrome P 450 (CYP) panel, cabozantinib and EXEL-1644 both inhibited most potently CYP2C8 (Kiapp = 4.6 and 1.1 μM, resp.). In an in vitro drug transporter panel, cabozantinib inhibited most potently MATE1 and MATE2-K (IC50 = 5.94 and 3.12 μM, resp.) and was a MRP2 substrate; EXEL-1644 inhibited most potently OAT1, OAT3, OATP1B1, MATE1, and OATP1B3 (IC50 = 4.3, 4.3, 6.1, 16.7, and 20.6 μM, resp.) and was a substrate of MRP2, OAT3, OATP1B1, OATP1B3, and possibly P-gp. Therefore, cabozantinib appears to be the primary pharmacol. active circulating analyte, whereas both cabozantinib and EXEL-1644 may represent potential for drug-drug interactions.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 58 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1127378 CAPLUS Full-text
TITLE: MET inhibitors for treatment of advanced hepatocellular carcinoma: a review
AUTHOR(S): Qi, Xing-Shun; Guo, Xiao-Zhong; Han, Guo-Hong; Li, Hong-Yu; Chen, Jiang
CORPORATE SOURCE: Department of Gastroenterology, General Hospital of Shenyang Military Area, Shenyang, Liaoning Province, 100840, Peop. Rep. China
SOURCE: World Journal of Gastroenterology (2015), 21(18), 5445-5453
CODEN: WJGAF2; ISSN: 2219-2840
DIGITAL OBJECT ID: 10.3748/wjg.v21.i18.5445
PUBLISHER: Baishideng Publishing Group Inc.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The current std. treatment option for advanced hepatocellular carcinoma (HCC) is sorafenib, but its clin. benefit is modest. In spite of many attempts, few drugs can provide any significant improvement of survival as the first- or second-line therapy of choice in phase III randomized controlled trials. Recently, the subgroup anal. of a phase II randomized controlled trial has shown that tivantinib, a selective MET inhibitor, can significantly improve the overall survival in patients with MET-pos. advanced HCC after the failure or intolerance of a prior systemic therapy. These findings enlighten the role of MET inhibitors in the treatment of advanced HCC. In this paper, we review all ongoing and completed clin. trials regarding this topic. As for the first-line therapy of advanced HCC, INC280 and foretinib are being evaluated in 2 phase II single-arm trials; and MSC2156119J and golvatinib plus sorafenib are being compared with sorafenib alone in 2 phase II randomized controlled trials. As for the second-line therapy of advanced HCC, tivantinib and cabozantinib are being compared with placebo in 2 phase II randomized controlled trials.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 59 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1124138 CAPLUS Full-text
DOCUMENT NUMBER: 163:187706
TITLE: Biomarker for predicting or monitoring efficacy of c-Met inhibitor
INVENTOR(S): Jung, Soo Yeon; Shim, Seon Hui; Song, Yun Jeong; Yoo, Hyeon-Seok
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: Eur. Pat. Appl., 147pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2891884	A2	20150708	EP 2015-150360	20150107
EP 2891884	A3	20151014		
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015082121	A	20150715	KR 2015-956	20150106
CN 104762371	A	20150708	CN 2015-10008065	20150107
US 20150192588	A1	20150709	US 2015-14591787	20150107
JP 2015129755	A	20150716	JP 2015-1880	20150107
PRIORITY APPLN. INFO.:			KR 2014-1799 A	20140107
			KR 2015-956 A	20150106

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A biomarker for predicting and/or monitoring the efficacy of a c-Met inhibitor; a composition for predicting and/or monitoring the efficacy of a c-Met inhibitor, comprising a material detecting the biomarker; a composition for selecting a subject suitable for the application of a c-Met inhibitor, comprising a material detecting the biomarker is presented. In addition a method for predicting and/or monitoring the efficacy of a c-Met inhibitor using the biomarker; a method for selecting a subject suitable for the application of a c-Met inhibitor using the biomarker; and a method for

preventing and/or treating cancer comprising administering a c-Met inhibitor to the selected subject is given. One embodiment provides a biomarker for use in predicting and/or monitoring the therapeutic effect of a c-Met inhibitor or selecting a subject suitable for the application of a c-Met inhibitor, wherein the biomarker includes at least one selected from the group consisting of IL-8, BIGH3, or MIF and nucleic acids encoding the proteins. Another embodiment provides a c-Met inhibitor or a pharmaceutical composition including a c-Met inhibitor, for use in inhibiting c-Met and/or treating a cancer in a subject, wherein the subject has a high level of IL-8 or a nucleic acid encoding IL-8 compared to a reference sample in which a c-Met inhibitor is not effective; shows a decreased level of IL-8, BIGH3, MIF, and/or nucleic acids encoding them after administering a c-Met inhibitor; and/or has a mutation of KRAS, BRAF, and/or nucleic acids encoding them. A specific example shows the IL-8 levels in cancer cell-implanted mouse models showing relationship between IL-8 level and responsiveness to an anti-c-Met antibody.

OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

L8 ANSWER 60 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1079985 CAPLUS Full-text
DOCUMENT NUMBER: 163:231592
TITLE: Heteroaromatic compound and its application in medicine for treating proliferative diseases
INVENTOR(S): Liu, Bing; Liu, Jinlei; Zhang, Yingjun; Zhang, Jiancun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 189pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104744446	A	20150701	CN 2014-10835175	20141229
PRIORITY APPLN. INFO.:			CN 2013-10746766 A	20131230
			CN 2014-10108590 A	20140322

OTHER SOURCE(S): MARPAT 163:231592

AB The invention provides a class of heteroarom. compd. or stereisomer, geometrical isomer, tautomer, racemate, oxynitride, hydrate, solvate, metabolite, metabolic precursor and pharmaceutically acceptable salt, or prodrug thereof, used for the treatment of proliferative disease. The invention also discloses the pharmaceutical composition containing such compound and application of the compound of this invention or its pharmaceutical composition in the preparation of medicine for the treatment of proliferative disease.

L8 ANSWER 61 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1073487 CAPLUS Full-text
DOCUMENT NUMBER: 163:480792
TITLE: Response and toxicity of small-molecule tyrosine kinase inhibitors in patients with thyroid carcinoma: a systematic review and meta-analysis
AUTHOR(S): N. Klein Hesselink, E.; Steenvoorden, D.; Kapiteijn, E.; Corssmit, E. P.; van der Horst-Schrivers, A. N. A.; Lefrandt, J. D.; Links, T. P.; Dekkers, O. M.
CORPORATE SOURCE: Department of Endocrinology, Department of Internal Medicine, Division of Vascular Medicine, University Medical Center Groningen, University of Groningen, Groningen, Neth.
SOURCE: European Journal of Endocrinology (2015), 172(5), R215-R225
CODEN: EJOEEP; ISSN: 0804-4643
DIGITAL OBJECT ID: 10.1530/EJE-14-0788
PUBLISHER: BioScientifica Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Context: Many tyrosine kinase inhibitors (TKIs) have been studied in patients with thyroid carcinoma (TC). However, the effect and toxicity of various TKIs in differentiated TC (DTC) and medullary TC (MTC) patients have not been directly compared. The aim of the present systematic review and meta-anal. was to systematically summarize response and toxicity of TKIs in TC patients. Methods: All major databases were systematically searched for publications on TKIs in TC. Primary endpoint was objective response; secondary endpoints were clin. benefit, percentage TKI dose reduction/discontinuation, hand-foot syndrome, diarrhea, and nausea/vomiting. Meta-anal. was performed using an exact likelihood approach and a logistic regression. Pooled percentages and 95% CIs were reported. Results: In total, 22 publications were included. For DTC patients, gefitinib induced no objective responses. Pooled percentage was highest for pazopanib, 49 (95% CI 33-64)%, and was 17 (95% CI 12-24)% for sorafenib. For MTC, gefitinib and imatinib induced no objective responses, whereas sunitinib induced objective response in 43 (95% CI 14-77)%. For vandetanib and cabozantinib, these nos. were 40 (95% CI 34-46)% and 27 (95% CI 22-32)% resp. Clin. benefit was found in 53 (95% CI 48-59)% of DTC patients on sorafenib, and in 84 (95% CI 79-88)% and 55 (95% CI 49-61)% of MTC patients on vandetanib and cabozantinib resp. All TKIs were associated with considerable toxicity. Conclusion: The currently studied TKIs show a modest response, while side effects are not negligible. Therefore, we suggest to solely consider TKIs in TC patients with rapid progressive disease, for whom the benefits of treatment outweigh toxicity.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 62 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1053832 CAPLUS Full-text
DOCUMENT NUMBER: 163:145772
TITLE: Preparation of heterocyclic modulators of lipid synthesis
INVENTOR(S): Heuer, Timothy Sean; Oslob, Johan D.; Mcdowell, Robert S.; Johnson, Russell; Yang, Hanbiao; Evanchik, Marc; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.
PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 488pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015095767	A1	20150625	WO 2014-US71617	20141219
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2013-61919235 P	20131220

OTHER SOURCE(S): CASREACT 163:145772; MARPAT 163:145772
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This invention relates to heterocyclic modulators of lipid synthesis as well as pharmaceutically acceptable salts thereof; to pharmaceutical compns. comprising such compds.; and to methods of treating conditions characterized by dysregulation of a fatty acid synthase pathway by the administration of such compds. and combinations of such compds. and other therapeutic agents. Method of treating a condition characterized by dysregulation of a fatty acid synthase pathway in a subject by administering to the subject a therapeutically effective amount of compound I [LAr = II-IV; Ar = V-IX (wherein Het = 5-6 membered heteroaryl; R1 = H, CN, halo, etc.; R2 = H, halo, alkyl; R3 = H or F; R11 = H or Me); R21 = H, halo, alkyl, etc.; R22 = H, halo, alkyl; R24 = H, CN, alkyl, etc.; R25 = halo, CN, alkyl, etc.], in combination with other therapeutic agent, was claimed. Over three-hundred-eighty compds. I and their heterocyclic analogs were prepared E.g., a multi-step synthesis of X, starting from tert-Bu 4-iodopiperidine-1-carboxylate and 4-bromobenzonitrile, was described. The antiviral activities of the exemplified compds. I were assessed using the HCV1b replicon system (data given).

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 63 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:999711 CAPLUS Full-text
TITLE: Iodide- and glucose-handling gene expression regulated by sorafenib or cabozantinib in papillary thyroid cancer
AUTHOR(S): Ruan, Maomei; Liu, Min; Dong, Qianggang; Chen, Libo
CORPORATE SOURCE: Department of Nuclear Medicine, Sixth People's Hospital, Shanghai Jiao Tong University, Shanghai, 200233, Peop. Rep. China
SOURCE: Journal of Clinical Endocrinology and Metabolism (2015), 100(5), 1771-1779
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2014-3023
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Context: The aberrant silencing of iodide-handling genes accompanied by up-regulation of glucose metabolism presents a major challenge for radioiodine treatment of papillary thyroid cancer (PTC). Objective: This study aimed to evaluate the effect of tyrosine kinase inhibitors on iodide-handling and glucose-handling gene expression in BHP 2-7 cells harboring RET/PTC1 rearrangement. Main Outcome Measures: In this in vitro study, the effects of sorafenib or cabozantinib on cell growth, cycles, and apoptosis were investigated by cell proliferation assay, cell cycle anal., and Annexin V-FITC apoptosis assay, resp. The effect of both agents on signal transduction pathways was evaluated using the Western blot. Quant. real-time PCR, Western blot, immunofluorescence, and radioisotope uptake assays were used to assess iodide-handling and glucose-handling gene expression. Results: Both compds. inhibited cell proliferation in a time-dependent and dose-dependent manner and caused cell cycle arrest in the G0/G1 phase. Sorafenib blocked RET, AKT, and ERK1/2 phosphorylation, whereas cabozantinib blocked RET and AKT phosphorylation. The restoration of iodide-handling gene expression and inhibition of glucose transporter 1 and 3 expression could be induced by either drug. The robust expression of sodium/iodide symporter induced by either agent was confirmed, and 125I uptake was correspondingly enhanced. 18F-fluorodeoxyglucose accumulation was significantly decreased after treatment by either sorafenib or cabozantinib. Conclusions: Sorafenib and cabozantinib had marked effects on cell proliferation, cell cycle arrest, and signal transduction pathways in PTC cells harboring RET/PTC1 rearrangement. Both agents could be potentially used to enhance the expression of iodide-handling genes and inhibit the expression of glucose transporter genes.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 64 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:981422 CAPLUS Full-text
DOCUMENT NUMBER: 163:88178
TITLE: Methods of selecting treatment regimens of cancer with chemotherapy plus VEGF signaling inhibitors using the predictive potential of serum protein and tumor gene expression
INVENTOR(S): Barry, Simon T.; Critchlow, Susan E.; Pommier, Aurelien J.C.
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015082880	A1	20150611	WO 2014-GB53485	20141125
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK,				

SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61910652 P 20131202

AB The present invention is directed to, inter alia, the predictive potential of serum protein and tumor gene expression in patients with metastatic colorectal cancer (mCRC) receiving either chemotherapy plus placebo or chemotherapy plus the VEGF signaling inhibitor cediranib, sunitinib, sorafenib, pazopanib, tivozanib, vandetanib, soraninib, axitinib, cabozantinib, bevacizumab, aflibercept or ramucirumab. The present invention, in addition, provides for patient selection methods, as well as kits, that may be used in determining suitable cancer treatment regimens in subjects with cancer, with particular reference to whether the subject will gain benefit from treatment with VEGF signaling inhibitors.

OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 65 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:960349 CAPLUS Full-text

TITLE: Cabozantinib as a new drug for treating metastatic medullary thyroid cancer

AUTHOR(S): Chen, Hui-ling; Zhang, Zhi-ye; Yang, Yan-biao

CORPORATE SOURCE: Department of Pharmacy, Lanzhou City First People's Hospital, Lanzhou, 730050, Peop. Rep. China

SOURCE: Zhongguo Yaofang (2014), 25(29), 2766-2769
CODEN: ZYHAA4; ISSN: 1001-0408

DIGITAL OBJECT ID: 10.6039/j.issn.1001-0408.2014.29.27

PUBLISHER: Zhongguo Yaofang Zazhishe

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Chinese

AB A review with 12 refs. is given on the cabozantinib as a new drug for treating metastatic medullary thyroid cancer. The topic discussed include:: (1) clin. pharmacol. research of cabozantinib(action mechanism and pharmacol. effects), (2) clin. research of cabozantinib, (3) adaptation disease and dosage and administration of cabozantinib, (4) drug interactions with cytochrome P 450 and p-glycoprotein, (5) attention and safety evaluation of cabozantinib, (6) administration for special population.

L8 ANSWER 66 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:948166 CAPLUS Full-text

TITLE: Update on Cardiovascular Safety of Tyrosine Kinase Inhibitors: With a Special Focus on QT Interval, Left Ventricular Dysfunction and Overall Risk/Benefit

AUTHOR(S): Shah, Rashmi R.; Morganroth, Joel

CORPORATE SOURCE: Rashmi Shah Consultancy Ltd, Buckinghamshire, SL9 7JA, UK

SOURCE: Drug Safety (2015), 38(8), 693-710
CODEN: DRSAEA; ISSN: 0114-5916

DIGITAL OBJECT ID: 10.1007/s40264-015-0300-1

PUBLISHER: Springer International Publishing AG

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. We previously reviewed the cardiovascular safety of 16 tyrosine kinase inhibitors (TKIs), approved for use in oncol. as of 30 Sept. 2012. Since then, the indications for some of them have been widened and an addnl. nine TKIs have also been approved as of 30 Apr. 2015. Eight of these nine are indicated for use in oncol. and one (nintedanib) for idiopathic pulmonary fibrosis. This report is an update on the cardiovascular safety of those 16 TKIs, including the post-marketing data concerning their pro-arrhythmic effects, and reviews the cardiovascular safety of the nine new TKIs approved since (afatinib, cabozantinib, ceritinib, dabrafenib, ibrutinib, lenvatinib, nintedanib, ponatinib, and trametinib). As before, we focus on specific aspects of cardiovascular safety, namely their potential to induce QT interval prolongation, left ventricular (LV) dysfunction and hypertension but now also summarise the risks of arterial thromboembolic events (ATEs) associated with these agents. Of the newer TKIs, cabozantinib and ceritinib have been shown to induce a mild to moderate degree of QTc interval prolongation while cardiac dysfunction has been reported with the use of afatinib, dabrafenib, lenvatinib, ponatinib and trametinib. The label for axitinib was revised to include a new association with cardiac dysfunction. Hypertension is associated with cabozantinib, lenvatinib, nintedanib, ponatinib and trametinib. Ponatinib, within 10 mo of its approval in Dec. 2012, required voluntary (temporary) suspension of its marketing until significant safety revisions (restricted indication, addnl. warnings and precautions about the risk of arterial occlusion and thromboembolic events and amended dose) were made to its label. Compared with the previous 16 TKIs, more of the recently introduced TKIs are associated with the risk of LV dysfunction, and fewer with QT prolongation. Available data on morbidity and mortality associated with TKIs, together with post-marketing experience with lapatinib and ponatinib, emphasize the need for effective pharmacovigilance and ongoing re-assessment of their risk/benefit after approval of these novel agents. If not adequately managed, these cardiovascular effects significantly decrease the quality of life and increase the morbidity and mortality in a population already at high risk. Evidence accumulated over the last decade suggests that their clin. benefit, although worthwhile, is modest and extends only to progression-free survival and complete response without any effect on overall survival. During uncontrolled use in routine clin. practice, their risk/benefit is likely to be inferior to that perceived from highly controlled clin. trials.

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 67 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:894377 CAPLUS Full-text

DOCUMENT NUMBER: 163:1020

TITLE: Compositions and methods for diagnosing, evaluating and treating cancer by means of the DNA methylation status

INVENTOR(S): Clement, Kendell; Getz, Gad; Landau, Dan-Avi; Meissner, Alexander; Wu, Catherine Ju-Ying

PATENT ASSIGNEE(S): The Broad Institute Inc., USA; Dana-Farber Cancer Institute, Inc.; The General Hospital Corporation; President and Fellows of Harvard College

SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015077717	A1	20150528	WO 2014-US67146	20141124

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61908316 P 20131125

AB The present invention relates to methods of detg. a cancer treatment prognosis for a subject in need thereof by evaluating epigenetic and genetic changes within a tumor sample from the subject. The present invention further provides methods of treating cancer in a subject by evaluating epigenetic and genetic changes within a tumor sample from the subject, in addition, the present invention provides methods of screening test agents to identify agents that decrease tumor cell plasticity.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 68 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:893490 CAPLUS Full-text

DOCUMENT NUMBER: 163:51687

TITLE: Process for the preparation of cabozantinib salt and its crystal form

INVENTOR(S): Shen, Anxiong; Tang, Dongjun; Kou, Jingping

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 19pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104649969	A	20150527	CN 2014-10676653	20141121

PRIORITY APPLN. INFO.: CN 2013-10596247 A 20131122

AB The invention relates to the cabozantinib L-malate crystal form A2, which has absorption peaks at 9.33°, 11.75°, 13.44°, 15.16°, 19.72°, 23.14°, and 25.92° determined by X-ray powder diffraction at 2θ. The invention also relates to cabozantinib hydrobromide crystal form I, which has absorption peaks at 8.68°, 13.01°, 7.45°, 19.52°, 20.05°, 21.71°, 23.29°, and 26.28° determined by X-ray powder diffraction at 2θ.

L8 ANSWER 69 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:893241 CAPLUS Full-text

DOCUMENT NUMBER: 163:66113

TITLE: Aminopyridine compounds as protein kinase receptor inhibitors and their preparation, pharmaceutical compositions and use in the treatment of proliferative disorders

INVENTOR(S): Xi, Ning; Wang, Liang; Wang, Tingjin

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company

SOURCE: Faming Zhuanli Shenqing, 109pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

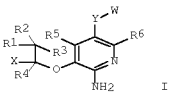
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104650049	A	20150527	CN 2014-10429046	20140827

PRIORITY APPLN. INFO.: CN 2013-10383121 A 20130828
CN 2014-10144178 A 20140410

OTHER SOURCE(S): MARPAT 163:66113

GI



I

AB The invention relates to aminopyridine compds. of formula I, their pharmaceutically acceptable salts, and pharmaceutical formulations, which is used for regulating protein kinase activity, and adjusting signal response within cells or between cells. The invention also relates to compds. I and their stereoisomer, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts or prodrugs which are used in treating mammal, particularly to human hyperproliferative disorders. The pharmaceutical compns. includes the title compds., pharmaceutically acceptable carriers, excipients, diluents, adjuvants, and/or mediums, and other treating agents. The pharmaceutical compns. are used in preparing medicines for preventing, handling, treating or relieving proliferative disorders such as metastatic cancer, colon cancer, gastric adenocarcinoma, bladder cancer, breast cancer, kidney cancer, liver cancer, lung cancer, thyroid cancer, head and neck cancer, prostate cancer, pancreatic cancer, central nervous system cancer, spongioblastoma, bone marrow hyperplasia, atherosclerosis or pulmonary fibrosis. Compds. of formula I wherein R1- R6 are independently H, D or F; X, Y are independently (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl; W is C3-8 cycloalkyl, -(C1-4 alkylene)-(C3-8 cycloalkyl), C3-7 heterocyclyl or -(C1-4 alkylene)-(C3-7 heterocyclyl), etc.; and their stereoisomer, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts or prodrugs as

protein kinase receptor inhibitors useful in the treatment of proliferative disorders thereof, are claimed. Compds. of formula I were prepared by using condensation, reduction, and cross-coupling as the key steps. All the invention compds. were evaluated for their protein kinase inhibitory activity.

L8 ANSWER 70 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:884680 CAPLUS Full-text
TITLE: Comprehensive transcriptomic analysis of molecularly targeted drugs in cancer for target pathway evaluation
AUTHOR(S): Mashima, Tetsuo; Ushijima, Masaru; Matsuura, Masaaki; Tsukahara, Satomi; Kunimasa, Kazuhiro; Furuno, Aki; Saito, Sakae; Kitamura, Masami; Soma-Nagae, Taeko; Seimiya, Hiroyuki; Dan, Shingo; Yamori, Takao; Tomida, Akihiro
CORPORATE SOURCE: Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo, Japan
SOURCE: Cancer Science (2015), 106(7), 909-920
CODEN: CSACCM; ISSN: 1349-7006
DIGITAL OBJECT ID: 10.1111/cas.12682
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Targeted therapy is a rational and promising strategy for the treatment of advanced cancer. For the development of clin. agents targeting oncogenic signaling pathways, it is important to define the specificity of compds. to the target mol. pathway. Genome-wide transcriptomic anal. is an unbiased approach to evaluate the compound mode of action, but it is still unknown whether the anal. could be widely applicable to classify molecularly targeted anticancer agents. We comprehensively obtained and analyzed 129 transcriptomic datasets of cancer cells treated with 83 anticancer drugs or related agents, covering most clin. used, molecularly targeted drugs alongside promising inhibitors of mol. cancer targets. Hierarchical clustering and principal component anal. revealed that compds. targeting similar target mols. or pathways were clustered together. These results confirmed that the gene signatures of these drugs reflected their modes of action. Of note, inhibitors of oncogenic kinase pathways formed a large unique cluster, showing that these agents affect a shared mol. pathway distinct from classical antitumor agents and other classes of agents. The gene signature anal. further classified kinome-targeting agents depending on their target signaling pathways, and we identified target pathway-selective signature gene sets. The gene expression anal. was also valuable in uncovering unexpected target pathways of some anticancer agents. These results indicate that comprehensive transcriptomic anal. with our database (http://scads.jfcr.or.jp/db/cs/) is a powerful strategy to validate and re-evaluate the target pathways of anticancer compds.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 71 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:866343 CAPLUS Full-text
DOCUMENT NUMBER: 163:1013
TITLE: mTOR protein kinase inhibitors for enhancing the immune response for treatment of diseases such as cancer
INVENTOR(S): Mannick, Joan; Glass, David Jonathan; Murphy, Leon
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 149pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015073644	A1	20150521	WO 2014-US65408	20141113
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150140036	A1	20150521	US 2014-14540867	20141113

PRIORITY APPLN. INFO.: US 2013-61903636 P 20131113
US 2014-62027121 P 20140721
US 2014-62052629 P 20140919
US 2014-62076142 P 20141106
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention relates, in part, to compns. and methods for enhancement of an immune response by partial mTOR inhibition, e.g., with low, immune enhancing, doses of an mTOR inhibitor, such as RAD001 or rapamycin. In an embodiment, the subject has cancer and the method comprises promoting the subject's immune response to treat cancer.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 72 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:847958 CAPLUS Full-text
TITLE: Cabozantinib: A MET, RET, and VEGFR2 Tyrosine Kinase Inhibitor
AUTHOR(S): Gruellich, Carsten
CORPORATE SOURCE: Department of Medical Oncology, National Center for Tumor Diseases, Heidelberg University Medical Center, Heidelberg, 69120, Germany
SOURCE: Recent Results in Cancer Research (2014), 201(Small Molecules in Oncology), 207-214
CODEN: RRCRBU; ISSN: 2197-6767
DIGITAL OBJECT ID: 10.1007/978-3-642-54490-3_12
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib is a receptor tyrosine kinase inhibitor with activity against MET, VEGFR2, FLT3, c-KIT, and RET. Activity of cabozantinib toward a broad range of tumor models could be detected in several preclin. studies. Of note, cabozantinib decreases metastasis potential and tumor invasiveness when compared with placebo or agents that target VEGFR and have no activity against MET. Clin. phase I and II studies with cabozantinib have been conducted in various malignancies including medullary thyroid cancer (MTC), NSCLC, breast, ovarian, pancreatic, and prostate cancer. In MTC, gain of function mutations of RET are central for tumorigenesis. Hereditary forms of MTC (MEN II) are caused by germline mutations of RET, in sporadic MTC in up to 50 % of cases RET mutations occur. Addnl., activating mol. changes in VEGFR and MET pathways have also been implicated in MTC progression. Clin. responses with cabozantinib in MTC could be observed in early clin. trials, and following confirmation of clin. benefit in a randomized phase III trial, cabozantinib gained FDA approval for first-line treatment of advanced MTC in 2012. In prostate cancer models, MET expression increases with androgen ablation and clin. progression of bone and lymph node metastasis. A phase II trial with cabozantinib also showed very promising response rates in patients with metastatic prostate cancer. Therefore, randomized phase III studies are currently ongoing to validate the efficacy of cabozantinib in heavily pretreated prostate cancer patients.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L8 ANSWER 73 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:827243 CAPLUS Full-text
DOCUMENT NUMBER: 162:650141
TITLE: Methods using TIE2 kinase inhibitors for the treatment of cancer
INVENTOR(S): Flynn, Daniel L.; Kaufman, Michael D.; Smith, Bryan; Rudoltz, Marc S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 121pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015069266	A1	20150514	WO 2013-US69005	20131107
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: WO 2013-US69005 20131107
AB The present invention relates to methods using TIE2 kinase inhibitors for the treatment of tumor growth, invasiveness, intravasation, dissemination, metastasis, and immunosuppression. Specifically, the invention relates to methods of using 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea and salts thereof.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 74 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:821056 CAPLUS Full-text
TITLE: Pharmacological Inhibition of KIT Activates MET Signaling in Gastrointestinal Stromal Tumors
AUTHOR(S): Cohen, Noah A.; Zeng, Shan; Seifert, Adrian M.; Kim, Teresa S.; Sorenson, Eric C.; Greer, Jonathan B.; Beckman, Michael J.; Santamaria-Barria, Juan A.; Crawley, Megan H.; Green, Benjamin L.; Rossi, Ferdinand; Besmer, Peter; Antonescu, Cristina R.; DeMatteo, Ronald P.
CORPORATE SOURCE: Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Cancer Research (2015), 75(10), 2061-2070
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-14-2564
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB These findings offer a preclin. rationale to immediately reposition the MET kinase inhibitor cabozantinib for clin. evaluation in treatment of gastrointestinal stromal tumors that are either sensitive or resistant to imatinib, the kinase inhibitor used to treat this type of sarcoma. Gastrointestinal stromal tumors (GIST) are the most common adult sarcomas and the oncogenic driver is usually a KIT or PDGFRA mutation. Although GISTs are often initially sensitive to imatinib or other tyrosine kinase inhibitors, resistance generally develops, necessitating backup strategies for therapy. In this study, we determined that a subset of human GIST specimens that acquired imatinib resistance acquired expression of activated forms of the MET oncogene. MET activation also developed after imatinib therapy in a mouse model of GIST (KitV558del/+ mice), where it was associated with increased tumor hypoxia. MET activation also occurred in imatinib-sensitive human GIST cell lines after imatinib treatment in vitro. MET inhibition by crizotinib or RNA interference was cytotoxic to an imatinib-resistant human GIST cell population. Moreover, combining crizotinib and imatinib was more effective than imatinib alone in imatinib-sensitive GIST models. Finally, cabozantinib, a dual MET and KIT small-mol. inhibitor, was markedly more effective than imatinib in multiple preclin. models of imatinib-sensitive and imatinib-resistant GIST. Collectively, our findings showed that activation of compensatory MET signaling by KIT inhibition may contribute to tumor resistance. Furthermore, our work offered a preclin. proof of concept for MET inhibition by cabozantinib as an effective strategy for GIST treatment. Cancer Res; 75(10); 2061-70. ©2015 AACR.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 75 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:803712 CAPLUS Full-text
TITLE: Physicochemical properties of novel protein kinase inhibitors in relation to their substrate specificity for drug transporters
AUTHOR(S): Da Silva, Candido G.; Honeywell, Richard J.; Dekker, Henk; Peters, Godefridus J.

CORPORATE SOURCE: Department of Medical Oncology, VU University Medical Center, Amsterdam, 1007 MB, Neth.
SOURCE: Expert Opinion on Drug Metabolism & Toxicology (2015), 11(5), 703-717
CODEN: EODMAP; ISSN: 1742-5255
DIGITAL OBJECT ID: 10.1517/17425255.2015.1006626
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Introduction: Small mol. tyrosine and serine-threonine kinase inhibitors (TKIs and STKIs) are emerging drugs that interfere with downstream signaling pathways involved in cancer proliferation, invasion, metastasis and angiogenesis. The understanding of their pharmacokinetics, the identification of their transporters and the modulating activity exerted on transporters is pivotal to predict therapy efficacy and to avoid unwarranted drug treatment combinations. Areas covered: Exptl. or in silico data were collected and summarized on TKIs and STKIs physico-chemical properties, which influence their transport, metabolism and efficacy, and TKIs and STKIs as influx transporter substrates and inhibitors. In addition, the uptake by tumor cell influx transporters and some factors in the tumor microenvironment affecting the uptake of TKIs and STKIs by cancer cells are briefly covered. Expert opinion: Membrane transporters play an important role in the pharmacokinetics and hence the efficacy of anticancer drugs, including TKIs and STKIs. These drugs are substrates and inhibitors of various transporters. Drug resistance may be bypassed not only by identifying the proper transporter but also by selective combinations, which may either downregulate or increase transporter activity. However, care has to be taken because this profile might be disease, drug and patient specific.
REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 76 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:739043 CAPLUS Full-text
DOCUMENT NUMBER: 162:567725
TITLE: Solid particulate formulations of tyrosine derivatives
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: PCT Int. Appl., 20pp.; Chemical Indexing Equivalent to 162:567667 (US)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015061288	A1	20150430	WO 2014-US61527	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150112116	A1	20150423	US 2013-14062194	20131024
PRIORITY APPLN. INFO.:			US 2013-61894279 P	20131022
			US 2013-14062194 A	20131024

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Provided are methods comprising providing a tyrosine deriv. such as α-methyltyrosine, and a solid particulate material (and, optionally, melanin) and applying force to said tyrosine derivative and said solid particulate material for a time and under conditions effective to impregnate at least one of said tyrosine derivative and said solid particulate material with the other of said tyrosine derivative and said solid particulate material.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 77 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:734279 CAPLUS Full-text
DOCUMENT NUMBER: 162:594407
TITLE: High-speed centrifugal mixing devices for uses in pharmaceuticals
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015061256	A1	20150430	WO 2014-US61481	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150110735	A1	20150423	US 2013-14059837	20131022
PRIORITY APPLN. INFO.:			US 2013-14059837 A	20131022

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A centrifugal mixing device can include a shaft assembly that is operably coupled to a motor such that the motor rotates the shaft assembly about a first axis. The devices can further include a turret that is rotatably coupled to the shaft assembly such that the turret rotates about the first axis relative to the shaft assembly. The turret can include a first support, a first canister rotatably coupled to the first support such that the first canister rotates about a second axis, and a second canister rotatably coupled to the first support such that the second canister rotates about a third axis. The turret is configured to rotate about the first axis in a first rotational direction and each of the first and second canisters is configured to rotate about the second and third axes, resp., in a second rotational direction that is opposite the first rotational direction. The centrifugal mixing device consists of the canisters comprising at least 2 different particulate materials. The particulate materials comprises an active pharmaceutical ingredient.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 78 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:694096 CAPLUS Full-text
DOCUMENT NUMBER: 163:240819
TITLE: New therapies for dedifferentiated papillary thyroid cancer
AUTHOR(S): Fallahi, Poupak; Mazzi, Valeria; Vita, Roberto; Ferrari, Silvia Martina; Materazzi, Gabriele; Galleri, David; Benvenga, Salvatore; Miccoli, Paolo; Antonelli, Alessandro
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56126, Italy
SOURCE: International Journal of Molecular Sciences (2015), 16(3), 6153-6182
CODEN: IJMCFK; ISSN: 1422-0067
DIGITAL OBJECT ID: 10.3390/ijms16036153
PUBLISHER: MDPI AG
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB The no. of thyroid cancers is increasing. Std. treatment usually includes primary surgery, TSH suppressive therapy, and ablation of the thyroid remnant with radioactive iodine (RAI). Despite the generally good prognosis of thyroid carcinoma, about 5% of patients will develop metastatic disease, which fails to respond to RAI, exhibiting a more aggressive behavior. The lack of specific, effective and well-tolerated drugs, the scarcity of data about the association of multi-targeting drugs, and the limited role of radioiodine for dedifferentiated thyroid cancer, call for further efforts in the field of new drugs development. Rearranged during transfection (RET)/papillary thyroid carcinoma gene rearrangements, BRAF (B-RAF proto-oncogene, serine/threonine kinase) gene mutations, RAS (rat sarcoma) mutations, and vascular endothelial growth factor receptor 2 angiogenesis pathways are some of the known pathways playing a crucial role in the development of thyroid cancer. Targeted novel compds. have been demonstrated to induce clin. responses and stabilization of disease. Sorafenib has been approved for differentiated thyroid cancer refractory to RAI.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 178 THERE ARE 178 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 79 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:691735 CAPLUS Full-text
DOCUMENT NUMBER: 162:567753
TITLE: High-speed centrifugal mixing devices for uses in pharmaceuticals
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 15pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150110735	A1	20150423	US 2013-14059837	20131022
WO 2015061256	A1	20150430	WO 2014-US61481	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2013-14059837 A	20131022

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A centrifugal mixing device can include a shaft assembly that is operably coupled to a motor such that the motor rotates the shaft assembly about a first axis. The devices can further include a turret that is rotatably coupled to the shaft assembly such that the turret rotates about the first axis relative to the shaft assembly. The turret can include a first support, a first canister rotatably coupled to the first support such that the first canister rotates about a second axis, and a second canister rotatably coupled to the first support such that the second canister rotates about a third axis. The turret is configured to rotate about the first axis in a first rotational direction and each of the first and second canisters is configured to rotate about the second and third axes, resp., in a second rotational direction that is opposite the first rotational direction. The centrifugal mixing device consists of the canisters comprising at least 2 different particulate materials. The particulate materials comprises an active pharmaceutical ingredient.

L8 ANSWER 80 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:691420 CAPLUS Full-text
DOCUMENT NUMBER: 162:567667
TITLE: Solid particulate formulations of tyrosine derivatives
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 6pp.; Chemical Indexing Equivalent to 162:567725 (WO)
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150112116	A1	20150423	US 2013-14062194	20131024
WO 2015061288	A1	20150430	WO 2014-US61527	20141021

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61894279 P 20131022
US 2013-14062194 A 20131024

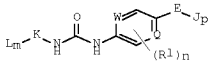
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided are methods comprising providing a tyrosine deriv. such as α-methyltyrosine, and a solid particulate material (and, optionally, melanin) and applying force to said tyrosine derivative and said solid particulate material for a time and under conditions effective to impregnate at least one of said tyrosine derivative and said solid particulate material with the other of said tyrosine derivative and said solid particulate material.

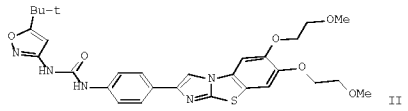
L8 ANSWER 81 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:656704 CAPLUS Full-text
DOCUMENT NUMBER: 162:487306
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Institut de Recerca Biomedica (IRB Barcelona), Spain; Institucio Catalana de Recerca i Estudis Avancats
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015052583	A2	20150416	WO 2014-IB2675	20141007
WO 2015052583	A3	20150723		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW



I



II

AB This invention provides substituted urea derivs. I [wherein K = 5- or 6-membered heteroaryl; Q and W = independently CH or N; L = independently NH2, NO2, alkylthio, alkyl, etc.; R1 = independently H, F, Cl, Br, I, etc.; E = bicyclic or tricyclic heteroaryl; J = G-(CH2)q-R; G = independently O, S, SO, SO2, CO, etc.; R = independently H, alkoxy, alkyl, alkenyl, etc.; m = 1-4; n = 0-4; p = 2-4; q = 1-4], stereoisomers, geometrical isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, esters, pharmaceutically acceptable salts, or prodrugs for treating FLT3 kinase mediated or induced diseases, such as autoimmune diseases, inflammatory diseases and proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 6.0 nM against FLT3 kinase.

L8 ANSWER 83 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:613471 CAPLUS Full-text
DOCUMENT NUMBER: 162:532738
TITLE: High drug loading system to co-deliver anticancer drugs and nucleic acids for cancer therapy
INVENTOR(S): Cheng, Gang; Tang, Qiong; Cao, Bin
PATENT ASSIGNEE(S): The University of Akron, USA
SOURCE: U.S. Pat. Appl. Publ., 10pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150099005	A1	20150409	US 2014-14510442	20141009

PRIORITY APPLN. INFO.: US 2013-61888709 P 20131009

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A high drug loading system is described comprising of at least one anticancer drug; at least one peptide; and at least one nucleic acid.

L8 ANSWER 84 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:560353 CAPLUS Full-text
DOCUMENT NUMBER: 162:488682
TITLE: Preparation of substituted urea derivatives for modulating the FLT3 kinase activity and inhibiting FLT3-ITD
INVENTOR(S): Cheng, Changchung; Liu, Bing; Zhang, Yingjun; Long, Bohua; Zhang, Weihong
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015043492	A1	20150402	WO 2014-CN87469	20140925

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

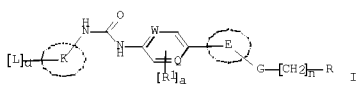
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CN 104513259	A	20150415	CN 2014-10498216	20140925
CN 104513252	A	20150415	CN 2014-10499464	20140925

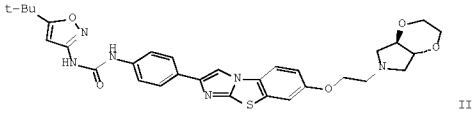
PRIORITY APPLN. INFO.: CN 2013-10445605 A 20130926
CN 2014-10107854 A 20140322

OTHER SOURCE(S): CASREACT 162:488682; MARPAT 162:488682

GI



I



II

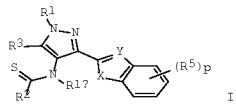
AB The title compds. I [each of Q and W = (independently) CH or N; G = O, S, C(O), etc.; R = alkoxy, alkyl, (un)substituted amino, etc.; ring K = 5-6 membered heteroaryl group, of which at least two ring members are heteroatoms independently selected from O, S, NR4 and N; each L = (independently) amino, nitro, alkylthio, etc.; ring E = bicyclic or tricyclic heteroarylene; R1 = H, halo, haloalkyl, etc.; R4 = H, alkyl, cycloalkyl, etc.; a = 0-4; d, n = 1-4; with the provisos] which are useful in modulating the FLT3 kinase activity, inhibiting FLT3-ITD, and treating the diseases mediated by FLT3 kinase or caused by FLT3-ITD, were prepared and claimed. E.g., a multi-step synthesis of II, starting from (4aS,7aS)-hexahydro-2H-[1,4]dioxino[2,3-c]pyrrole and 2-chloroethanol, was described. Exemplified compds. I were tested for FLT3 kinase inhibition (data given for representative compds. I). Pharmaceutical compns. comprising compound I, alone or in combination with other therapeutic agents, were disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

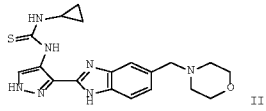
L8 ANSWER 85 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:527604 CAPLUS Full-text
DOCUMENT NUMBER: 162:475187
TITLE: Preparation of pyrazole derivatives as protein kinase over expression inhibitors
INVENTOR(S): Zhang, Jiancun; Liu, Bing; Zhang, Yingjun; Nie, Linlin; Yang, Xueqi
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 80pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104447701	A	20150325	CN 2014-10471458	20140916
PRIORITY APPLN. INFO.:			CN 2013-10426478 A	20130917
			CN 2014-10109414 A	20140321

OTHER SOURCE(S): MARPAT 162:475187
GI



I



II

AB The title compds. with general formula I [wherein R1 and R1a are independently H or C1-4 alkyl; R2 is alkyl amino, aryl, heteroaryl, etc.; X is CR4aR4 or NR6; Y is CR4a or N; R3 is H, F, Cl, etc.; R3 is H, F, Cl, Br, etc.; R5 is H, alkyl, alkenyl, alkynyl, etc.; p = 1 -4] or isomers, N-oxide, hydrates, solvates, metabolites, esters, prodrugs, or pharmaceutically acceptable salts there of were prepared as protein kinase over expression inhibitors. For example, compound II was prepared in a multi-step synthesis. The title substituted pyrazole derivative for inhibiting protein kinase over expression, or stereoisomer, geometric isomer, tautomer, oxynitride, solvate, hydrate, metabolite, ester, pharmaceutically acceptable salt or prodrug thereof, pharmaceutical compns. containing these compds. as active ingredients, and the application of these compds. or pharmaceutical compns. in preparing the drugs for preventing, treating of reducing cell growth disorders. (assay data given).

L8 ANSWER 86 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:494404 CAPLUS Full-text
DOCUMENT NUMBER: 162:570128
TITLE: Dermatologic adverse events in pediatric patients receiving targeted anticancer therapies: A pooled analysis
AUTHOR(S): Belum, Viswanath Reddy; Washington, Courtney; Pratilas, Christine A.; Sibaud, Vincent; Boralevi, Franck; Lacouture, Mario E.
CORPORATE SOURCE: Department of Dermatology, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Pediatric Blood & Cancer (2015), 62(5), 798-806
CODEN: PBCEAQ; ISSN: 1545-5017
DIGITAL OBJECT ID: 10.1002/pbc.25429
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background : The dermatol. adverse events (AEs) of various molecularly targeted therapies are well-described in adult cancer patients. Little has been reported on the incidence and clin. presentation of such AEs in pediatric patients with cancer. To address this gap, we analyzed the dermatol. AEs reported across clin. trials of targeted anticancer therapies in pediatric patients. Procedures : We conducted an electronic literature search (PubMed, American Society of Clin. Oncol. annual meetings' abstrs., , NCI's Pediatric Oncol. Branch webpage) to identify clin. trials involving targeted anticancer therapies that reported dermatol. AEs in their safety data. Studies were limited to the pediatric population, monotherapy trials (oncol.), and English language publications. Results : Pooled data from 19 clin. studies investigating 11 targeted anticancer agents (alemtuzumab, rituximab, imatinib, dasatinib, erlotinib, vandetanib, sorafenib, cabozantinib, pazopanib, everolimus, and temsirolimus) were analyzed. The most frequently encountered dermatol. AEs were rash (127/660; 19%), xerosis (18/100; 18%), mucositis (68/402; 17%), and pruritus (12/169; 7%). Other AEs included pigmentary abnormalities of the skin/hair (13%), hair disorders (trichomegaly, hypertrichosis, alopecia, and madarosis; 14%), urticaria (7%), palmoplantar erythrodysesthesia (7%), erythema, acne, purpura, skin fissures, other 'unknown skin changes', exanthem, infection, flushing, telangiectasia, and photosensitivity. Conclusion : This study describes the dermatol. manifestations of targeted anticancer therapy-related AEs in the pediatric population. Since these AEs are often associated with significant morbidity, it is imperative that pediatric oncologists be familiar with their recognition and management, to avoid unnecessary dose modifications and/or termination, and to prevent impairments in patients' quality of life. Pediatr Blood Cancer 2015;62:798-806. © 2015 Wiley Periodicals, Inc.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 87 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:460229 CAPLUS Full-text
DOCUMENT NUMBER: 162:398722
TITLE: Anti-human angiopoietin 2 antibody for enhancing efficacy of antitumor agent and for combination cancer therapy
INVENTOR(S): Kim, Kyung Eun; Han, Sang Yeul; Koh, Gou Young; Lee, Hyo Seon; Kim, Chan
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd, S. Korea; Korea Advanced Institute of Science and Technology
SOURCE: Eur. Pat. Appl., 66pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2848631	A1	20150318	EP 2014-178842	20140729
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015032075	A	20150325	KR 2013-112089	20130917
US 20150079112	A1	20150319	US 2014-14446199	20140729
PRIORITY APPLN. INFO.:			KR 2013-112089 A	20130917

AB A method of preventing or treating cancer using an anti-Ang2 antibody or an antigen-binding fragment thereof that specifically binds to an angiogenesis-inducing factor Angiopoietin-2 (Ang2) and complexes to a Tie2 receptor while bound with Ang2.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 88 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:458209 CAPLUS Full-text
DOCUMENT NUMBER: 162:447668
TITLE: Anti-human VSTM5 antibodies, fragments and conjugates for therapy and diagnosis of cancer, infection and immune disease
INVENTOR(S): Levine, Zurit; Rotman, Galit; Dassa, Liat; Levy, Ofer; Cojocaru, Gad S.; Toporik, Amir; Kliger, Yossef; Pow, Andrew; Liang, Spencer
PATENT ASSIGNEE(S): Compugen Ltd., Israel
SOURCE: PCT Int. Appl., 490pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015037005	A1	20150319	WO 2014-IL50814	20140911
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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PRIORITY APPLN. INFO.:			US 2013-61876324 P	20130911

AB The present invention relates to VSTM5-specific antibodies, antibody fragments, and VSTM5 polypeptides, conjugates and compns. comprising same, for modulating (antagonizing or agonizing) one or more of the effects of VSTM5 expression on immunity. More specifically, the present invention relates to VSTM5-specific antibodies, antibody fragments, and VSTM5 polypeptides, conjugates and compns. comprising same for treating and aiding in the diagnosis of cancer, infectious diseases and immune related diseases, e.g., those associated with aberrant (higher or lower than normal) VSTM5 expression by diseased and/or immune cells and/or aberrant (increased or reduced) VSTM5-mediated effects on immunity.

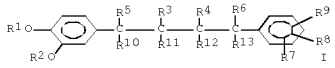
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 89 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:423197 CAPLUS Full-text
DOCUMENT NUMBER: 162:419539
TITLE: Cancer therapy using dual kinase inhibitors such as catecholic butanes
INVENTOR(S): White, Thomas F.; Hoth, Daniel
PATENT ASSIGNEE(S): Triact Therapeutic, Inc., USA
SOURCE: PCT Int. Appl., 76pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015035410	A1	20150312	WO 2014-US54832	20140909
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150071919	A1	20150312	US 2014-14481837	20140909

PRIORITY APPLN. INFO.: US 2013-61875502 P 20130909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 162:419539
GI



AB The application relates to methods for treating a proliferative disorder by administering to a subject a pharmaceutical composition of a dual kinase inhibitor e.g. catecholic butanes of formula I [R1, R2 = independently H, lower alkyl, lower acyl; R3 - R6, R10 - R13 = independently H, lower alkyl; R7 - R9 = independently H, OH, lower alkoxy, lower acyloxy]. Patients to be treated include those that have been treated with Tarceva or other therapeutic compds. and relapsed or are resistant to treatment. The compds. described herein may exhibit a synergistic effect when administered with another agent.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 90 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:422447 CAPLUS Full-text
DOCUMENT NUMBER: 162:371151
TITLE: Combination therapy for the treatment of cancer using c-met inhibitor and c-myc inhibitor
INVENTOR(S): Lee, Ji Min; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 83pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150071932	A1	20150312	US 2014-14481509	20140909
KR 2015029175	A	20150318	KR 2013-107995	20130909

PRIORITY APPLN. INFO.: KR 2013-107995 A 20130909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 162:371151
AB The invention relates to a method of preventing and/or treating a cancer including co-administering a c-Met inhibitor and a c-Myc Inhibitor to a subject in need thereof. The invention relates to a pharmaceutical composition comprising a c-Met inhibitor and a c-Myc inhibitor. The inhibitor comprises at least one selected from the group consisting of an antibody, an antigen-binding fragment thereof, aptamers, siRNA, shRNA, microRNA, or a small mol. The invention relates to a kit comprising a pharmaceutically effective amount of a c-Met inhibitor as an active ingredient, and a second pharmaceutical composition comprising a pharmaceutically effective amount of a c-Myc inhibitor as an active ingredient, packaged together.

L8 ANSWER 91 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:422412 CAPLUS Full-text
DOCUMENT NUMBER: 162:423721
TITLE: Combination cancer therapy using c-met inhibitor and β-catenin inhibitor
INVENTOR(S): Lee, Ji Min; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 98pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150071930	A1	20150312	US 2014-14480174	20140908
KR 2015028652	A	20150316	KR 2013-107568	20130906

PRIORITY APPLN. INFO.: KR 2013-107568 A 20130906
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose a method of preventing and/or treating cancer. The method comprises the administration of a c-Met inhibitor and a β-catenin inhibitor. In several examples, an anti-MET receptor antibody in combination with a β-catenin inhibitor are shown to be effective in inhibiting the proliferation of breast, colon, and renal cancer cells.

L8 ANSWER 92 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:414572 CAPLUS Full-text
DOCUMENT NUMBER: 162:425170
TITLE: Preparation of substituted pyridine compounds as tyrosine kinase inhibitors for treating proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Liang; Wang, Tingjin
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 142pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015034729	A1	20150312	WO 2014-US53017	20140827
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2013-61873963 P 20130905
OTHER SOURCE(S): CASREACT 162:425170; MARPAT 162:425170
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridine compds. of general formula I (wherein each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; each of X and Y is independently C6-10aryl or 5-10 membered heteroaryl, both optionally substituted; W is C3-8cycloalkyl, -(C1-4-alkylene)(C3-8cycloalkyl), C3-7heterocyclyl or -(C1-4-alkylene)-C3-7heterocyclyl, each optionally substituted), pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 4-step synthesis that involved reaction of intermediate tert-Bu 4-(5-bromopyridin-2-yl)piperazine-1-carboxylate with III, and deprotecting the intermediate formed. The stability of the example compds. in human and rat liver microsomes, their pharmacokinetic profile in rats, and their ALK kinase and c-met kinase inhibitory activities were measured.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 93 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:383707 CAPLUS Full-text
DOCUMENT NUMBER: 162:337080
TITLE: Gene expression signatures predictive of subject response to a multi-kinase inhibitor and methods of using the same
INVENTOR(S): Guo, Sheng; Chen, Dawei; Zhang, Juan; Cai, Jie; Li, Henry Qixiang
PATENT ASSIGNEE(S): Crown Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015031604	A1	20150305	WO 2014-US53142	20140828
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: WO 2013-CN82487 A 20130828
AB Gene expression signature predictive of cancer patient response to multi-kinase inhibitor is disclosed. Also disclosed are methods predicting the efficacy of the multi-kinase inhibitor for treating cancer in a patient. Also disclosed are methods for distinguishing responders from non-responders to a multi-kinase inhibitor in treating cancer. Also disclosed are methods for treating a cancer patient with a multi-kinase inhibitor.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 94 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:359181 CAPLUS Full-text
DOCUMENT NUMBER: 163:714261
TITLE: Patient-Derived Xenografts from Non-Small Cell Lung Cancer Brain Metastases Are Valuable Translational Platforms for the Development of Personalized Targeted Therapy
AUTHOR(S): Lee, Hye Won; Lee, Jung-il; Lee, Se Jeong; Cho, Hyun Jung; Song, Hye Jin; Jeong, Da Eun; Seo, Yun Jee; Shin, Sang; Joung, Je-Gun; Kwon, Yong-Jun; Choi, Yoon-La; Park, Woong-Yang; Lee, Hyun Moo; Seol, Ho Jun; Shim, Young Mog; Joo, Kyeung Min; Nam, Do-Hyun
CORPORATE SOURCE: Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, S. Korea
SOURCE: Clinical Cancer Research (2015), 21(5), 1172-1182
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-14-1589
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: The increasing prevalence of distant metastases from non-small cell lung cancer (NSCLC) indicates an urgent need for novel therapeutic modalities. Brain metastasis is particularly common in NSCLC, with severe adverse effects on clin. prognosis. Although the mol. heterogeneity of NSCLC and availability of various targeted agents suggest personalized therapeutic approaches for such brain metastases, further development of appropriate preclin. models is needed to validate the strategies. Exptl. Design: We established patient-derived xenografts (PDX) using NSCLC brain metastasis surgical samples and elucidated their possible preclin. and clin. implications for personalized treatment. Results: NSCLC brain metastases (n = 34) showed a significantly higher successful PDX establishment rate than primary specimens (n = 64; 74% vs. 23%). PDXs derived from NSCLC brain metastases recapitulated the pathol., genetic, and functional properties of corresponding parental tumors. Furthermore, tumor spheres established in vitro from the xenografts under serum-free conditions maintained their in vivo brain metastatic potential. Differential phenotypic and mol. responses to 20 targeted agents could subsequently be screened in vitro using these NSCLC PDXs derived from brain metastases. Although PDX establishment from primary NSCLCs was significantly influenced by histol. subtype, clin. aggressiveness, and genetic alteration status, the brain metastases exhibited consistently adequate in vivo tumor take rate and in vitro tumor sphere formation capacity, regardless of clin. and mol. conditions. Conclusions: Therefore, PDXs from NSCLC brain metastases may better represent the heterogeneous advanced NSCLC population and could be utilized as preclin. models to meet unmet clin. needs such as drug screening for personalized treatments. Clin Cancer Res; 21(5); 1172-82. ©2014 AACR.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 95 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:316867 CAPLUS Full-text
DOCUMENT NUMBER: 162:399931
TITLE: Novel crystal form of quinoline compound and preparation method thereof
INVENTOR(S): Tang, Dongjun; Liu, Yanping; Kou, Jingping
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104370811	A	20150225	CN 2014-10399795	20140814
PRIORITY APPLN. INFO.:			CN 2013-10356174 A	20130815

AB The present invention relates to a novel crystal form of quinoline compd. N-(4-{[6,7-dimethoxyquinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarbonamide and preparation method thereof, and belongs to medicinal chemical field. The crystal form is basically pure crystal form I or crystal form II. In the X-ray powder diffraction pattern of crystal form I, there are peaks at 2θ angles of about 11.9, 12.9, 14.4, 16.0, 22.1 and 26.0 degrees. In the X-ray powder diffraction pattern of crystal form II, there are peaks at 2θ angles of about 11.6, 14.1, 18.5, 21.1, 22.2, 23.2, 24.1 and 29.0 degrees. The novel crystal form possesses good stability and mobility, which is conducive to operate in storage, transfer and production, and the novel crystal form can be used for preparing pharmaceutically acceptable salt thereof for application in pharmaceutics.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 96 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:312826 CAPLUS Full-text
DOCUMENT NUMBER: 163:407215
TITLE: Treating medullary thyroid cancer in the age of targeted therapy
AUTHOR(S): Cabanillas, Maria E.; Hu, Mimi I.; Jimenez, Camilo; Grubbs, Elizabeth G.; Cote, Gilbert J.
CORPORATE SOURCE: Department of Endocrine Neoplasia & Hormonal Disorders, Unit 1461, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX, 77030, USA
SOURCE: International Journal of Endocrine Oncology (2014), 1(2), 203-216
CODEN: IJEOBC; ISSN: 2045-0869
DIGITAL OBJECT ID: 10.2217/ije.14.26
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor deriving from the thyroid parafollicular cell. Thyroidectomy continues to serve as the primary initial treatment for this cancer. Because standard cytotoxic chemotherapy has proven ineffective, reoperation and external beam radiation therapy had been the only tools to treat recurrences or distant disease. The discovery that aberrant activation of RET, a receptor tyrosine kinase, is a primary driver of MTC tumorigenesis led to clin. trials using RET-targeting tyrosine kinase inhibitors. The successes of those trials led to the approval of vandetanib and cabozantinib for treating patients with progressive or symptomatic MTC. The availability of these drugs, along with addnl. targeted therapies in development, requires a thoughtful reconsideration of the approach to treating patients with unresectable locally advanced and/or metastatic progressive MTC.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 97 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:312823 CAPLUS Full-text
DOCUMENT NUMBER: 163:437839
TITLE: Protein kinase inhibitor therapy in advanced thyroid cancer: ethical challenges and potential solutions
AUTHOR(S): Bible, Keith C.; Ain, Kenneth B.; Rosenthal, M. Sara
CORPORATE SOURCE: Mayo Clinic, Division of Medical Oncology, Rochester, MN, USA
SOURCE: International Journal of Endocrine Oncology (2014), 1(2), 145-151
CODEN: IJEOBC; ISSN: 2045-0869
DIGITAL OBJECT ID: 10.2217/ije.14.24
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Protein kinase inhibitors (PKIs) have emerged as highly promising therapies in progressive metastatic radioiodine-refractory differentiated thyroid cancer and in medullary thyroid cancer; two were recently approved in the USA for use in medullary thyroid cancer (vandetanib, cabozantinib), and another for use in progressive metastatic radioiodine-refractory differentiated thyroid cancer (sorafenib). Although more than 90% of thyroid cancer patients fare well in response to conventional treatment, PKI therapy has the potential to provide benefit. Nonetheless, PKIs produce numerous side effects, may worsen quality of life, may hasten mortality (by 1-2%), require discerning clin. acumen, are not yet proven to improve thyroid cancer survival and are very costly. This raises questions about who should prescribe PKIs, and about whether their use in thyroid cancer is truly beneficent and ethically justified. Restraint should be exercised in their use in thyroid cancer, with potential risks and benefits carefully weighed and solns. devised to help ameliorate many of the problems associated with their use.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 98 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:293134 CAPLUS Full-text
DOCUMENT NUMBER: 162:337073
TITLE: 1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy
INVENTOR(S): Jefford, Charles William; Hoessli, Daniel
PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 69pp.; Chemical Indexing Equivalent to 162:337069 (GB)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015022497	A1	20150219	WO 2014-GB52392	20140805
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
GB 2517199	A	20150218	GB 2013-14639	20130815
PRIORITY APPLN. INFO.:			GB 2013-14639 A	20130815

OTHER SOURCE(S): MARPAT 162:337073
AB The invention provides 1,2,4-trioxane compds. or pharmaceutically acceptable salts, esters, solvates, tautomers, stereoisomers thereof, for use as adjuvants for tyrosine kinase inhibitors in the treatment of cancer. Preferably the tyrosine kinase inhibitor is selected from imatinib, gefitinib, erlotinib, lapatinib, canertinib, vatalanib, sorafenib or genistein. The cancer may be selected from lymphoma, breast cancer, leukemia, gastrointestinal tumors, nonsmall cell lung cancer, melanoma, renal carcinoma, multiple myeloma, kidney cancer, colon cancer, pancreatic cancer, lung cancer, ovarian cancer and prostate cancer.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 99 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:283370 CAPLUS Full-text
DOCUMENT NUMBER: 163:438161
TITLE: Is there an antiandrogen withdrawal syndrome with enzalutamide?
AUTHOR(S): Rodriguez-Vida, Alejo; Bianchini, Diletta; Van Hemelrijck, Mieke; Hughes, Simon; Malik, Zafar; Powles, Thomas; Bahl, Amit; Rudman, Sarah; Payne, Heather; de Bono, Johann; Chowdhury, Simon
CORPORATE SOURCE: Great Maze Pond, Guy's and St Thomas' NHS Foundation Trust, London, UK
SOURCE: BJU International (2015), 115(3), 373-380
CODEN: BJINFO; ISSN: 1464-410X
DIGITAL OBJECT ID: 10.1111/bju.12826
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Objective : To examine prostate-specific antigen (PSA) levels after enzalutamide discontinuation to assess whether an antiandrogen withdrawal syndrome (AAWS) exists with enzalutamide. Methods : We retrospectively identified 30 consecutive patients with metastatic prostate cancer who were treated with enzalutamide after docetaxel. Post-discontinuation PSA results were available for all patients and were determined at 2-weekly intervals until starting further anticancer systemic therapy. PSA withdrawal response was defined as a PSA decline by ≥50% from the last on-treatment PSA, with a confirmed decrease ≥3 wk later. Patient characteristics were evaluated in relation to the AAWS using univariate logistic regression anal. Results : The median (range) patient age was 70.5 (56-86) years and the median (range) follow-up was 9.0 (0.5-16) months. The most common metastatic sites were the bone (86.7%) and lymph nodes (66.7%). Most patients (70%) had previously received abiraterone and 12 patients (40%) had also received cabazitaxel. The median (range) treatment duration with enzalutamide was 3.68 (1.12-21.39) months. PSA levels after enzalutamide withdrawal were monitored for a median (range) time of 35 (10-120) days. Only one patient (3.3%) had a confirmed PSA response ≥50% after enzalutamide discontinuation. One patient (3.3%) had a confirmed PSA response of between 30 and 50% and another patient (3.3%) had an unconfirmed PSA response of between 30 and 50%. The median overall survival was 15.5 mo (95% CI 8.1-24.7). None of the factors analyzed in the univariate anal. were significant predictors of PSA decline after enzalutamide discontinuation. Conclusions : This retrospective study provides the first evidence that enzalutamide may have an AAWS in a minority of patients with metastatic castration-resistant prostate cancer. Further studies are needed to

confirm the existence of an enzalutamide AAWS and to assess its relevance in prostate cancer management.
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 100 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:283246 CAPLUS Full-text
DOCUMENT NUMBER: 163:418637
TITLE: Cabozantinib reverses multidrug resistance of human hepatoma HepG2/adr cells by modulating the function of P-glycoprotein
AUTHOR(S): Xiang, Qing-feng; Zhang, Dong-mei; Wang, Jing-nan; Zhang, Hong-wu; Zheng, Zhe-yu; Yu, Da-cheng; Li, Ying-jie; Xu, Jun; Chen, Ya-jin; Shang, Chang-zhen
CORPORATE SOURCE: Department of Hepatopancreatobiliary Surgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Peop. Rep. China
SOURCE: Liver International (2015), 35(3), 1010-1023
CODEN: LIINCM; ISSN: 1478-3223
DIGITAL OBJECT ID: 10.1111/liv.12524
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background & Aims : Cabozantinib, a small-mol. multitargeted tyrosine kinase inhibitor, has entered into a phase III clin. trial for the treatment of hepatocellular carcinoma (HCC). This study assessed the mechanistic effect of cabozantinib on the reversal of P-glycoprotein (P-gp)-mediated multidrug resistance (MDR). Methods : CCK-8 assays and tumor xenografts were used to investigate the reversal of MDR in vitro and in vivo resp. Substrate retention assays were evaluated by fluorescence microscope and flow cytometry. Western blotting was used to detect protein expression levels. mRNA expression was determined by qPCR. The ATPase activity of P-gp was investigated using Pgp-Glo® assay systems. The binding mechanism of cabozantinib to P-gp at the mol. level was evaluated using docking anal. Results : Cabozantinib enhanced the cytotoxicity of P-gp substrate drugs in HepG2/adr and HEK293-MDR1 cells but had no effect on non-P-gp substrates. In addition, cabozantinib increased the accumulation of P-gp substrates in HepG2/adr cells but had no effect in HepG2 cells. Furthermore, cabozantinib did not alter the expression of P-gp mRNA or protein but did stimulate the activity of P-gp ATPase. The docking study indicated that cabozantinib and verapamil may partially share a binding site on P-gp. The reversal concns. of cabozantinib did not affect the expression of MET, AKT and ERK1/2. Significantly, cabozantinib increased the inhibitory efficacy of doxorubicin in P-gp-overexpressing HepG2/adr cell xenografts in nude mice. Conclusion : Cabozantinib reverses P-gp-mediated MDR by directly inhibiting the efflux function of P-gp, indicating that cabozantinib may help to reverse P-gp-mediated MDR in HCC and other cancer chemotherapy.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 101 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:281739 CAPLUS Full-text
DOCUMENT NUMBER: 162:337069
TITLE: 1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy
INVENTOR(S): Jefford, Charles William; Hoessli, Daniel Christian
PATENT ASSIGNEE(S): Switz.
SOURCE: Brit. UK Pat. Appl., 66pp.; Chemical Indexing Equivalent to 162:337073 (WO)
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2517199	A	20150218	GB 2013-14639	20130815
WO 2015022497	A1	20150219	WO 2014-GB52392	20140805

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2013-14639 A 20130815
AB The invention provides 1,2,4-trioxane compds. or pharmaceutically acceptable salts, esters, solvates, tautomers, stereoisomers thereof, for use as adjuvants for tyrosine kinase inhibitors in the treatment of cancer. Preferably the tyrosine kinase inhibitor is selected from imatinib, gefitinib, erlotinib, lapatinib, canertinib, vatalanib, sorafenib or genistein. The cancer may be selected from lymphoma, breast cancer, leukemia, gastrointestinal tumors, nonsmall cell lung cancer, melanoma, renal carcinoma, multiple myeloma, kidney cancer, colon cancer, pancreatic cancer, lung cancer, ovarian cancer and prostate cancer.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 102 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:258957 CAPLUS Full-text
DOCUMENT NUMBER: 162:370540
TITLE: Design and Optimization of a Series of 1-Sulfonylpyrazolo[4,3-b]pyridines as Selective c-Met Inhibitors
AUTHOR(S): Ma, Yuchi; Sun, Guangqiang; Chen, Danqi; Peng, Xia; Chen, Yue-Lei; Su, Yi; Ji, Yinchun; Liang, Jin; Wang, Xin; Chen, Lin; Ding, Jian; Xiong, Bing; Ai, Jing; Geng, Meiyu; Shen, Jingkang
CORPORATE SOURCE: Department of Medicinal Chemistry, State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 201203, Peop. Rep. China
SOURCE: Journal of Medicinal Chemistry (2015), 58(5), 2513-2529
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/jm502018y
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 162:370540
AB C-Met has emerged as an attractive target for targeted cancer therapy because of its abnormal activation in many cancer cells. To identify high potent and selective c-Met inhibitors, we started with profiling the potency and in vitro metabolic stability of a reported hit 7. By rational design, a novel sulfonylpyrazolo[4,3-b]pyridine 9 with improved DMPK properties was discovered. Further elaboration of π-π stacking interactions and solvent accessible polar moieties led to a series of highly potent and selective type I c-Met inhibitors. On the basis of in vitro and in vivo pharmacol. and pharmacokinetics studies, compound 46 was selected as a preclin. candidate for further anticancer drug development.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 103 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:232900 CAPLUS Full-text
DOCUMENT NUMBER: 163:340057
TITLE: Potent antitumor activity of cabozantinib, a c-MET and VEGFR2 inhibitor, in a colorectal cancer patient-derived tumor explant model
AUTHOR(S): Song, Eun-Kee; Tai, W. M.; Messersmith, Wells A.; Bagby, Stacey; Purkey, Alicia; Quackenbush, Kevin S.; Pitts, Todd M.; Wang, Guoliang; Blatchford, Patrick; Yahn, Rachel; Kaplan, Jeffrey; Tan, Aik Choon; Atreya, Chloe E.; Eckhardt, Gail; Kelley, Robin K.; Venook, Alan; Kwak, Eunice L.; Ryan, David; Arcaroli, John J.
CORPORATE SOURCE: Division of Medical Oncology, University of Colorado Denver and University of Colorado Cancer Center, Aurora, CO, USA
SOURCE: International Journal of Cancer (2015), 136(8), 1967-1975
CODEN: IJCNAW; ISSN: 0020-7136
DIGITAL OBJECT ID: 10.1002/ijc.29225
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Antiangiogenic therapy is commonly used for the treatment of colorectal cancer (CRC). Although patients derive some clin. benefit, treatment resistance inevitably occurs. The MET signaling pathway has been proposed to be a major contributor of resistance to antiangiogenic therapy. MET is upregulated in response to vascular endothelial growth factor pathway inhibition and plays an essential role in tumorigenesis and progression of tumors. In this study, we set out to determine the efficacy of cabozantinib in a preclin. CRC patient-derived tumor xenograft model. We demonstrate potent inhibitory effects on tumor growth in 80% of tumors treated. The greatest antitumor effects were observed in tumors that possess a mutation in the PIK3CA gene. The underlying antitumor mechanisms of cabozantinib consisted of inhibition of angiogenesis and Akt activation and significantly decreased expression of genes involved in the PI3K pathway. These findings support further evaluation of cabozantinib in patients with CRC. PIK3CA mutation as a predictive biomarker of sensitivity is intriguing and warrants further elucidation. A clin. trial of cabozantinib in refractory metastatic CRC is being activated.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

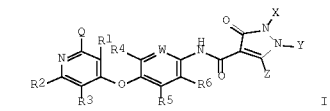
L8 ANSWER 104 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:226654 CAPLUS Full-text
DOCUMENT NUMBER: 163:214328
TITLE: Dual effects of a targeted small-molecule inhibitor (cabozantinib) on immune-mediated killing of tumor cells and immune tumor microenvironment permissiveness when combined with a cancer vaccine
AUTHOR(S): Kwilas, Anna R.; Ardiani, Andressa; Donahue, Renee N.; Aftab, Dana T.; Hodge, James W.
CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Translational Medicine (2014), 12, 294/1-294/15, 15 pp.
CODEN: JTMOBV; ISSN: 1479-5876
DIGITAL OBJECT ID: 10.1186/s12967-014-0294-y
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Growing awareness of the complexity of carcinogenesis has made multimodal therapies for cancer increasingly compelling and relevant. In recent years, immunotherapy has gained acceptance as an active therapeutic approach to cancer treatment, even though cancer is widely considered an immunosuppressive disease. Combining immunotherapy with targeted agents that have immunomodulatory capabilities could significantly improve its efficacy. Methods: We evaluated the ability of cabozantinib, a receptor tyrosine kinase inhibitor, to modulate the immune system in vivo as well as alter the phenotype of tumor cells in vitro in order to determine if this inhibitor could act synergistically with a cancer vaccine. Results: Our studies indicated that cabozantinib altered the phenotype of MC38-CEA murine tumor cells, rendering them more sensitive to immune-mediated killing. Cabozantinib also altered the frequency of immune sub-populations in the periphery as well as in the tumor microenvironment, which generated a more permissive immune environment. When cabozantinib was combined with a poxviral-based cancer vaccine targeting a self-antigen, the combination significantly reduced the function of regulatory T cells and increased cytokine production from effector T cells in response to the antigen. These alterations to the immune landscape, along with direct modification of tumor cells, led to markedly improved antitumor efficacy. Conclusions: These studies support the clin. combination of cabozantinib with immunotherapy for the treatment of cancer.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

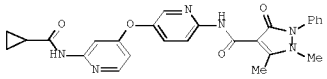
L8 ANSWER 105 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:213358 CAPLUS Full-text
DOCUMENT NUMBER: 162:245319
TITLE: Preparation of pyrazolone compounds that are protein tyrosine kinase activity modulators useful in

treatment of proliferative and other diseases
INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150037280	A1	20150205	US 2013-13945924	20130719
US 8975282	B2	20150310		
US 20150050239	A1	20150219	US 2013-13945925	20130719
US 8969388	B2	20150303		
US 20150141463	A1	20150521	US 2015-14601207	20150120
PRIORITY APPLN. INFO.:			US 2012-61676944 P	20120728
			US 2012-61679416 P	20120803
			US 2013-13945924 A3	20130719

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 162:245319; MARPAT 162:245319
GI


I


II

AB The invention provides novel substituted pyrazolone compds. of formula I [each of R1-R7 is independently H, F, Cl, (C1-C6)alkyl, (C1-C6)haloalkyl, etc.; each of X, Y and Z is independently H, (C1-C6)alkyl, (C6-C10)aryl, etc.; W is CR7 or N; Q as defined in the disclosure], pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The example compound II was prepared in two-step synthesis (procedure shown) was tested in multiple bioassay for activity in modulation of protein tyrosine kinase, pharmacokinetics and metabolic stability, as well as for antiproliferative activity. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns.

in the treatment of hyperproliferative disorders in mammals, especially humans.

L8 ANSWER 106 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:210763 CAPLUS Full-text
DOCUMENT NUMBER: 162:283487
TITLE: Dielectrophoresis methods for determining a property of a plurality of cancer cells to determine drug efficacy and/or resistance
INVENTOR(S): Schmelz, Eva M.; Elvington, Elizabeth S.; Salmanzadeh, Alireza; Sano, Mike; Roberts, Paul C.; Davalos, Rafael V.
PATENT ASSIGNEE(S): Virginia Tech Intellectual Properties, Inc., USA
SOURCE: PCT Int. Appl., 82pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015017729	A1	20150205	WO 2014-US49296	20140731
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20100224493	A1	20100909	US 2010-720406	20100309
US 8968542	B2	20150303		
US 20120085649	A1	20120412	US 2011-13269286	20111007
PRIORITY APPLN. INFO.:			US 2010-720406 A2	20100309
			US 2011-13269286 A2	20111007
			US 2013-61860309 P	20130731
			US 2009-61158553 P	20090309
			US 2009-61252942 P	20091019
			US 2010-61390748 P	20101007

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Provided are dielectrophoresis (DEP) devices and methods that allow cell sorting to identify, isolate, and/or sep. cells of interest based on elec. and phys. properties of the cells. Particularly, provided are systems and methods for manipulating particles suspended in a fluid, e.g., cells, micro- or nano-particles, using their elec. signatures. Such methods can be performed using DEP, iDEP, and/or cDEP (contactless dielectrophoresis, where direct contact between the electrodes and the sample is avoided). Typically, an elec. field is induced in a sample comprising the target particles and/or cells, such as cancer cells, and the spatial distribution of cells is measured to identify one or more characteristics or properties of the cancer cells.

The identified characteristics of the sorted cells can be used to determine drug efficacy and/or resistance with respect to the cells.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 107 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:203193 CAPLUS Full-text
DOCUMENT NUMBER: 162:294277
TITLE: Methods of treating a cancer through targeted disruption of alpha connexin 43-zonula occludens-1 (zo-1) interaction
INVENTOR(S): Gourdie, Robert G.; Sheng, Zhi
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 152pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015017034	A1	20150205	WO 2014-US42528	20140616
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2013-61861686 P	20130802

AB The present disclosure describes methods of treating a cancer based on the targeted disruption of alpha connexin 43-zonula occludens-1 (ZO-1) interaction. The methods may include administering to a subject an effective amount of a composition comprising a peptide with a contiguous sequence of amino acids representing a portion of the C-terminus of an alpha connexin protein or conservative variant thereof, wherein said C-terminus includes the sequence up to the transmembrane domain, optionally in combination with administration of a chemotherapeutic agent. In embodiments, the cancer is glioma and the chemotherapeutic agent is temozolomide. The methods may also include administration of vectors encoding the peptide or host cells comprising the vectors. Also described are compns. for treating a cancer comprising one or more peptides, nucleic acids, vectors, and/or host cells, optionally in combination with a chemotherapeutic agent such as temozolomide.
OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 108 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:173876 CAPLUS Full-text
DOCUMENT NUMBER: 162:320090
TITLE: An LC-MS/MS method for the quantitation of cabozantinib in rat plasma: Application to a pharmacokinetic study
AUTHOR(S): Su, Qinghong; Li, Jian; Ji, Xiwei; Li, Jingyun; Zhou, Tianyan; Lu, Wei; Li, Liang
CORPORATE SOURCE: Department of Pharmaceutics, School of Pharmaceutical Sciences, Peking University Health Science Center, Beijing, 100191, Peop. Rep. China
SOURCE: Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences (2015), 985, 119-123
CODEN: JCBAAI; ISSN: 1570-0232
DIGITAL OBJECT ID: 10.1016/j.jchromb.2015.01.024
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB A simple, rapid and sensitive high-performance liq. chromatog. tandem mass-spectrometric method (LC-MS/MS) for the novel multiple tyrosine kinase inhibitor (TKI) cabozantinib was developed and validated using erlotinib as internal standard (IS). Plasma samples were pre-treated by liquid-liquid extraction with Et acetate. Separation was achieved on a reversed phase C18 column (50 × 2 mm, 5 μm) at ambient temperature using isocratic elution with acetonitrile-water (45:55, volume/volume) containing 5 mM ammonium formate buffer (finally adjusted to apparent pH* = 5.0 with formic acid) at a flow rate of 0.4 mL/min. The analytes were monitored by a triple quadrupole tandem mass spectrometer with electrospray ionization source in the pos. ion mode. Calibration curve was linear (r > 0.99) in a concentration range of 0.5-1000 ng/mL with the lower limit of quantification (LLOQ) of 0.5 ng/mL. Intra- and inter-day accuracy and precision were validated by relative error values (RE) and relative standard deviation values (RSD), resp., which were both lower than the limit of 15%. This method was successfully applied to a pharmacokinetic study of cabozantinib in rats.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 109 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:159139 CAPLUS Full-text
DOCUMENT NUMBER: 162:560084
TITLE: Progress in Discovery of KIF5B-RET Kinase Inhibitors for the Treatment of Non-Small-Cell Lung Cancer
AUTHOR(S): Song, Minsoo
CORPORATE SOURCE: New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Taegu, 701 310, S. Korea
SOURCE: Journal of Medicinal Chemistry (2015), 58(9), 3672-3681
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/jm501464c
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. A new chimeric fusion transcript of KIF5B (the kinesin family 5B gene) and the RET (Rearranged during Transcription) oncogene, KIF5B-RET, was found in 1-2% of lung adenocarcinomas (LADCs) in late 2011. Several related

clin. trials for non-small-cell lung cancer (NSCLC) with KIF5B-RET rearrangements using existing RET inhibitors, such as lenvatinib, vandetanib, sunitinib, ponatinib, cabozantinib, and AUY922, have been swiftly initiated by the discovery of the KIF5B-RET fusion gene. Anti-RET activity and the status of clin. development of these known RET tyrosine kinase inhibitors (TKIs) for KIF5B-RET fusion-pos. NSCLC are discussed. A kinase inhibitor that can target a driver mutation specifically may lead to a superior clin. benefit compared with broad-spectrum kinase inhibitors. In this regard, an anal. of the structure of RET kinase and its complex with known RET inhibitors are also briefly discussed.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 110 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:152289 CAPLUS Full-text

DOCUMENT NUMBER: 162:320143

TITLE: Pharmacokinetics and tissue distribution model of cabozantinib in rat determined by UPLC-MS/MS

AUTHOR(S): Wang, Xianqin; Wang, Shuanghu; Lin, Feiyan; Zhang, Qingwei; Chen, HuiLing; Wang, Xianchuan; Wen, Congcong; Ma, Jianshe; Hu, Lufeng

CORPORATE SOURCE: Analytical and Testing Center, Wenzhou Medical University, Wenzhou, 325035, Peop. Rep. China

SOURCE: Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences (2015), 983-984, 125-131
CODEN: JCBAAI; ISSN: 1570-0232

DIGITAL OBJECT ID: 10.1016/j.jchromb.2015.01.020

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Cabozantinib (XL184) is a novel small mol. inhibitor of receptor tyrosine kinases (RTKs) targeted at mesenchymal-epithelial transition factor (MET). To study the pharmacokinetics and tissue distribution in rat, a specific ultra-performance liquid chromatog.-tandem mass spectrometry (UPLC-MS/MS) method was developed with midazolam as internal standard The calibration curves in plasma and tissues were linear in the range of 5-5000 ng/mL (R2 > 0.99). The recoveries were better than 80.4% and matrix effects ranged from 96.9% to 105.1%. Then, the developed UPLC-MS/MS method was applied to determine the concentration of XL184 in blood and tissues. The pharmacokinetics of four different dosages (iv 5, 10 mg/kg and ig 15, 30 mg/kg) revealed that XL184 was eliminated slowly, the t1/2 was longer than 10 h and the absolute bioavailability was 25.6±8.3%. The concentration distribution of XL184 in tissues was liver > lung > kidney > spleen > heart. Based on the concentration-time of XL184 in tissues, a BP-ANN distribution model was developed with good performance, and can be used to predict the concentration of XL184 in tissues.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 111 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:142298 CAPLUS Full-text

DOCUMENT NUMBER: 163:360237

TITLE: QTc interval prolongation with vascular endothelial growth factor receptor tyrosine kinase inhibitors

AUTHOR(S): Ghatalia, P.; Je, Y.; Kaymakcalan, M. D.; Sonpavde, G.; Choueiri, T. K.

CORPORATE SOURCE: Department of Internal Medicine, University of Alabama at Birmingham (UAB), Birmingham, AL, USA

SOURCE: British Journal of Cancer (2015), 112(2), 296-305
CODEN: BJCAAI; ISSN: 0007-0920

DIGITAL OBJECT ID: 10.1038/bjc.2014.564

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Background: Multi-targeted vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) are known to cause cardiac toxicity, but the relative risk (RR) of QTc interval prolongation and serious arrhythmias associated with them are not reported. Methods: We conducted a trial-level meta-anal. of randomized phase II and III trials comparing arms with and without a US Food and Drug Administration-approved VEGFR TKI (sunitinib, sorafenib, pazopanib, axitinib, vandetanib, cabozantinib, ponatinib and regorafenib). A total of 6548 patients from 18 trials were selected. Statistical analyses were conducted to calculate the summary incidence, RR and 95% CIs. Results: The RR for all-grade and high-grade QTc prolongation for the TKI vs no TKI arms was 8.66 (95% CI 4.92-15.2, P<0.001) and 2.69 (95% CI 1.33-5.44, P=0.006), resp., with most of the events being asymptomatic QTc prolongation. Resp., 4.4% and 0.83% of patients exposed to VEGFR TKI had all-grade and high-grade QTc prolongation. On subgroup anal., only sunitinib and vandetanib were associated with a statistically significant risk of QTc prolongation, with higher doses of vandetanib associated with a greater risk. The rate of serious arrhythmias including torsades de pointes did not seem to be higher with high-grade QTc prolongation. The risk of QTc prolongation was independent of the duration of therapy. Conclusions: In the largest study to date, we show that VEGFR TKI can be associated with QTc prolongation. Although most cases were of low clin. significance, it is unclear whether the same applies to patients treated off clin. trials.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 112 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:138904 CAPLUS Full-text

DOCUMENT NUMBER: 163:511501

TITLE: Current role of cabozantinib in metastatic castration-resistant prostate cancer

AUTHOR(S): Fay, Andre P.; Albiges, Laurence; Bellmunt, Joaquim

CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02215, USA

SOURCE: Expert Review of Anticancer Therapy (2015), 15(2), 151-156
CODEN: ERATBJ; ISSN: 1473-7140

DIGITAL OBJECT ID: 10.1586/14737140.2015.1003047

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB Over 80% of men with castration-resistant prostate cancer have bone metastases. This condition can dramatically impact quality of life and is associated with short-term survival. Consequently, the development of bone-targeted therapies is a relevant topic on prostate cancer management. Hepatocyte growth factor receptor and vascular endothelial growth factor signaling pathways have been identified to play a role in prostate cancer progression and bone metastasis and are potential targets for therapeutic intervention. Early-phase studies have shown encouraging responses in bone metastases and pain control with cabozantinib, a multi-tyrosine kinase inhibitor targeting hepatocyte growth factor receptor and vascular endothelial growth factor receptor. Despite striking responses seen in some patients, preliminary results from a pivotal Phase III study have failed to produce survival benefit. This review encompasses preclin. and clin. data of cabozantinib in metastatic castration-resistant prostate cancer highlighting future research options for this agent.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 113 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:104550 CAPLUS Full-text

DOCUMENT NUMBER: 162:265265

TITLE: Thyroid carcinoma, version 2.2014: featured updates to the NCCN guidelines

AUTHOR(S): Tutele, R. Michael; Haddad, Robert I.; Ball, Douglas W.; Byrd, David; Dickson, Paxton; Duh, Quan-Yang; Ehya, Hormoz; Haymart, Megan; Hoh, Carl; Hunt, Jason P.; Iagaru, Andrei; Kandeel, Fouad; Kopp, Peter; Lamonica, Dominick M.; Lydiatt, William M.; McCaffrey, Judith; Moley, Jeffrey F.; Parks, Lee; Raeburn, Christopher D.; Ridge, John A.; Ringel, Matthew D.; Scheri, Randall P.; Shah, Jatin P.; Sherman, Steven I.; Sturgeon, Cord; Waguespack, Steven G.; Wang, Thomas N.; Wirth, Lori J.; Hoffmann, Karin G.; Hughes, Miranda

CORPORATE SOURCE: Memorial Sloan Kettering Cancer Center, USA

SOURCE: Journal of the National Comprehensive Cancer Network (2014), 12(12), 1671-1680
CODEN: JNCCA4; ISSN: 1540-1405

PUBLISHER: Harborside Press

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. These NCCN Guidelines Insights focus on some of the major updates to the 2014 NCCN Guidelines for Thyroid Carcinoma. Kinase inhibitor therapy may be used to treat thyroid carcinoma that is symptomatic and/or progressive and not amenable to treatment with radioactive iodine. Sorafenib may be considered for select patients with metastatic differentiated thyroid carcinoma, whereas vandetanib or cabozantinib may be recommended for select patients with metastatic medullary thyroid carcinoma. Other kinase inhibitors may be considered for select patients with either type of thyroid carcinoma. A new section on "Principles of Kinase Inhibitor Therapy in Advanced Thyroid Cancer" was added to the NCCN Guidelines to assist with using these novel targeted agents.

REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 114 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:100945 CAPLUS Full-text

DOCUMENT NUMBER: 163:480691

TITLE: Targeting Angiogenesis in Thyroid Cancer

AUTHOR(S): Lkhoyaali, S.; Benhmida, S.; Aitelhaj, M.; Layachi, M.; Abahssain, H.; Ismaili, H. N.; Errihani, H.

CORPORATE SOURCE: Department of Medical Oncology, Mohammed VI University Hospital, Marrakech, Morocco

SOURCE: Current Angiogenesis (2014), 3(2), 107-112
CODEN: CAUNBS; ISSN: 2211-5528

DIGITAL OBJECT ID: 10.2174/22115528026661407161705 21

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. Thyroid cancers are characterized by a good prognosis but 10 to 15% of patients progress and become refractory to current therapies. Systemic treatment based on chemotherapy in these settings has shown limited efficacy, with response rates not exceeding 25%. At progression, differentiated thyroid cancer is characterized by a high level of expression of vascular endothelial growth factor (VEGF). This high expression of VEGF is associated with an aggressive tumor behavior and a poor clin. outcome.; We will review the recent advances in targeting angiogenesis in the treatment of recurrent and metastatic thyroid carcinoma.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 115 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:100878 CAPLUS Full-text

DOCUMENT NUMBER: 163:292268

TITLE: Should the Incorporation of Structural Alerts be Restricted in Drug Design? An Analysis of Structure-Toxicity Trends with Aniline-Based Drugs

AUTHOR(S): Kalgutkar, A. S.

CORPORATE SOURCE: Pharmacokinetics, Dynamics and Metabolism Department-New Chemical Entities, Pfizer Worldwide Research and Development, Cambridge, MA, 02139, USA

SOURCE: Current Medicinal Chemistry (2015), 22(4), 438-464
CODEN: CMCHE7; ISSN: 0929-8673

DIGITAL OBJECT ID: 10.2174/0929867321666141112222118

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Certain idiosyncratic adverse drug reactions (IADRs) can be triggered by electrophilic protein-reactive metabolites that are formed in the process of drug metabolism While methodologies (e.g., structural alert concept in drug design, glutathione (GSH) trapping, and protein covalent binding) for examining reactive metabolite (RM) formation are available, predicting the IADR potential applying these parameters remains a significant challenge. The present work examines toxicity trends associated with the aniline structural alert in the top 200 prescribed drugs of 2011 and recently approved (2009-2013) small mol. drugs, in relation with 30 aniline-based drugs withdrawn from com. use or associated with a black box warning for IADRs. The aniline sub-structure was found in several drugs from the toxic, mostprescribed, and recently approved category. RMs resulting from the bioactivation of the aniline alert was also noted in the three categories chosen for comparison. A major discriminator between the toxic drugs and the majority of drugs in the most-prescribed list, however, was the daily dose - drugs most frequented associated with IADRs were the ones with higher daily doses (exceeding hundreds of milligrams). A greater tolerance for

IADRs was also noted with certain drugs intended to treat rare, unmet medical needs (e.g., cancer). Overall, the anal. suggests that optimization of pharmacol. potency and pharmacokinetics that would lead to a lower daily dose, and therefore, a lower body burden of parent drug/metabolites, should be taken into consideration in drug discovery.
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 116 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:28803 CAPLUS Full-text
DOCUMENT NUMBER: 162:393504
TITLE: Development of therapeutic drug for castration-resistant prostate cancer
AUTHOR(S): Zhou, Xiang-jun; Zhang, Jie
CORPORATE SOURCE: Department of Urology, Renmin Hospital of Wuhan University, Wuhan, 430060, Peop. Rep. China
SOURCE: Shijie Linchuang Yaowu (2014), 35(2), 74-79
CODEN: SLYHAA; ISSN: 1672-9188
PUBLISHER: Shijie Linchuang Yaowu Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 28 ref. is given on development of therapeutic drug for castration-resistant prostate cancer. The treatment of castration-resistant prostate cancer (CRPC) is still a challenge, as there are few effective therapies to lengthen life of patients. Many novel approaches with extended survival benefit currently in development yielded promising results for patients. This review describes the therapeutic drug for CRPC. The therapeutic drug comprises antiandrogen drug such as abiraterone, enzalutamide, orteronel, galeterone; cytotoxic chemotherapy such as docetaxel, cabazitaxel; immunotherapy such as sipuleucel-T, rilimogene galvacirepvec, ipilimumab; targeting therapy including endothelin-A receptor antagonist such as atrasentan, zibotentan, tyrosine kinase inhibitor such as dasatinib and sorafenib, cabozantinib, anti-angiogenesis agent such as bevacizumab, aflibercept, tasquinimod, clusterin inhibitor such as custirsen, and radium chloride.

L8 ANSWER 117 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:26950 CAPLUS Full-text
DOCUMENT NUMBER: 163:325796
TITLE: Cabozantinib Overcomes Crizotinib Resistance in ROS1 Fusion-Positive Cancer
AUTHOR(S): Katayama, Ryohei; Kobayashi, Yuka; Friboulet, Luc; Lockerman, Elizabeth L.; Koike, Sumie; Shaw, Alice T.; Engelman, Jeffrey A.; Fujita, Naoya
CORPORATE SOURCE: Division of Experimental Chemotherapy, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo, Japan
SOURCE: Clinical Cancer Research (2015), 21(1), 166-174
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-14-1385
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: ROS1 rearrangement leads to constitutive ROS1 activation with potent transforming activity. In an ongoing phase I trial, the ALK tyrosine kinase inhibitor (TKI) crizotinib shows remarkable initial responses in patients with non-small cell lung cancer (NSCLC) harboring ROS1 fusions; however, cancers eventually develop crizotinib resistance due to acquired mutations such as G2032R in ROS1. Thus, understanding the crizotinib-resistance mechanisms in ROS1-rearranged NSCLC and identification of therapeutic strategies to overcome the resistance are required. Exptl. Design: The sensitivity of CD74-ROS1-transformed Ba/F3 cells to multiple ALK inhibitors was examined Acquired ROS1 inhibitor-resistant mutations in CD74-ROS1 fusion were screened by N-ethyl-N-nitrosourea mutagenesis with Ba/F3 cells. To overcome the resistance mutation, we performed high-throughput drug screening with small-mol. inhibitors and anticancer drugs used in clin. practice or being currently tested in clin. trials. The effect of the identified drug was assessed in the CD74-ROS1-mutant Ba/F3 cells and crizotinib-resistant patient-derived cancer cells (MGH047) harboring G2032R-mutated CD74-ROS1. Results: We identified multiple novel crizotinib-resistance mutations in the ROS1 kinase domain, including the G2032R mutation. As the result of high-throughput drug screening, we found that the cMET/RET/VEGFR inhibitor cabozantinib (XL184) effectively inhibited the survival of CD74-ROS1 wild-type (WT) and resistant mutants harboring Ba/F3 and MGH047 cells. Furthermore, cabozantinib could overcome all the resistance by all newly identified secondary mutations. Conclusions: We developed a comprehensive model of acquired resistance to ROS1 inhibitors in NSCLC with ROS1 rearrangement and identified cabozantinib as a therapeutic strategy to overcome the resistance. Clin Cancer Res; 21(1); 166-74. cpr2014 AACR.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L8 ANSWER 118 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:21816 CAPLUS Full-text
DOCUMENT NUMBER: 162:172165
TITLE: A Novel Multiple Tyrosine-kinase Targeted Agent to Explore the Future Perspectives of Anti-Angiogenic Therapy for the Treatment of Multiple Solid Tumors: Cabozantinib
AUTHOR(S): Roy, Subhajit; Narang, Bawneet K.; Rastogi, Shiva K.; Rawal, Ravindra K.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Indo-Soviet Friendship College of Pharmacy, Punjab, 142 001, India
SOURCE: Anti-Cancer Agents in Medicinal Chemistry (2015), 15(1), 37-47
CODEN: AAMCE4; ISSN: 1871-5206
DIGITAL OBJECT ID: 10.2174/1871520614666140902153840
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The process of angiogenesis involves the formation of new blood vessels from pre-existing vasculature by the over expression of certain factors leading to the growth and development of all solid tumor types. Hepatocyte growth factor receptor abbreviated as c-Met and vascular endothelial growth factor abbreviated as VEGF are some of the factors responsible for the induction in tumor growth and development. Recently a number of analogs associated with these receptors are under study. US FDA on Nov. 29, 2012 approved a drug named cabozantinib formerly known as XL184 which is being marketed under the trade name of Cometriq for the treatment of Medullary Thyroid Cancer (MTC). Designing of the drug has been done in such a fashion that it can inhibit both VEGFR2 and c-Met simultaneously without over expressing any of the factors leading to the inhibition of angiogenesis. The drug is still under study for the evaluation of its efficacy in cases of many other solid tumor types including breast cancer, castration resistant prostate cancer (CRPC), renal cell carcinoma (RCC), hepatocellular carcinoma (HCC), gastric or gastroesophageal junction cancer, melanoma, small cell lung cancer (SCLC), ovarian cancer and primary peritoneal or fallopian tube carcinoma. This review article consists of preclin. and clin. data of cabozantinib and its efficacy and safety towards various types of solid tumors.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 119 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2163755 CAPLUS Full-text
DOCUMENT NUMBER: 162:309823
TITLE: Antiangiogenic drugs for castration-resistant prostate cancer: Recent findings
AUTHOR(S): Huang, Dao-guang; Gan, Wei-dong
CORPORATE SOURCE: Department of Urology, Nanjing Drum Tower Hospital, the Affiliated Hospital, School of Medicine, Nanjing University, Nanjing, Jiangsu Province, 210008, Peop. Rep. China
SOURCE: Zhonghua Nankexue Zazhi (2014), 20(10), 932-937
CODEN: ZNZHB5
DIGITAL OBJECT ID: 10.13263/j.cnki.nja.2014.10.014
PUBLISHER: Zhonghua Nankexue Zazhi Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. In the recent years, treatment options for castration-resistant prostate cancer had evolved from conventional antiandrogens and chemotherapy to novel androgen receptor signaling inhibitors, a new generation of taxanes, and immunotherapy. Randomized clin. trials had shown that docetaxel, cabazitaxel, enzalutamide, abiraterone acetate, radium-223, and sipuleucel-T could improve the overall survival of the patients with androgen-independent prostate cancer. However, drug resistance was inevitable and androgen-independent prostate cancer remained a major clin. burden, which urgently called for novel therapeutic options for the improvement of the patients' survival and quality of life. Angiogenesis played a central role in the formation and progression of prostate cancer, and the anti angiogenic targeted therapy was shown in many clin. trials to be an effective therapeutic supplement for advanced prostate cancer beyond surgery and endocrine treatment. The recent findings of antiangiogenic mugs for castration-resistant prostate cancer was reviewed.

L8 ANSWER 120 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2157654 CAPLUS Full-text
DOCUMENT NUMBER: 162:99756
TITLE: New drug cabozantinib malate for medullary thyroid cancer treatment
AUTHOR(S): Lu, Juanli; Liu, Yang; Sun, Huiping
CORPORATE SOURCE: Department of Pharmacy, General Hospital of Armed Police Forces, Beijing, 100039, Peop. Rep. China
SOURCE: Zhongguo Linchuang Yaoxue Zazhi (2014), 23(1), 58-62
CODEN: ZLYZA5; ISSN: 1007-4406
PUBLISHER: Zhongguo Linchuang Yaoxue Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 21 refs. to introduce the new drug cabozantinib malate for medullary thyroid cancer treatment, including its basic properties, action mechanism, pharmacokinetic parameters, clin. trial, drug interactions, adverse reactions, and comparison on therapeutic effect with vandetanib.

L8 ANSWER 121 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2146461 CAPLUS Full-text
DOCUMENT NUMBER: 162:114047
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 12pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
US 20140378401	A1	20141225	US 2013-14132822	20131218
WO 2014204791	A1	20141224	WO 2014-US42221	20140613

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-13924189 A2 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The ophthalmic drug delivery vehicles provide comfort and compliance; drug solubility, residence time and permeability; and reduce side effects. In addition, the delivery vehicle can be slightly modified to provide an artificial tear formulation. The ophthalmic drug delivery vehicles include 2-12% nonionic surfactant, one or more non-Newtonian high blend viscosity enhancing, non-gelling agents and 0.1-0.90% sodium chloride. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.

L8 ANSWER 122 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:2146420 CAPLUS Full-text
DOCUMENT NUMBER: 162:144424
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 924,189.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140378401	A1	20141225	US 2013-14132822	20131218
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
WO 2014204791	A1	20141224	WO 2014-US42221	20140613

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-13924189 A2 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The ophthalmic drug delivery vehicles provide comfort and compliance; drug solubility, residence time and permeability; and reduce side effects. In addition, the delivery vehicle can be slightly modified to provide an artificial tear formulation. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.

L8 ANSWER 123 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2145974 CAPLUS Full-text
DOCUMENT NUMBER: 163:58679
TITLE: Cabozantinib in chemotherapy-pretreated metastatic castration-resistant prostate cancer: results of a phase II nonrandomized expansion study
AUTHOR(S): Smith, Matthew R.; Sweeney, Christopher J.; Corn, Paul G.; Rathkopf, Dana E.; Smith, David C.; Hussain, Maha; George, Daniel J.; Higano, Celestia S.; Harzstark, Andrea L.; Sartor, A. Oliver; Vogelzang, Nicholas J.; Gordon, Michael S.; de Bono, Johann S.; Haas, Naomi B.; Logothetis, Christopher J.; Elfiky, Aymen; Scheffold, Christian; Laird, A. Douglas; Schimmoller, Frauke; Basch, Ethan M.; Scher, Howard I.
CORPORATE SOURCE: USA
SOURCE: Journal of Clinical Oncology (2014), 32(30), 3391-3399
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2013.54.5954
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose Cabozantinib (XL184), an oral inhibitor of multiple receptor tyrosine kinases such as MET and VEGFR2, was evaluated in a phase II nonrandomized expansion study in castration-resistant prostate cancer (CRPC). Patients and Methods Patients received open-label cabozantinib at daily starting doses of 100 mg or 40 mg until disease progression or unacceptable toxicity. The primary end point was bone scan response, defined as ≥ 30% reduction in bone scan lesion area. Other efficacy end points included overall survival, pain, analgesic use, and biomarkers. Results One hundred forty-four patients sequentially enrolled in either a 100-mg (n = 93) or 40-mg (n = 51) study cohort. Ninety-one patients (63%) had a bone scan response, often by week 6. Treatment resulted in clin. meaningful pain relief (57% of patients) and reduction or discontinuation of narcotic analgesics (55% of patients), as well as improvements in measurable soft tissue disease, circulating tumor cells, and bone biomarkers. Improvements in each of these outcomes were observed in both cohorts: bone scan response in 73% and 45%, resp.; redns. in measurable soft tissue disease in 80% and 79%, resp. Median overall survival was 10.8 mo for the entire population. Most common grade 3 or 4 adverse events were fatigue (22%) and hypertension (14%). Fewer dose redns. because of toxicity were required in the 40-mg group. Conclusion The evidence suggests that cabozantinib has clin. meaningful activity in CRPC. Cabozantinib resulted in improvements in bone scans, pain, analgesic use, measurable soft tissue disease, circulating tumor cells, and bone biomarkers. Taken together, these phase II observations warrant further development of cabozantinib in prostate cancer.
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 124 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2128221 CAPLUS Full-text
DOCUMENT NUMBER: 162:127174
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: PCT Int. Appl., 57pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014204791	A1	20141224	WO 2014-US42221	20140613

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
US 20140378401	A1	20141225	US 2013-14132822	20131218

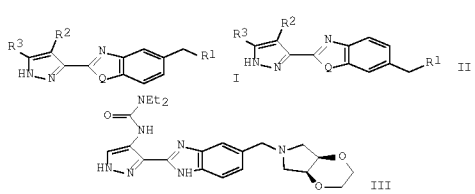
PRIORITY APPLN. INFO.: US 2013-13924189 A 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The ophthalmic drug delivery vehicles include 1-15% nonionic surfactant, one or more non-Newtonian high blend viscosity enhancing, non-gelling agents and 0.025-0.90% sodium chloride. Particularly, formulations that have the non-Newtonian characteristics at 37° of creating a viscosity increase in ratio of 3:1 within 1-2 s at the low shear force between blinks and drops within the fraction of a second to the high shear force of each blink, which on dilution maintain a viscosity of ≥10 cPs during each blink and which do not cause excessive stinging or discomfort, are disclosed. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 125 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2126341 CAPLUS Full-text
DOCUMENT NUMBER: 162:148367
TITLE: Medullary thyroid cancer in the era of tyrosine kinase inhibitors: to treat or not to treat-and with which drug-those are the questions
AUTHOR(S): Cabanillas, Maria E.; Hu, Mimi I.; Jimenez, Camilo
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2014), 99(12), 4390-4396
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2014-2811
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Context: Medullary thyroid cancer (MTC) is a rare form of thyroid cancer comprising approx. 4% of all thyroid cancers. The majority of patients have a relatively good prognosis; however, a subgroup of patients will require systemic therapy. Large phase III randomized trials led to the approval of two drugs-vandetanib and cabozantinib-for progressive or symptomatic MTC. The decision regarding which drug to initiate first is not entirely clear and is a common concern amongst treating physicians. Evidence Acquisition and Synthesis: A review of the literature in English was conducted, and data were summarized and integrated into a decision matrix. Conclusions: The decision regarding which drug to initiate first for progressive MTC should be based on a careful review of the medical history, phys. examination findings, medication list, ECG, laboratory results, and tumor characteristics. It is necessary to consider the relative contraindications when choosing which drug to initiate first.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 126 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2105568 CAPLUS Full-text
DOCUMENT NUMBER: 162:137867
TITLE: Substituted pyrazole-type deriv. as aurora kinase inhibitor useful in treatment of various diseases and its preparation
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Zhang, Jiquan; Li, Yanping; Yang, Xueqi; Zhang, Jiancun; Zheng, Changchun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 96pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104211692	A	20141217	CN 2014-10245663	20140604

PRIORITY APPLN. INFO.: CN 2013-10217864 A 20130604
CN 2014-10109643 A 20140321
OTHER SOURCE(S): MARPAT 162:137867
GI

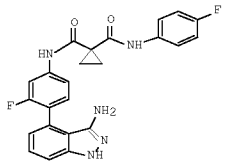


I II III

AB The invention relates to substituted pyrazole-type deriv. of formula I and II as aurora kinase inhibitor useful in treatment of various diseases and their preparation Compds. I and II, wherein Q is NH or O; R1 is one of morpholinyl, C5-12 bridged bicyclic group, etc.; R2 is R4R4aN-CO-NH, R5R5aCHCONH, or R6OCONH; and R3 is H or C1-6 alkyl; R4 is H, C1-6 alkyl, C3-6 cycloalkyl, etc.; R4a is C1-6 alkyl, C3-6 cycloalkyl, C6-10 aryl, etc.; R5 and R5a are independently H, C3-6 cycloalkyl, etc.; R6 is C1-6 alkyl or C6-10 aryl; their stereoisomer, geometric isomer, tautomer, nitrogen oxide,

hydrate, solvate, metabolite, ester, pharmaceutically acceptable salt or prodrug are claimed. Compound III was prepared by multi-step procedure (procedure given). The invention compds. were evaluated for their aurora kinase inhibitor activity. From assay, it was determined that III exhibited the IC50 value of 2.16 nM against aurora A kinase .

L8 ANSWER 127 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2087478 CAPLUS Full-text
DOCUMENT NUMBER: 162:183726
TITLE: Discovery and SAR study of c-Met kinase inhibitors bearing an 3-amino-benzo[d]isoxazole or 3-aminoindazole scaffold
AUTHOR(S): Jiang, Xiaolong; Liu, Hongyan; Song, Zilan; Peng, Xia; Ji, Yinchun; Yao, Qizheng; Geng, Meiyu; Ai, Jing; Zhang, Ao
CORPORATE SOURCE: Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry (2015), 23(3), 564-578
CODEN: BMECEP; ISSN: 0968-0896
DIGITAL OBJECT ID: 10.1016/j.bmc.2014.12.002
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 162:183726
GI



I

AB A series of 3-amino-benzo[d]isoxazole-/3-aminoindazole-based compds. were designed, synthesized and pharmacol. evaluated as tyrosine kinase c-Met inhibitors. The SAR study was conducted leading to identification of nine compds. with IC50s less than 10 nM against c-Met. Compound I stood out as the most potent c-Met inhibitor displaying potent inhibitory effects both at enzymic (IC50 = 1.8 nM) and cellular (IC50 = 0.18 μM on EBC-1 cells) levels. In addition, I had a relatively good selectivity compared to a panel of the inhouse 14 RTKs.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 128 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2072471 CAPLUS Full-text
DOCUMENT NUMBER: 163:156450
TITLE: Adaptive Responses to Dasatinib-Treated Lung Squamous Cell Cancer Cells Harboring DDR2 Mutations
AUTHOR(S): Bai, Yun; Kim, Jae-Young; Watters, January M.; Fang, Bin; Kinose, Fumi; Song, Lanxi; Koomen, John M.; Teer, Jamie K.; Fisher, Kate; Chen, Yian Ann; Rix, Uwe; Haura, Eric B.
CORPORATE SOURCE: Department of Thoracic Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA
SOURCE: Cancer Research (2014), 74(24), 7217-7228
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-14-0505
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study of cancer cell signaling perturbed by the tyrosine kinase inhibitor dasatinib suggests rational combinations to improve the efficacy of this drug in the subset of lung cancers where it is used. DDR2 mutations occur in approx. 4% of lung squamous cell cancer (SCC) where the tyrosine kinase inhibitor dasatinib has emerged as a new therapeutic option. We found that ERK and AKT phosphorylation was weakly inhibited by dasatinib in DDR2-mutant lung SCC cells, suggesting that dasatinib inhibits survival signals distinct from other oncogenic receptor tyrosine kinases (RTK) and/or compensatory signals exist that dampen dasatinib activity. To gain better insight into dasatinib's action in these cells, we assessed altered global tyrosine phosphorylation (pY) after dasatinib exposure using a mass spectrometry-based quant. phosphoproteomics approach. Overlaying protein-protein interaction relationships upon this dasatinib-regulated pY network revealed decreased phosphorylation of Src family kinases and their targets. Conversely, dasatinib enhanced tyrosine phosphorylation in a panel of RTK and their signaling adaptor complexes, including EGFR, MET/GAB1, and IGF1R/IRS2, implicating a RTK-driven adaptive response associated with dasatinib. To address the significance of this observation, these results were further integrated with results from a small-mol. chemical library screen. We found that dasatinib combined with MET and insulin-like growth factor receptor (IGF1R) inhibitors had a synergistic effect, and ligand stimulation of EGFR and MET rescued DDR2-mutant lung SCC cells from dasatinib-induced loss of cell viability. Importantly, we observed high levels of tyrosine-phosphorylated EGFR and MET in a panel of human lung SCC tissues harboring DDR2 mutations. Our results highlight potential RTK-driven adaptive-resistant mechanisms upon DDR2 targeting, and they suggest new, rationale cotargeting strategies for DDR2-mutant lung SCC. Cancer Res; 74(24); 7217-28. cpr2014 AACR.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 129 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2068289 CAPLUS Full-text
DOCUMENT NUMBER: 162:228992
TITLE: Anti-angiogenic agents in metastatic NSCLC
AUTHOR(S): Das, Millie; Wakelee, Heather
CORPORATE SOURCE: VA Palo Alto Heath Care System, Palo Alto, CA, USA
SOURCE: Lung Cancer (4th Edition) (2014), 527-540. Editor(s): Roth, Jack A.; Hong, Waun Ki; Komaki, Ritsuko U.
Wiley-Blackwell: Hoboken, N. J.
CODEN: 69THV4; ISBN: 978-1-118-46874-6
DIGITAL OBJECT ID: 10.1002/9781118468791.ch34
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB This review highlights the role of anti-angiogenic agents in metastatic non-small cell lung cancer (NSCLC). Anti-angiogenic agents being studied in NSCLC include monoclonal antibodies against VEGF, tyrosine kinase inhibitors directed at VEGF receptors, as well as vascular disrupting agents which do not involve inhibition of VEGF.
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

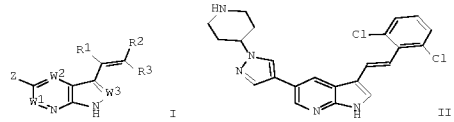
L8 ANSWER 130 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2037552 CAPLUS Full-text
DOCUMENT NUMBER: 163:187272
TITLE: RET-Rearranged Lung Adenocarcinomas with Lymphangitic Spread, Psammoma Bodies, and Clinical Responses to Cabozantinib
AUTHOR(S): Mukhopadhyay, Sanjay; Pennell, Nathan A.; Ali, Siraj M.; Ross, Jeffrey S.; Ma, Patrick C.; Velcheti, Vamsidhar
CORPORATE SOURCE: Solid Tumor Oncology, and Translational Hematology and Oncology Research, Cleveland Clinic, Cleveland, OH, 9500, USA
SOURCE: Journal of Thoracic Oncology (2014), 9(11), 1714-1719
CODEN: JTOOB7; ISSN: 1556-0864
DIGITAL OBJECT ID: 10.1097/JTO.0000000000000323
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Oncogenic rearrangements of the RET gene have recently been described in 1% to 2% of lung adenocarcinomas. We report five cases of RET-rearranged lung adenocarcinoma with an unusual constellation of clin. and histol. features that has not previously been described in tumors with this genomic alteration. The age at diagnosis of the five patients (4F, 1M) ranged from 44 to 77 years. All were never-smokers. Radiol., four tumors showed lymphangitic spread within the lungs at presentation; three of these had multiple bilateral lung nodules. Histol. showed psammoma bodies within the tumor in four of five cases. Mol. testing for activating EGFR mutations by standard genotyping and ALK expression by immunohistochem. was neg. in all cases. Addnl. mol. anal. was prompted by the clin. profile in that all five patients were never-smokers with metastatic, relapsed, and/or refractory disease; and also by unusual histol. findings in two cases. Comprehensive genomic profiling performed by means of a clin. grade cancer gene panel next-generation sequencing assay demonstrated a KIF5B-RET fusion in three; and fluorescence in-situ hybridization documented a RET rearrangement in two. Three of the patients were treated with the RET inhibitor cabozantinib. By Response Evaluation Criteria In Solid Tumors (RECIST) criteria, two had a confirmed partial response (at 6 wk and 4 wk) and one had stable disease. Our findings suggest that the combination of lymphangitic spread and psammoma bodies may be characteristic of a subset of advanced stage RET-rearranged lung adenocarcinomas. These findings should prompt addnl. mol. testing for RET translocations, particularly in never-smokers with EGFR- and ALK-neg. lung adenocarcinoma.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 131 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2015786 CAPLUS Full-text
DOCUMENT NUMBER: 162:37339
TITLE: Preparation of alkenyl-pyrrolo[2,3-b]pyridine compounds as protein tyrosine kinase modulators useful for treatment of proliferative disorders
INVENTOR(S): Xi, Ning; Li, Xiaobo
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 117pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014193647	A2	20141204	WO 2014-US37856	20140513
WO 2014193647	A3	20150129		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61827599 P 20130526
OTHER SOURCE(S): CASREACT 162:37339; MARPAT 162:37339
GI



I II

AB The invention provides substituted alkenyl pyrrolo[2,3-b]pyridine compds. of formula I, pharmaceutical acceptable salts and formulations thereof as protein tyrosine kinase modulators capable of modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion

and, thus useful for the treatment of proliferative disorders. I [wherein W1, W2, and W3 are independently N or (un)substituted C; R1, R2, and R3 are independently H, CN, (hetero)aryl, etc.; Z is (un)substituted 5- to 6-membered heteroaryl] or a stereoisomer, geometric isomer, tautomer, N-oxide, hydrate, solvate, metabolite, prodrug, or pharmaceutically acceptable salt thereof is claimed. (E)-II was prepared in a multistep process (preparation given). I were evaluated for kinase inhibitor activity using radiochem. anal. and [γ33P-ATP]. From this assay it was determined that (E)-II demonstrated IC50 values of 44 nM and 8 nM for ALK kinase and c-Met kinase, resp.

L8 ANSWER 132 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1955485 CAPLUS Full-text
DOCUMENT NUMBER: 164:33863
TITLE: Novel therapies for thyroid cancer
AUTHOR(S): Krajewska, Jolanta; Jarzab, Barbara
CORPORATE SOURCE: Nuclear Medicine and Endocrine Oncology Department, Gliwice Branch, M.Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Pol.
SOURCE: Expert Opinion on Pharmacotherapy (2014), 15(18), 2641-2652
CODEN: EOPHF7; ISSN: 1465-6566
DIGITAL OBJECT ID: 10.1517/14656566.2014.969240
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Introduction: New therapeutic options for both differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC) have opened up during the past few years, as the key role of tyrosine kinases in the pathogenesis of thyroid carcinoma has been proved. Recently, two tyrosine kinase inhibitors (TKIs) targeting VEGFR vandetanib (Caprelsa) and cabozantinib (Cometriq) have been approved for advanced MTC, whereas, sorafenib (Nexavar) has been accepted to treat late-stage of DTC. Their efficacy was demonstrated in Phase III studies, compared to placebo; each of them significantly prolonged the progression-free survival. Areas covered: Common adverse reactions related to VEGFR blockade are hypertension, proteinuria, impaired wound healing, hemorrhage and thrombosis, and congestive heart failure. Fatigue, different gastrointestinal disturbances with diarrhea, appetite decrease and weight loss are observed in the majority of patients. Another frequent TKI side effect is TSH increase secondary to inhibition of MCT8-dependent T3 and T4 uptake in pituitary. Expert opinion: So far, no direct comparison of both treatment outcomes and toxicity between particular drugs has been carried out. The evidence-based medicine guidelines are necessary to precisely indicate what drug to use: more effective or less toxic and when to start the treatment.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 133 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1943046 CAPLUS Full-text
DOCUMENT NUMBER: 161:714155
TITLE: Method for the prognosis and treatment of renal cell carcinoma metastasis
INVENTOR(S): Gomis, Roger; Lacey, David L.
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014184679	A2	20141120	WO 2014-IB1715	20140313
WO 2014184679	A3	20150319		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61801642 P 20130315
AB The present invention relates to a method for the prognosis of bone metastasis in renal cell carcinoma which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering renal cell carcinoma. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of renal cell carcinoma metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering renal cell carcinoma and for classifying a subject from renal cell carcinoma into a cohort.

L8 ANSWER 134 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1940485 CAPLUS Full-text
DOCUMENT NUMBER: 161:765704
TITLE: Short-chain phosphatidylcholine lipids and their use in therapy
INVENTOR(S): Van Hell, Albert; Verheij, Marcel; Marrink, Siewert Jan; Koning, Gerben
PATENT ASSIGNEE(S): Stichting Het Nederlands Kanker Instituut - Antoni Van Leeuwenhoek Ziekenhuis, Neth.; Erasmus University Medical Centre; Rijksuniversiteit Groningen
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014184726	A2	20141120	WO 2014-IB61379	20140512
WO 2014184726	A3	20150219		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2013-8753 A 20130515
OTHER SOURCE(S): MARPAT 161:765704
AB The invention pertains generally to the field of therapy and medical treatment, and more specifically to certain compds. of the following formula (for convenience, collectively referred to herein as "short-chain phosphatidylcholine lipids" and "SCPC lipids"), which, inter alia, are useful in methods of improving drug delivery, bioavailability, and efficacy. The invention also pertains to pharmaceutical formulations, and more specifically to co-formulations of known drugs (e.g., amphiphilic drugs) (e.g., anthracyclines) (e.g., doxorubicin) with these SCPC lipids, and their use in therapy, such as cancer treatment.

L8 ANSWER 135 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1921290 CAPLUS Full-text
DOCUMENT NUMBER: 163:87631
TITLE: Axitinib and crizotinib combination therapy inhibits bone loss in a mouse model of castration resistant prostate cancer
AUTHOR(S): Eswaraka, Jeetendra; Giddabasappa, Anand; Han, Guangzhou; Lalwani, Kush; Eisele, Koleen; Feng, Zheng; Affolter, Timothy; Christensen, James; Li, Gang
CORPORATE SOURCE: Global Science and Technology (WCM), Pfizer Global Research and Development, San Diego, CA, 92121, USA
SOURCE: BMC Cancer (2014), 14, 742/1-742/10
CODEN: BCMACL; ISSN: 1471-2407
DIGITAL OBJECT ID: 10.1186/1471-2407-14-742
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Castration resistant prostate cancer (CRPC) is a leading cause of cancer-related deaths in men. The primary cause of mortality and morbidity in patients is bone metastases and remodeling resulting in osteoblastic and osteolytic lesions. Recently, cabozantinib, a multi-kinase inhibitor (VEGFR2 and c-MET inhibitor), was shown to have efficacy on bone lesions in patients. In this study we tested multi-kinase inhibitors: axitinib (VEGFR inhibitor) and crizotinib (c-MET inhibitor) in a combination trial in mice models. Methods: VCaP-Luc cells were grown as s.c. implants in intact and castrated NOD-SCID-gamma (NSG) mice to confirm the androgen dependency. For bone metastasis model two cohorts of NSG mice (castrated and intact) received orthotopic injection of VCaP-Luc cells into the bone marrow cavity of left tibia. Mice were monitored weekly for tumor growth using bioluminescence imaging. Animals were randomized into 4 groups based on the tumor bioluminescence signal: vehicle, crizotinib alone, axitinib alone, crizotinib and axitinib in combination. Animals were imaged weekly by in vivo 2-D X-ray imaging to monitor bone remodeling. At the end of the study animals were euthanized and both tibias were extracted for ex vivo high-resolution 3-D micro-computed tomog. (μCT) imaging. Results: S.c. model showed that androgen stimulation may be helpful but not essential for the growth of VCaP-Luc cells. VCaP-Luc cells grown intra-tibially in intact animals caused extensive remodeling of bone with mixed osteoblastic (bone formation) and osteolytic (bone matrix dissoln.) lesions. The osteoblastic lesions were predominant and at times extended beyond the tibial shaft into the surrounding tissue. In contrast, only osteolytic lesions were prominent throughout the study in castrated animals. Treatment with crizotinib alone reduced the osteolytic lesions in castrated animals. Axitinib alone reduced the osteoblastic lesions in the intact animals. Combination therapy with axitinib and crizotinib remarkably inhibited the tibial remodeling by VCaP-Luc cells which resulted in a significant reduction of both osteoblastic and osteolytic lesions. Conclusion: Our data show that combined inhibition of c-MET and VEGFR can be beneficial for treatment of metastatic bone disease in CRPC and that the drugs act on two different stages of the disease.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 136 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1853168 CAPLUS Full-text
DOCUMENT NUMBER: 162:33543
TITLE: Significances of RET fusion gene in non-small cell lung cancer
AUTHOR(S): Liu, Jingjing; Bi, Minghong
CORPORATE SOURCE: Department of Medical Oncology, First Affiliated Hospital of Bengbu Medical College, Bengbu, 233004, Peop. Rep. China
SOURCE: Zhongguo Feiai Zazhi (2013), 16(11), 615-620
CODEN: ZFZHAG; ISSN: 1009-3419
DIGITAL OBJECT ID: 10.3779/j.issn.1009-3419.2013.11.11
PUBLISHER: Zhongguo Feiai Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 33 refs. Lung cancer is the leading cause of cancer-related death worldwide, mol. target therapy has become a hot research direction of non-small cell lung cancer(NSCLC) treatment. RET fusion gene with an identifiable clin. pathol. features, is present in some subsets of lung cancer, and its treatment is effective by RET inhibitor, suggesting that RET fusion gene may be a new target for individualized treatment to the subgroup of NSCLC. This article reviews the structural characteristics of RET fusion gene and expression model in clin. samples, and treatment of NSCLC.

L8 ANSWER 137 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1827672 CAPLUS Full-text
DOCUMENT NUMBER: 161:690410
TITLE: Pharmaceutical combinations of a protein kinase C (PKC) inhibitor and a c-MET receptor tyrosine kinase

inhibitor for treatment of proliferative diseases
INVENTOR(S): Porter, Dale; Emery, Caroline; Tan, Lujian
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014174478	A1	20141030	WO 2014-IB60976	20140424

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61816266 P 20130426

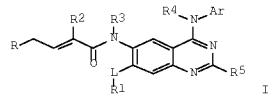
AB A pharmaceutical combination comprising (a) a protein kinase C (PKC) inhibitor, or a pharmaceutically acceptable salt thereof, and (b) at least one c-MET receptor tyrosine kinase inhibitor, or a pharmaceutically acceptable salt, and optionally a pharmaceutically acceptable carrier, for simultaneous, sep. or sequential administration; the uses of such combination in the treatment of proliferative diseases; and methods of treating a subject suffering from a proliferative disease comprising administering a therapeutically effective amount of such combination.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

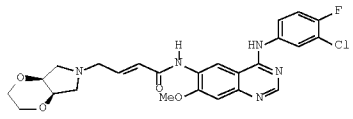
L8 ANSWER 138 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1821658 CAPLUS Full-text
DOCUMENT NUMBER: 161:715766
TITLE: Preparation of quinazolineamine derivatives for treating proliferative diseases
INVENTOR(S): Zhang, Yingjun; Liu, Bing; Liu, Jinlei; Zhang, Jiancun; Zheng, Changchun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 147pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104119350	A	20141029	CN 2014-10175636	20140428
WO 2014177038	A1	20141106	WO 2014-CN76377	20140428

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: CN 2013-10156470 A 20130428
CN 2014-10108773 A 20140323
OTHER SOURCE(S): MARPAT 161:715766
GI



I



II

AB The present invention provides quinazolineamine derivs. I [wherein R = bicyclic heterocyclyl; R1 = H, D, F, Cl, Br, I, etc.; R2 = H, F, Cl, Br, I, NH2, etc.; R3 and R4 = independently H, D, or alkyl; R5 = H, D, F, Cl, Br, I, alkyl, etc.; Ar = (un)substituted Ph or indazole-5-yl] stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts, or prodrugs thereof for prevention, treatment, or relieving proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 3.2, 14, and 8.3 nM against EGFR, HER-2, and EGFR T790M kinases, resp. Pharmaceutical compns. comprising the title compound were also described.

L8 ANSWER 139 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1792793 CAPLUS Full-text
DOCUMENT NUMBER: 162:498601
TITLE: Enrichment of c-Met+ tumorigenic stromal cells of giant cell tumor of bone and targeting by cabozantinib
AUTHOR(S): Liu, L.; Aleksandrowicz, E.; Fan, P.; Schoensiegel, F.; Zhang, Y.; Saehr, H.; Gladkich, J.; Mattern, J.; Depeweg, D.; Lehner, B.; Fellenberg, J.; Herr, I.
CORPORATE SOURCE: Department of Molecular OncoSurgery, General, Visceral and Transplantation Surgery, University of Heidelberg and German Cancer Research Center (DKFZ), Heidelberg, Germany
SOURCE: Cell Death & Disease (2014), 5(10), e1471
CODEN: CDDEA4; ISSN: 2041-4889
DIGITAL OBJECT ID: 10.1038/cddis.2014.440
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Giant cell tumor of bone (GCTB) is a very rare tumor entity, which is little examined owing to the lack of established cell lines and mouse models and the restriction of available primary cell lines. The stromal cells of GCTB have been made responsible for the aggressive growth and metastasis, emphasizing the presence of a cancer stem cell population. To identify and target such tumor-initiating cells, stromal cells were isolated from eight freshly resected GCTB tissues. Tumorigenic properties were examined by colony and spheroid formation, differentiation, migration, MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay, immunohistochem., antibody protein array, Alu in situ hybridization, FACS anal. and xenotransplantation into fertilized chicken eggs and mice. A sub-population of the neoplastic stromal cells formed spheroids and colonies, differentiated to osteoblasts, migrated to wounded regions and expressed the metastasis marker CXC-chemokine receptor type 4, indicating self-renewal, invasion and differentiation potential. Compared with adherent-growing cells, markers for pluripotency, stemness and cancer progression, including the CSC surface marker c-Met, were enhanced in spheroidal cells. This c-Met-enriched sub-population formed xenograft tumors in fertilized chicken eggs and mice. Cabozantinib, an inhibitor of c-Met in phase II trials, eliminated CSC features with a higher therapeutic effect than standard chemotherapy. This study identifies a c-Met+ tumorigenic sub-population within stromal GCTB cells and suggests the c-Met inhibitor cabozantinib as a new therapeutic option for targeted elimination of unresectable or recurrent GCTB.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 140 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1791911 CAPLUS Full-text
DOCUMENT NUMBER: 161:680644
TITLE: Cancer-associated chimeric genes arising from translocations and their use in diagnosis, prognosis, and therapy of cancer
INVENTOR(S): Rhodes, Daniel; Sadis, Seth; Wyngaard, Peter; Khazanov, Nikolay; Bandla, Santhoshi; Tomilo, Mark; Eddy, Sean; Bowden, Emma
PATENT ASSIGNEE(S): Life Technologies Corporation, USA
SOURCE: PCT Int. Appl., 272pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014172046	A2	20141023	WO 2014-US29592	20140314

EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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WO 2014172046 A3 20150618

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

AU 2014254394 A1 20151203 AU 2014-254394 20140314
PRIORITY APPLN. INFO.: US 2013-61813182 P 20130417
US 2013-61813465 P 20130418
US 2013-61824253 P 20130516
US 2013-61860115 P 20130730
US 2013-61907939 P 20131122
US 2013-61915392 P 20131212
US 2014-61935650 P 20140204
US 2014-61940226 P 20140214
WO 2014-US29592 W 20140314

AB Chimeric genes arising from chromosomal translocations that play a role in the etiol. of cancer are identified for use in diagnosis, prognosis, and selection and monitoring of therapies. These chimeric genes were identified by a large-scale survey of 19 cancers in 4,225 patients.

L8 ANSWER 141 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1790149 CAPLUS Full-text
DOCUMENT NUMBER: 161:686526
TITLE: Cabozantinib malate and its preparation method
INVENTOR(S): Meng, Qingyi; Zhang, Aiming; Xu, Wenwei; Zhang, Xiquan
PATENT ASSIGNEE(S): Lianyungang Runzhong Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 7pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104109128	A	20141022	CN 2013-10164410	20130419

PRIORITY APPLN. INFO.: CN 2013-10164410 20130419

AB The present invention relates to cabozantinib malate and its prepn. method, and specifically, the present invention relates to cabozantinib·n malate, its preparation method, and a pharmaceutical composition comprising the same. The inventive cabozantinib·n malate has excellent stability, and can be used for preparing medicines for the treatment of tumors, especially in preparation of medicine for the treatment of medullary thyroid cancer. The preparation method of cabozantinib·n malate includes: (a) adding cabozantinib to an organic solvent, (b) adding malic acid n times molar amount

of cabozantinib to mixture of step (a), and (c) precipitating to obtain cabozantinib·n malate, wherein, n is selected from 0.4-0.6, preferably 0.5.

L8 ANSWER 142 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1782124 CAPLUS Full-text
DOCUMENT NUMBER: 161:705479
TITLE: Crystal of cabozantinib· 0.5 malate
INVENTOR(S): Meng, Qingyi; Zhang, Aiming; Xu, Wenwei; Zhang, Xiquan
PATENT ASSIGNEE(S): Chia Tai Tianqing Pharmaceutical Group Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104109124	A	20141022	CN 2013-10138216	20130419
PRIORITY APPLN. INFO.:			CN 2013-10138216	20130419

AB The invention relates to crystal of cabozantinib·0.5malate, a crystal composition and a pharmaceutical composition of the crystal, preparing method thereof, and application thereof in manufacture of drugs treating tumor-related diseases. In the x-ray powder diffraction spectrum of the crystal using Cu-Kα radiation, there are diffraction peaks at 2θ of 5.48°, 10.88°, 15.24°, 21.97° and 24.56°.

L8 ANSWER 143 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1754957 CAPLUS Full-text
DOCUMENT NUMBER: 161:635758
TITLE: Platform for targeted delivery to stem cells and tumor cells and methods thereof
INVENTOR(S): Carvalho Da Fonseca, Nuno Andre; Gomes Da Silva, Ligia Catarina; Dantas Nunes Caldeira De Moura, Vera Lucia; De Magalhaes Simoes, Sergio Paulo; Sereno De Almeida Moreira, Joao Nuno
PATENT ASSIGNEE(S): Universidade de Coimbra, Port.
SOURCE: PCT Int. Appl., 59pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014167126	A2	20141016	WO 2014-EP57446	20140411
WO 2014167126	A3	20150108		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
AU 2014253040 A1 20151105 AU 2014-253040 20140411
PRIORITY APPLN. INFO.: PT 2013-128240 A 20130413
WO 2014-EP57446 W 20140411

AB The invention involves therapy and diagnostics using nanoparticles that provide targeted delivery of agents to cancer cells and stem cells, including cancer stem cells, the nanoparticles being pH sensitive and incorporating cytotoxic ceramides.

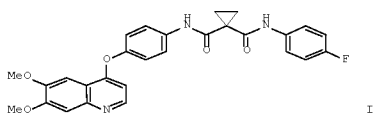
L8 ANSWER 144 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1754784 CAPLUS Full-text
DOCUMENT NUMBER: 163:225877
TITLE: Sequencing of lung cancer genomes and its translation to the therapy
AUTHOR(S): Iwakawa-Kawabata, Reika; Kohno, Takashi
CORPORATE SOURCE: Div. of Genome Biology, National Cancer Center, Japan
SOURCE: Jikken Igaku (2014), 32(12), 1865-1870
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review discussing the sequencing of lung cancer genomes and its translation to the therapy.

L8 ANSWER 145 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1742452 CAPLUS Full-text
DOCUMENT NUMBER: 163:438125
TITLE: A Phase I Study of Cabozantinib (XL184) in Patients with Differentiated Thyroid Cancer
AUTHOR(S): Cabanillas, Maria E.; Brose, Marcia S.; Holland, Jaymes; Ferguson, Kimberly C.; Sherman, Steven I.
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Thyroid (2014), 24(10), 1508-1514
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2014.0125
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Cabozantinib targets tyrosine kinases including MET, vascular endothelial growth factor (VEGF) receptor 2, and rearranged during transfection (RET). Differentiated thyroid cancer (DTC) is a tumor type that may be sensitive to cabozantinib. Therefore, we evaluated cabozantinib in a cohort of heavily pretreated patients with metastatic DTC. .Methods: This single-arm open-label phase I trial assessed the safety, tolerability, and antitumor activity of cabozantinib in DTC patients taking part in a drug-drug interaction study. Adult patients with histol. confirmed metastatic or surgically unresectable DTC (including papillary, follicular, or Huerthle cell) were enrolled. Patients received daily oral dosing of 140 mg cabozantinib. Safety was assessed by evaluation of adverse events (AEs), vital signs, electrocardiograms, laboratory tests, and concomitant medications. Tumor response by magnetic resonance imaging or computed tomog. scan was investigator assessed using Response Evaluation Criteria In Solid Tumors (RECIST) v1.0. Results: The study enrolled 15 patients who had failed standard radioactive iodine therapy. Patients had received a median of two prior systemic agents, and 11 patients (73%) had previously received at least one VEGF pathway inhibiting therapy. Common AEs included diarrhea, nausea, fatigue, and decreased appetite. Partial response was reported in eight patients (53%). Median progression-free survival and median overall survival were not reached. Conclusions: Cabozantinib demonstrates a safety profile similar to other multitargeted VEGFR inhibitors in advanced DTC patients. The antitumor activity observed in this study warrants further investigation of cabozantinib in patients with advanced DTC.
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 146 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1716754 CAPLUS Full-text
DOCUMENT NUMBER: 161:582215
TITLE: Preparation of cabozantinib and dosage forms for treatment of cancer
INVENTOR(S): Decillis, Arthur
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165786	A1	20141009	WO 2014-US33016	20140404

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2013-61808511 P 20130404
OTHER SOURCE(S): CASREACT 161:582215
GI



I

AB This invention relates to a dosage form of cabozantinib (I) and a method of employing the dosage form to treat cancer. I was prepared starting with 6,7-dimethoxy-4-quinolinol through a number of steps. I S-maleate was also prepared and tablets containing I were prepared
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 147 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1715795 CAPLUS Full-text
DOCUMENT NUMBER: 161:577833
TITLE: Methods and compositions for treating cancers having acquired resistance to chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): Tactical Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 23pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165412	A2	20141009	WO 2014-US32253	20140328
WO 2014165412	A3	20150129		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140294806	A1	20141002	US 2013-13986103	20130401
US 9089570	B2	20150728		
CA 2902144	A1	20141009	CA 2014-2902144	20140328
AU 2014248377	A1	20150903	AU 2014-248377	20140328
IL 241827	A	20151130	IL 2014-241827	20140328

CN 105120663	A	20151202	CN 2014-80019712		20140328
PRIORITY APPLN. INFO.:			US 2013-13986103	A	20130401
			WO 2014-US32253	W	20140328

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

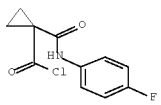
AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.

L8 ANSWER 148 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1710486 CAPLUS Full-text
DOCUMENT NUMBER: 161:577829
TITLE: Drug combinations to treat cancer
INVENTOR(S): Sweeney, Christopher J.; Kantoff, Philip W.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 78pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165779	A1	20141009	WO 2014-US33008	20140404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2908815	A1	20141009	CA 2014-2908815	20140404
AU 2014248001	A1	20151119	AU 2014-248001	20140404
IL 241868	A	20151130	IL 2014-241868	20140404
KR 2015138268	A	20151209	KR 2015-7030445	20140404
PRIORITY APPLN. INFO.:			US 2013-61808516	P 20130404
			WO 2014-US33008	W 20140404

OTHER SOURCE(S): CASREACT 161:577829; MARPAT 161:577829
GI



AB This invention relates to the combination of cabozantinib and abiraterone to treat cancer, particularly castration resistant prostate cancer.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 149 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1689164 CAPLUS Full-text
DOCUMENT NUMBER: 162:58578
TITLE: Cabozantinib inhibits growth of androgen-sensitive and castration-resistant prostate cancer and affects bone remodeling [Erratum to document cited in CA160:363229]
AUTHOR(S): Nguyen, Holly M.; Ruppender, Nazanin; Zhang, Xiaotun; Brown, Lisha G.; Gross, Ted S.; Morrissey, Colm; Gulati, Roman; Vessella, Robert L.; Schimmoller, Frauke; Aftab, Dana T.; Corey, Eva
CORPORATE SOURCE: Department of Urology, University of Washington, Seattle, WA, USA
SOURCE: PLoS One (2014), 9(8), e106797/1, 1 pp.
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0106797
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB On page 1, the funding information was incomplete; the cor. funding statement is given.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 150 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1684883 CAPLUS Full-text
DOCUMENT NUMBER: 161:588524
TITLE: Emerging molecular targets in oncology: clinical potential of MET/hepatocyte growth-factor inhibitors
AUTHOR(S): Smyth, Elizabeth C.; Sclafani, Francesco; Cunningham, David
CORPORATE SOURCE: Department of Gastrointestinal Oncology, Royal Marsden Hospital, Sutton, UK
SOURCE: OncoTargets and Therapy (2014), 7, 1001-1014, 14 pp.
CODEN: OTNHAZ; ISSN: 1178-6930
DIGITAL OBJECT ID: 10.2147/OTT.S44941
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. The MET/hepatocyte growth-factor (HGF) signaling pathway plays a key role in the processes of embryogenesis, wound healing, and organ regeneration. Aberrant activation of MET/HGF occurs through multiple mechanisms including gene amplification, mutation, protein overexpression, and abnormal gene splicing interrupting autocrine and paracrine regulatory feedback mechanisms. In many cancers including non-small-cell lung cancer, colorectal, gastric, renal, and hepatocellular cancer, dysregulation of MET may lead to a more aggressive cancer phenotype and may be a neg. prognostic indicator. Successful therapeutic targeting of the MET/HGF pathway has been achieved using monoclonal antibodies against the MET receptor and its ligand HGF in addition to MET-specific and multitargeted small-mol. tyrosine-kinase inhibitors with several drugs in late-phase clin. trials including onartuzumab, rilotumumab, tivantinib, and cabozantinib. MET frequently interacts with other key oncogenic tyrosine kinases including epidermal growth-factor receptor (EGFR) and HER-3 and these interactions may be responsible for resistance to anti-EGFR therapies. Similarly, resistance to MET inhibition may be mediated through EGFR activation, or alternatively by increasing levels of MET amplification or acquisition of novel "gatekeeper" mutations. In order to optimize development of effective inhibitors of the MET/HGF pathway clin. trials must be enriched for patients with demonstrable MET-pathway dysregulation for which robustly standardized and validated assays are required.
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 140 THERE ARE 140 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 151 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1684761 CAPLUS Full-text
DOCUMENT NUMBER: 161:588517
TITLE: Cabozantinib for progressive metastatic medullary thyroid cancer: a review
AUTHOR(S): Colombo, Joshua R.; Wein, Richard O.
CORPORATE SOURCE: Department of Otolaryngology, Head and Neck Surgery, Tufts Medical Center, Boston, MA, USA
SOURCE: Therapeutics and Clinical Risk Management (2014), 10, 395-404, 10 pp.
CODEN: TCRMA6; ISSN: 1178-203X
DIGITAL OBJECT ID: 10.2147/TCRM.S46041
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Medullary thyroid cancer is uncommon and patients typically present with advanced disease. Treatment options for patients with progressive, metastatic medullary thyroid cancer had been limited until recently. Tyrosine kinase inhibitors have garnered increasing interest in this subset of patients. The US Food and Drug Administration recently approved cabozantinib, a tyrosine kinase inhibitor, after promising results were shown in a large Phase III clin. trial. This review summarizes the clin. pharmacol., clin. trials, and safety data for cabozantinib and concludes with a discussion of possible future directions for the treatment of medullary thyroid cancer.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 152 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1660666 CAPLUS Full-text
DOCUMENT NUMBER: 161:546938
TITLE: Methods and compositions for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): Tactical Therapeutics Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140294806	A1	20141002	US 2013-13986103	20130401
US 9089570	B2	20150728		
CA 2902144	A1	20141009	CA 2014-2902144	20140328
WO 2014165412	A2	20141009	WO 2014-US32253	20140328
WO 2014165412	A3	20150129		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014248377	A1	20150903	AU 2014-248377	20140328
IL 241827	A	20151130	IL 2014-241827	20140328
CN 105120663	A	20151202	CN 2014-80019712	20140328
PRIORITY APPLN. INFO.:			US 2013-13986103	A 20130401
			WO 2014-US32253	W 20140328

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.

L8 ANSWER 153 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1657302 CAPLUS Full-text
DOCUMENT NUMBER: 161:559304
TITLE: Methods of treating proliferative diseases such as cancer using natural compounds and/or ketogenic diet
INVENTOR(S): Reynolds, Brent; Deleyrolle, Loic
PATENT ASSIGNEE(S): University of Florida Research Foundation,

Incorporated, USA
SOURCE: PCT Int. Appl., 115pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014159500	A1	20141002	WO 2014-US23934	20140312
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2912518	A1	20141002	CA 2014-2912518	20140312
AU 2014240467	A1	20151105	AU 2014-240467	20140312

PRIORITY APPLN. INFO.: US 2013-61784386 P 20130314
WO 2014-US23934 W 20140312

AB The current invention is directed to a treatment of a proliferative disease comprising administering to a subject in need of such treatment, a composition comprising epigallocatechin-3-gallate (EGCG), curcumin, glucosinolates and, optionally Daikon radish sprout, alone or in combination with providing a ketogenic diet or a modified ketogenic diet to the subject. The invention also provides a composition comprising medium chain triglycerides, epigallocatechin-3-gallate, curcumin, compns. comprising glucosinolates and/or derivs. thereof, such as glucoraphanin and its breakdown product sulforaphane (SFN) (which are found at high levels in broccoli sprouts or sprouts of other cruciferous vegetables), and, optionally Daikon radish sprout.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 154 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1653556 CAPLUS Full-text
DOCUMENT NUMBER: 161:542164
TITLE: Articles and methods for preventing and treating dermatologic adverse events
INVENTOR(S): Lacouture, Mario E.; Abou-Alfa, Ghassan Khaled
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 22pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014160628	A2	20141002	WO 2014-US31545	20140324
WO 2014160628	A3	20141204		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2013-61804907 P 20130325

AB The present invention provides articles and methods for preventing or treating dermatol. adverse events.

L8 ANSWER 155 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1651697 CAPLUS Full-text
DOCUMENT NUMBER: 161:710328
TITLE: Hepatocellular carcinoma: novel molecular targets in carcinogenesis for future therapies
AUTHOR(S): Bertino, Gaetano; Demma, Shirin; Ardiri, Annalisa; Proiti, Maria; Gruttadauria, Salvatore; Toro, Adriana; Malaguarnera, Giulia; Bertino, Nicoletta; Malaguarnera, Michele; Malaguarnera, Mariano; Di Carlo, Isidoro
CORPORATE SOURCE: Hepatology Unit, Department of Medical and Pediatric Sciences, University of Catania, Policlinic, Catania, 95123, Italy
SOURCE: BioMed Research International (2014) 203693/1-203693/15, 16 pp.
CODEN: BRIIDT; ISSN: 2314-6141
DIGITAL OBJECT ID: 10.1155/2014/203693
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background. Hepatocellular carcinoma is one of the most common and lethal malignant tumors worldwide. Over the past 15 years, the incidence of HCC has more than doubled. Due to late diagnosis and/or advanced underlying liver cirrhosis, only limited treatment options with marginal clin. benefit are available in up to 70% of patients. During the last decades, no effective conventional cytotoxic systemic therapy was available contributing to the dismal prognosis in patients with HCC. A better knowledge of mol. hepatocarcinogenesis provides today the opportunity for targeted therapy. Materials and Methods. A search of the literature was made using cancer literature, the PubMed, Scopus, and Web of Science (WOS) database for the following keywords: "hepatocellular carcinoma," "mol. hepatocarcinogenesis," "targeted therapy," and "immunotherapy." Discussion and Conclusion. Treatment decisions are complex and dependent upon tumor staging, presence of portal hypertension, and the underlying degree of liver dysfunction. The knowledge of mol. hepatocarcinogenesis broadened the horizon for patients with advanced HCC. During the last years, several mol. targeted agents have been evaluated in clin. trials in advanced HCC. In the future, new therapeutic options will be represented by a blend of immunotherapy-like vaccines and T-cell modulators, supplemented by molecularly targeted inhibitors of tumor signaling pathways.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 156 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1600971 CAPLUS Full-text
DOCUMENT NUMBER: 161:533327
TITLE: c-met cancer biomarkers for patient prognosis and selection for the therapy with c-met antagonist, particularly anti-c-met antibody
INVENTOR(S): Yauch, Robert; Koeppen, Hartmut
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 99pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014150819	A2	20140925	WO 2014-US24316	20140312
WO 2014150819	A3	20150108		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2013-61801276 P 20130315

AB The invention concerns c-met biomarkers for patient selection and prognosis in cancer, as well as methods of therapeutic treatment and diagnostic kits using anti-c-met antibodies.

L8 ANSWER 157 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1599013 CAPLUS Full-text
DOCUMENT NUMBER: 161:533781
TITLE: Antibodies for treating angiogenesis-related disorders
INVENTOR(S): Gurewich, Victor
PATENT ASSIGNEE(S): FFE Therapeutics LLC, USA
SOURCE: PCT Int. Appl., 76pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014151917	A1	20140925	WO 2014-US26675	20140313
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2013-61785345 P 20130314

AB The author discloses anti-angiogenic monoclonal antibodies and antigen-binding antibody fragments that selectively and specifically bind to an epitope in both fibronectin and either fibrinogen or fibrin fragment E. In one example, administration of the monoclonal antibodies is shown to inhibit tumor growth and vascularization in a colon adenocarcinoma xenograft model.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 158 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1596401 CAPLUS Full-text
DOCUMENT NUMBER: 161:528901
TITLE: Stapling eIF4E-eIF4G interacting peptides and their therapeutic use in cancer treatment
INVENTOR(S): Brown, Christopher John; Lane, David Philip; Quah, Soo Tng; Lama, Dilraj; Verma, Chandra Shekhar
PATENT ASSIGNEE(S): Agency for Science, Technology and Research, Singapore
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014149001	A1	20140925	WO 2014-SG94	20140228
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,				

SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
SG 201400336 A1 20150828 SG 2014-336 20140115
PRIORITY APPLN. INFO.: SG 2013-2065 A 20130321
SG 2014-336 A 20140115
OTHER SOURCE(S): MARPAT 161:528901
AB The present invention relates to crosslinked peptides that are assocd. with human eIF4G and bind to eIF4E, uses thereof and pharmaceutical compns. comprising the peptides. Described below are crosslinked peptides related to a portion of human eIF4E. These crosslinked peptides contain at least two modified amino acids that together form an internal crosslink (also referred to as a staple) that can help to stabilize the alpha-helical secondary structure of a portion of eIF4G1 that is thought to be important for binding of eIF4E to eIF4G. Accordingly, a crosslinked peptide described herein can have improved biol. activity relative to a corresponding peptide that is not crosslinked. The crosslinked eIF4G1 peptides are thought to interfere with binding of eIF4G1 to eIF4G thereby inhibiting the increased translation of mRNAs with highly structured 5'UTRs. The crosslinked eIF4G1 peptide described herein can be used therapeutically, e.g., to treat or prevent a variety of cancers in a subject.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 159 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1594844 CAPLUS Full-text
DOCUMENT NUMBER: 162:544299
TITLE: Congestive heart failure risk in cancer patients treated with vascular endothelial growth factor tyrosine kinase inhibitors: a systematic review and meta-analysis of 36 clinical trials
AUTHOR(S): Qi, Wei-Xiang; Shen, Zan; Tang, Li-Na; Yao, Yang
CORPORATE SOURCE: Department of Oncology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE: British Journal of Clinical Pharmacology (2014), 78(4), 748-762
CODEN: BCPHBM; ISSN: 1365-2125
DIGITAL OBJECT ID: 10.1111/bcp.12387
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Aims : Congestive heart failure (CHF) assocd. with vascular endothelial growth factor tyrosine-kinase inhibitors (VEGFR-TKIs) has emerged as a relevant problem in clin. and scientific communities. We performed an up-to-date, comprehensive meta-anal. to determine the overall incidence and risk of CHF in cancer patients receiving VEGFR-TKIs. Methods : The databases of PubMed, Web of Science and abstrs. presented at the American Society of Clin. Oncol. up to August 31 2013 were searched for relevant articles. Statistical analyses were conducted to calculate the summary incidence, odds ratio (OR) and 95% confidence intervals (CIs) by using either random effects or fixed effect models according to the heterogeneity of included studies. Results : A total of 10 553 patients from 36 clin. trials were included. The overall incidence of all grade and high grade CHF associated with VEGFR-TKIs was 3.2% (95% CI 1.8%, 5.8%) and 1.4% (95% CI 0.9%, 2.3%), resp. The use of VEGFR-TKIs significantly increased the risk of developing all grade (OR 2.37, 95% CI 1.76, 3.20, P < 0.001) and high grade (OR 3.51, 95% CI 1.74, 7.05, P < 0.001) CHF. In subgroup analyses, the risk of CHF did not significantly vary with tumor types (P = 0.071 for all grade; P = 0.72 for high grade) and VEGFR-TKIs (P = 0.55 for all grade; P = 0.99 for high grade). Meta-regression indicated that CHF might possibly occur early in the treatment of VEGFR-TKIs. No evidence of publication bias was observed Conclusion : The use of VEGFR-TKIs is associated with a significantly increased risk of developing congestive heart failure in cancer patients. Clinicians should be aware of this risk and provide close monitoring in patients receiving these therapies.
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 160 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1563739 CAPLUS Full-text
DOCUMENT NUMBER: 161:496846
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Privada Institut de Recerca Biomedica, Spain; Fundacio Privada Institucio Catalana de Recerca i Estudis Avancats
SOURCE: PCT Int. Appl., 97pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

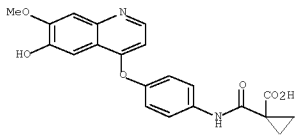
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014140933	A2	20140918	WO 2014-IB1253	20140314
WO 2014140933	A3	20141231		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2906394	A1	20140918	CA 2014-2906394	20140314
AU 2014229505	A1	20150903	AU 2014-229505	20140314
KR 2015122731	A	20151102	KR 2015-7026432	20140314

PRIORITY APPLN. INFO.: US 2013-61801718 P 20130315
WO 2014-IB1253 W 20140314
AB The invention relates to a method for the prognosis of bone metastasis in cancer which comprises using a probe to determine if a gene of interest is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise using a probe to determine the expression level of a gene of interest, or the amplification or translocation of a gene of interest. The invention also relates to a method for predicting early bone metastasis in a subject suffering cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering cancer and for classifying a subject from cancer into a cohort.

L8 ANSWER 161 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1554223 CAPLUS Full-text
DOCUMENT NUMBER: 161:496839
TITLE: Metabolites of n-[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]-n'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven; Nguyen, Linh
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014145693	A1	20140918	WO 2014-US30498	20140317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2013-61792562 P 20130315
OTHER SOURCE(S): CASREACT 161:496839; MARPAT 161:496839
GI



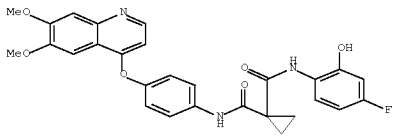
AB The invention relates to metabolites of foretinib as well as uses thereof.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 162 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1554191 CAPLUS Full-text
DOCUMENT NUMBER: 161:496838
TITLE: Metabolites of N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl) cyclopropane-1,1-dicarboxamide
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven; Nguyen, Linh
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 65pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014145715	A1	20140918	WO 2014-US30524	20140317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2907334	A1	20140918	CA 2014-2907334	20140317
AU 2014232714	A1	20151008	AU 2014-232714	20140317
KR 2015130376	A	20151123	KR 2015-7027712	20140317
IL 241577	A	20151130	IL 2014-241577	20140317
CN 105121412	A	20151202	CN 2014-80021215	20140317

PRIORITY APPLN. INFO.: US 2013-61792413 P 20130315
WO 2014-US30524 W 20140317

OTHER SOURCE(S): CASREACT 161:496838; MARPAT 161:496838
GI



AB The invention relates to metabolites of cabozantinib as well as uses thereof.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 163 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1509904 CAPLUS Full-text
DOCUMENT NUMBER: 162:419468
TITLE: Antitumor Agent Cabozantinib Decreases RANKL Expression in Osteoblastic Cells and Inhibits Osteoclastogenesis and PTHrP-Stimulated Bone Resorption
AUTHOR(S): Stern, Paula H.; Alvares, Keith
CORPORATE SOURCE: Department of Pharmacology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
SOURCE: Journal of Cellular Biochemistry (2014), 115(11), 2033-2038
CODEN: JCEBD5; ISSN: 0730-2312
DIGITAL OBJECT ID: 10.1002/jcb.24879
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cabozantinib, an inhibitor of vascular endothelial growth factor and hepatocyte growth factor signaling, decreases bone lesions in patients with prostate cancer. To determine direct effects of cabozantinib on bone, resorption in neonatal mouse bone organ culture and on gene expression, proliferation, and phenotypic markers in osteoblast and osteoclast cell lines were examined Cabozantinib, 0.3 and 3 μM, prevented PTHrP-stimulated calcium release from neonatal mouse calvaria. Since the effect on resorption could reflect effects on osteoblasts to prevent osteoclast activation, or direct inhibition of osteoclasts, responses in osteoblastic and osteoclast precursor cell lines were examined Twenty-four-hour treatment of osteoblastic MC3T3-E1 cells with 3 μM cabozantinib decreased expression of receptor activator of NFkB ligand (RANKL) and alkaline phosphatase. Forty-eight-hour treatment of MC3T3-E1 cells with 3 μM cabozantinib inhibited cell proliferation and decreased MTT activity. Effects on alkaline phosphatase activity were biphasic, with small stimulatory effects at concns. below 3 μM. When RAW 264.7 osteoclast precursor cells differentiated with 20 ng/mL RANKL were co-treated for 24 h with 3 μM cabozantinib, expression of RANK, TRAP, cathepsin K, alpha v or beta 3 integrin, or NFATc1 were unaffected. Five-day treatment of RANKL-treated RAW 264.7 cells with 3 μM cabozantinib decreased TRAP and MTT activity. The results suggest that the osteoblast could be the initial target, with subsequent direct and indirect effects on osteoclastogenesis leading to decreased resorption. The multiple effects of cabozantinib on the cell microenvironment of bone are consistent with its effectiveness in reducing lesions from prostate cancer metastases. J. Cell. Biochem. 115: 2033-2038, 2014. © 2014 Wiley Periodicals, Inc.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 164 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1476801 CAPLUS Full-text
DOCUMENT NUMBER: 161:446646
TITLE: Preparation of pyridine compounds as protein tyrosine kinase inhibitors for treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wang, Ruyong; Wang, Liang
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 118pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104016979	A	20140903	CN 2013-10597520	20131122
PRIORITY APPLN. INFO.:			CN 2012-10480698 A	20121123
			CN 2013-10116667 A	20130403

OTHER SOURCE(S): MARPAT 161:446646
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridinyl compds. of general formula I, pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. For I, each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; X is C6-C10 aryl or 5-10 membered heteroaryl that are optionally substituted; and Y is an (un)substituted bicyclic heterocyclyl. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 6-step reaction that culminated in coupling of intermediates III and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-o

l. Example compds. of the invention were also tested in ALK and c-Met kinase inhibition assays. Pharmacokinetic profiles were also examined in rats, as was compound stability in human and rat liver microsomes.

L8 ANSWER 165 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1460877 CAPLUS Full-text
DOCUMENT NUMBER: 162:17927
TITLE: Comparison of the cancer gene targeting and biochemical selectivities of all targeted kinase inhibitors approved for clinical use
AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; de Man, Jos; Tanizawa, Yoshinori; Kawase, Yusuke; Yoshino, Kohichiro; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE: Netherlands Translational Research Center B.V., Oss, Neth.
SOURCE: PLoS One (2014), 9(3), e92146/1-e92146/13, 13 pp.
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0092146
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The anti-proliferative activities of all twenty-five targeted kinase inhibitor drugs that are in clin. use were measured in two large assay panels: (1) a panel of proliferation assays of forty-four human cancer cell lines from diverse tumor tissue origins; and (2) a panel of more than 300 kinase enzyme activity assays. This study provides a head-on comparison of all kinase inhibitor drugs in use, and for six of these drugs, the first kinome profiling data in the public domain. Correlation of drug activities with cancer gene mutations revealed novel drug sensitivity markers, suggesting that cancers dependent on mutant CTNNB1 will respond to trametinib and other MEK inhibitors, and cancers dependent on SMAD4 to small mol. EGFR inhibitor drugs. Comparison of cellular targeting efficacies reveals the most targeted inhibitors for EGFR-, ABL1- and BRAF(V600E)-driven cell growth, and demonstrates that the best targeted agents combine high biochem. potency with good selectivity. For ABL1 inhibitors, we computationally deduce optimized kinase profiles for use in a next generation of drugs. Our study shows the power of combining biochem. and cellular profiling data in the evaluation of kinase inhibitor drug action.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 166 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1425621 CAPLUS Full-text
DOCUMENT NUMBER: 161:400645
TITLE: Treatment of cancer using an oncolytic virus and a receptor tyrosine kinase inhibitor
INVENTOR(S): Conner, Joe
PATENT ASSIGNEE(S): Virttu Biologics Limited, UK
SOURCE: PCT Int. Appl., 310pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014128487	A1	20140828	WO 2014-GB50522	20140221
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
GB 2516521	A	20150128	GB 2014-3083	20140221
US 20150374767	A1	20151231	US 2015-14768549	20150818
PRIORITY APPLN. INFO.:			GB 2013-3184 A	20130222
			WO 2014-GB50522 W	20140221

AB A method of treating cancer is disclosed, the method comprising simultaneous or sequential administration of an oncolytic virus and a receptor tyrosine kinase (RTK) inhibitor.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 167 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1416968 CAPLUS Full-text
DOCUMENT NUMBER: 162:442908
TITLE: High-Grade Undifferentiated Sarcomas of the Uterus: Diagnosis, Outcomes, and New Treatment Approaches
AUTHOR(S): Philip, Charles-Andre; Pautier, Patricia; Duffaud, Florence; Ray-Coquard, Isabelle
CORPORATE SOURCE: Department of Adult Medical Oncology, Centre Leon Berard, Lyon, 69008, Fr.
SOURCE: Current Oncology Reports (2014), 16(10), 1-8
CODEN: CORUAT; ISSN: 1534-6269
DIGITAL OBJECT ID: 10.1007/s11912-014-0405-1
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. High-grade undifferentiated sarcomas (HGUS) are rare malignancies accounting for 6 % of all uterine sarcomas and have a very poor outcome. Histol. classification of HGUS is currently debated as a subgroup with uniform nucleoli, and frequently YWHAE-FAM22 transcript has been described, constituting a potential target for new therapies. In localized HGUS, surgery involving total hysterectomy and bilateral oophorectomy is recommended. Adjuvant radiotherapy has recently been suggested in a retrospective study to decrease local recurrence and improve survival vs. observation in localized HGUS. In metastatic or recurrent disease, chemotherapy with doxorubicin with or without ifosfamide constitutes the standard of care. Gemcitabine plus docetaxel also seems to be an interesting alternative. Targeted therapies such as pazopanib are now available for soft tissue sarcomas and so could be proposed for uterine sarcoma patients after first- or second-line chemotherapy in the metastatic phase. Further investigations are needed to determine their indications and targets. A

European Organization for Research and Treatment of Cancer (EORTC) randomized trial testing maintenance therapy with cabozantinib after first-line chemotherapy in HGUS is ongoing.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 168 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1390694 CAPLUS Full-text
DOCUMENT NUMBER: 161:375913
TITLE: Preparation of pyrazolopyridine compounds as protein kinase modulators useful for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 41pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

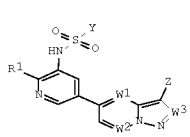
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140234254	A1	20140821	US 2014-14181670	20140215
CA 2898294	A1	20140828	CA 2014-2898294	20140215
WO 2014130375	A1	20140828	WO 2014-US16643	20140215

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

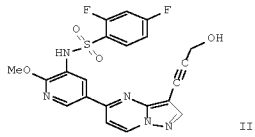
AU 2014219256	A1	20150730	AU 2014-219256	20140215
KR 2015118102	A	20151021	KR 2015-7019069	20140215
EP 2958564	A1	20151230	EP 2014-754663	20140215

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

PRIORITY APPLN. INFO.: US 2013-61767721 P 20130221
WO 2014-US16643 W 20140215
OTHER SOURCE(S): CASREACT 161:375913; MARPAT 161:375913
GI



I



II

AB The invention provides heteroarom. derivs. and pharmaceutically acceptable salts and formulations thereof useful in modulating the protein kinase activity, especially phosphatidylinositol 3-kinases (PI3K) and mammalian target of rapamycin (mTOR), and in modulating inter- and/or intra-cellular signaling activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Compds. of formula I [wherein W1, W2, and W3 are independently N or CRc; Z is D, CN, N3, etc.; Y is C1-6 alkyl, C3-6 cycloalkyl, C3-C6 heterocyclyl, etc.; Rl is H, Cl, C3-6 cycloalkyl, etc.; each Rc is independently H, D, F, etc.] or stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, prodrugs, or pharmaceutically acceptable salts thereof are claimed and exemplified. Example compound II was prepared in seven steps (procedure given). Candidate compds. of I were assayed for their stability in liver microsomes, their oral and i.v. bioavailability, and inhibitory activity against PI3K and mTOR kinase (data given).

L8 ANSWER 169 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1389525 CAPLUS Full-text
DOCUMENT NUMBER: 161:379820
TITLE: Efflux inhibitor compositions containing effect transporter protein inhibitors
INVENTOR(S): Bunt, Antonius Martinus Gustave; Tellingen, Olaf Van
PATENT ASSIGNEE(S): Izumi Biosciences LLC, USA; The Netherlands Cancer Institute
SOURCE: U.S. Pat. Appl. Publ., 33pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140235631	A1	20140821	US 2013-13952476	20130726

PRIORITY APPLN. INFO.: US 2013-61767689 P 20130221
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention relates to efflux inhibitor compns. and methods of using these agents for treating conditions where the activity of efflux transporter proteins (e.g., Breast Cancer Resistance Protein (BCRP) and P-Glycoprotein (P-GP)) inhibit effective delivery of a therapeutic agent to a target tissue (e.g., brain, spinal cord, nerves, cerebrospinal fluid, testis, eyeballs, retina, inner ear, placenta, mammary gland, liver, biliary tract, kidney, intestines, lung, adrenal cortex, endometrium, hematopoietic cells, and/or stem cells). E.g., elacridar nanoparticles were prepared

L8 ANSWER 170 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1348855 CAPLUS Full-text
DOCUMENT NUMBER: 161:346659
TITLE: Drug selection for non-small cell lung cancer therapy
INVENTOR(S): Singh, Sharat; Kim, Phillip
PATENT ASSIGNEE(S): Nestec S.A., Switz.
SOURCE: PCT Int. Appl., 77pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014122582	A1	20140814	WO 2014-IB58790	20140204

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2954068	A1	20151216	EP 2014-706699	20140204

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

PRIORITY APPLN. INFO.: US 2013-61761105 P 20130205
WO 2014-IB58790 W 20140204
AB The invention provides methods for therapy selection for a patient with non-small cell lung cancer (NSCLC) based on detecting, quantifying, and comparing the activity of particular signal transduction pathways, and components thereof, which can be represented as the patient's analyte index (e.g., EGFR/cMET index) and can be used to determine whether the patient is likely to respond to a particular therapy such as EGFR inhibitor therapy alone, cMET inhibitor therapy alone, or a combination thereof. The EGFR inhibitor is selected from the group consisting of cetuximab, panitumumab, matuzumab, nimotuzumab, Erbl vaccine, erlotinib, gefitinib, CL-387785 and a combination thereof, wherein the c-MET inhibitor is selected from the group consisting of ARQ197, XL184, GSK1363089/XL880, MP470, MGCD265, SGX523, PF04217903, JNJ38877605, INCB28060, AMG-458, E7050, MK-2461, BMS-777607 and a combination thereof. The invention also provides methods for determining drug resistance in non-small cell lung cancer (NSCLC) patients receiving above mentioned therapy.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 171 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1339983 CAPLUS Full-text
DOCUMENT NUMBER: 161:329247
TITLE: Improved treatment for adenoid cystic carcinoma comprising growth factor receptor kinase and MET kinase inhibitors
INVENTOR(S): Stenman, Goeran; Andersson, Mattias
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 116pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014123476	A1	20140814	WO 2014-SE50140	20140204

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

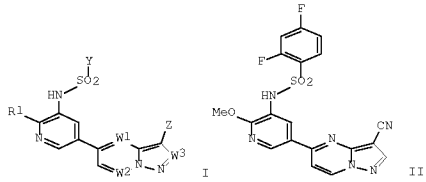
PRIORITY APPLN. INFO.: US 2013-61849920 P 20130205
AB The present application relates to inhibitors of epidermal growth factor receptor (EGFR) kinase, MET kinase, insulin receptor (IR) kinase and insulin-like growth factor 1 (IGF1R) kinase for use in the treatment of neoplastic disease such as adenoid cystic carcinoma (ACC) and dermal cylindroma characterized by MYB activation. In an optional embodiment, the kinase inhibitor inhibits the MET kinase and the EGFR kinase and/or the IGF1R/IR kinase. In an optional embodiment, the kinase inhibitor is BMS-754807. In an optional embodiment, the IGF1R/IR kinase inhibitor is selected from a group consisting of linsitinib and BMS-754807. In an optional embodiment, the EGFR kinase inhibitor is selected from a group consisting of gefitinib, erlotinib, BMS-690514 and cetuximab. In an optional embodiment, the MET kinase inhibitor is selected from a group consisting of crizotinib, BMS-907351, BMS-777607 and BMS-754807.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 172 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1274352 CAPLUS Full-text
DOCUMENT NUMBER: 161:361023
TITLE: Preparation of aryl-heterocyclic compounds for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 59pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103965199	A	20140806	CN 2014-10041929	20140128
PRIORITY APPLN. INFO.:			CN 2013-10040391 A	20130202
			CN 2013-10117077 A	20130404

OTHER SOURCE(S): CASREACT 161:361023; MARPAT 161:361023
GI



AB The present invention discloses aryl-heterocyclic compd. (with structure as shown in formula I), stereo isomers, geometrical isomers, tautomers, oxynitride, hydrates, solvates, metabolic products, pharmaceutically acceptable salts or prodrugs, pharmaceutical compns. containing thereof and application thereof in preparing agents for inhibiting or regulating the activity of protein kinases in biol. specimens. For example, compound II was prepared in a multi-step synthesis. The present invention also relates to pharmaceutical compns. containing the inventive compound, and application of the pharmaceutical compns. for treating mammal, particular human hyperproliferative disorders.

L8 ANSWER 173 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1273412 CAPLUS Full-text
DOCUMENT NUMBER: 162:67014
TITLE: Development of cabozantinib for the treatment of prostate cancer
AUTHOR(S): Vaishampayan, Ulka N.
CORPORATE SOURCE: Department of Oncology, Wayne State University/Karmanos Cancer Institute, Detroit, MI, USA
SOURCE: Core Evidence (2014), 9, 61-67, 7 pp.
CODEN: CEOVAF; ISSN: 1555-1741
DIGITAL OBJECT ID: 10.2147/CE.S67095
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (XL184) is a multitargeted receptor tyrosine kinase with predominantly MET and vascular endothelial growth factor inhibition properties. It is currently approved by the US Food and Drug Administration for the treatment of progressive metastatic medullary thyroid cancer. The agent has a convenient once-daily oral dosing schedule and has demonstrated encouraging activity in metastatic castrate-resistant prostate cancer (CRPC). A Phase I/II trial demonstrated responses in soft tissue, visceral disease, and bone metastases in CRPC. An objective response rate of 5%, a stable disease rate of 75%, and a median progression-free survival of 6 mo was observed As compared with the 140 mg daily dose used in thyroid cancer, a lower dose of 60 mg daily is currently being utilized in prostate cancer studies due to the fact that toxicity could be reduced without compromising efficacy. Randomized trials are ongoing in comparison with prednisone or with mitoxantrone and prednisone in pretreated metastatic CRPC. Cabozantinib has demonstrated a unique mechanism of action and preliminary efficacy in the crowded therapeutic field of prostate cancer. Since multiple therapies have recently demonstrated overall survival benefit in metastatic CRPC, cabozantinib will likely face some challenges in clin. application. At present, in this rapidly evolving field, it is unclear what proportion of patients with prostate cancer will be eligible to receive this therapy. The cost of cabozantinib is likely to be another deterrent, especially if it remains more expensive than other oral therapies, such as abiraterone and enzalutamide. Defining the role of MET overexpression and RET mutations as biomarkers in prostate cancer may help to guide patient selection, and enrich and enhance the future applications of this targeted novel agent.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 174 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1270460 CAPLUS Full-text
DOCUMENT NUMBER: 161:351479
TITLE: Degradation kinetics study of cabozantinib by a novel stability-indicating LC method and identification of its major degradation products by LC/TOF-MS and LC-MS/MS
AUTHOR(S): Wu, Chunyong; Xu, Xue; Feng, Chao; Shi, Yuanyuan; Liu, Wenyuan; Zhu, Xiaoyun; Zhang, Junying
CORPORATE SOURCE: Key Laboratory of Drug Quality Control and Pharmacovigilance, Ministry of Education, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2014), 98, 356-363
CODEN: JPBADA; ISSN: 0731-7085
DIGITAL OBJECT ID: 10.1016/j.jpba.2014.06.008
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The chem. stability of cabozantinib (CBZ) was investigated using a novel stability-indicating LC method. Forced degradation of CBZ was carried out under acidic, basic, thermal, oxidative and photolytic stress conditions. Hydrolysis and oxidation were the primary pathways for this compound and three major unknown degradation products were characterized by LC/TOF-MS and LC-MS/MS. The major oxidative degradation product was isolated by preparative LC and identified by UV, HRMS and NMR techniques to be N-{4-[(N-oxide-6,7-dimethoxyquinolin-4-yl)oxy]phenyl}-N'-(4-fluorophenyl)- cyclopropane-1,1-dicarboxamide. The developed method was validated as per ICH guidelines and then successfully applied to investigate the degradation kinetics of CBZ. Degradation of CBZ followed first-order kinetics under all exptl. conditions. A V-shaped pH-rate profile over the pH range 2-10 was observed with maximum stability at pH 6. The effect of temperature on the rate of CBZ degradation was characterized using the Arrhenius equation. The activation energy for hydrolysis was 57.31 kJ mol-1 in alkaline solution
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 175 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1237165 CAPLUS Full-text
DOCUMENT NUMBER: 162:55826
TITLE: Recent orphan drugs that are first-in-class
AUTHOR(S): Phillips, M. Ian; Lee, Jongserk R.
CORPORATE SOURCE: Keck Graduate Institute, Center for Rare Disease Therapies, 535 Watson Drive, Claremont, CA, 91711, USA
SOURCE: Expert Opinion on Orphan Drugs (2014), 2(8), 759-763
CODEN: EOODAJ; ISSN: 2167-8707
DIGITAL OBJECT ID: 10.1517/21678707.2014.931806
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Although the pipeline for new drugs seemed to be drying up, the number of new 'first-in-class' drugs appeared to be increasing. First-in-class drugs are those which use a new and unique mechanism for treating a disease or medical condition. They are a subset of new mol. entities (NMEs). The FDA reports that in 2012, 39 NMEs were approved. Twenty of these NMEs (.apprx. 50%) were identified by the FDA as first-in-class drugs. Of the 39 NMEs, 13 were designated orphan drugs and 9 of those orphan drugs were first-in-class. In 2013, there were 27 NMEs of which 9 were first-in-class. In 2013, nos. of NMEs are lower than the 2011 or 2012 but are based on fewer applications than in those years. There were 33% of NMEs that were first-in-class and 33% of the NMEs were orphan drugs. The FDA data indicate that creative new products are being developed for rare diseases.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 176 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1222486 CAPLUS Full-text
DOCUMENT NUMBER: 161:744871
TITLE: Cabozantinib-Induced Thyroid Dysfunction: A Review of Two Ongoing Trials for Metastatic Bladder Cancer and Sarcoma
AUTHOR(S): Yavuz, Sahzene; Apolo, Andrea B.; Kummar, Shivaani; del Rivero, Jaydira; Madan, Ravi A.; Shawker, Thomas; Reynolds, James; Celi, Francesco S.
CORPORATE SOURCE: National Institute of Diabetes and Digestive and Kidney Diseases, Diabetes, Endocrine, and Obesity Branch, National Institutes of Health, Bethesda, MD, USA
SOURCE: Thyroid (2014), 24(8), 1223-1231
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2013.0621
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Background: Thyroid dysfunction is a common adverse event associated with tyrosine kinase inhibitors (TKI), but its underlying pathophysiol. is unclear. Cabozantinib is a novel TKI currently Food and Drug Administration approved for advanced medullary thyroid cancer and tested in clin. trials on solid tumors including prostate, liver, bladder, breast, and ovarian cancer. Methods: We analyzed the thyroid function of patients enrolled in two phase 2 clin. trials using cabozantinib at the National Institutes of Health Clin. Center. Two cases of thyroiditis associated with cabozantinib therapy are presented in detail, and a systematic review of the literature on TKI-associated thyroid dysfunction is also discussed. Results: Between Sept. 2012 and Sept. 2013, 33 patients were treated with cabozantinib, and follow-up thyroid function tests were available for 31 (20 males, 11 females; age 59±1 years). Thyroid dysfunction was recorded in the majority of patients (93.1%), with a predominance of subclin. hypothyroidism. Two cases showed a biphasic pattern of thyroid dysfunction characterized by a transient thyrotoxicosis followed by hypothyroidism. Color Doppler demonstrated an increase in vascularization during the thyrotoxic phase, but no uptake was visualized on nuclear medicine imaging. A systematic review of the literature resulted in the identification of 40 original manuscripts, of which 13 were case series and 6 were case reports describing TKI-associated thyroid dysfunction. Conclusion: TKI therapy often results in clin. significant thyroid dysfunction. Cabozantinib treatment commonly results in thyroid dysfunction varying from subclin. hypothyroidism to symptomatic thyrotoxicosis. Early detection and characterization of cabozantinib-associated thyroid dysfunction and close follow-up are essential to provide adequate management of this common adverse event.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 177 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1212244 CAPLUS Full-text
DOCUMENT NUMBER: 161:731791
TITLE: Cabozantinib: A Review of Its Use in Patients with Medullary Thyroid Cancer
AUTHOR(S): Hoy, Sheridan M.
CORPORATE SOURCE: Springer, Auckland, N. Z.
SOURCE: Drugs (2014), 74(12), 1435-1444
CODEN: DRUGAY; ISSN: 0012-6667
DIGITAL OBJECT ID: 10.1007/s40265-014-0265-x
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (Cometriq) is an orally administered small mol. inhibitor of multiple tyrosine kinase receptors, including those involved in the pathogenesis of medullary thyroid cancer (MTC) [i.e. rearranged during transfection (RET), MET and vascular endothelial growth factor receptor (VEGFR)-2]. Cabozantinib is indicated for the treatment of adults with progressive, unresectable locally advanced (in the EU) or metastatic (in the EU and USA) MTC. Compared with placebo, cabozantinib significantly prolonged progression-free survival, reflecting a 72 % reduction in the risk of disease progression or death, in patients with unresectable, locally

advanced or metastatic MTC participating in a multinational, phase III study. A significantly higher proportion of patients receiving cabozantinib than those receiving placebo achieved an objective response or disease stabilization (i.e. a complete or partial response, or stable disease). The overall survival benefit with cabozantinib is as yet unclear, with no significant benefit observed in two interim analyses (one prespecified, and one unplanned and conducted at the request of the US FDA). The tolerability profile of oral cabozantinib is typical for a small mol. targeting the VEGFR and other tyrosine kinase-mediated pathways, with adverse events associated with the inhibition of the VEGF pathway (e.g. gastrointestinal perforation, hemorrhage, hypertension and venous thrombosis) reported in the phase III study. Treatment-emergent adverse events were generally managed with supportive therapy, dose redns. and/or dose interruptions. Although final overall survival data are awaited, current evidence suggests cabozantinib to be a valuable treatment option for adults with progressive, unresectable locally advanced or metastatic MTC.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 178 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1205266 CAPLUS Full-text

DOCUMENT NUMBER: 161:269288

TITLE: Hydrogen-bond surrogate peptides and peptidomimetics for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer

INVENTOR(S): Arora, Paramjit S.; Pan, Quintin; Mapp, Anna

PATENT ASSIGNEE(S): New York University, USA; The Ohio State University Research Foundation; University of Michigan

SOURCE: PCT Int. Appl., 98pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014113792	A1	20140724	WO 2014-US12331	20140121
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20140205681	A1	20140724	US 2014-14160018	20140121
US 20140220159	A1	20140807	US 2014-14160001	20140121

PRIORITY APPLN. INFO.: US 2013-61754574 P 20130119
US 2013-61874190 P 20130905

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 161:269288

AB The present invention relates to peptidomimetics for reactivating p53. Methods of using the peptidomimetics are also disclosed. One aspect of the present invention relates to a peptidomimetic, where the peptidomimetic mimics a helix having the formula X1-X2-X2-X3-X2-X2-X1-X4, wherein each X1 is any neg. charged residue, each X2 is any hydrophobic residue, X3 is any pos.-charged residue, and X4 is any polar residue. Addnl., the peptidomimetic may contain one or more bridges linking the side chains of its component amino acids. Another aspect of the present invention relates to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, the method comprising administering to the subject a peptidomimetic of the present invention under conditions effective to treat or prevent the disorder. Another aspect of the present invention relates to a method of inducing apoptosis and decreasing survival and/or proliferation of a cell, the method comprising contacting the cell with a peptidomimetic. In this study, the authors took a novel approach and functionally reactivated p53 in Human papillomaviruses (HPV)-pos. head and neck squamous cell carcinoma (HNSCC) by blocking the interaction between E6 and p300. Ectopic expression of the CH1 domain of p300 squelched E6 to disrupt E6-p300 association resulting in an increase in p53 acetylation, accumulation, and activity. CH1 domain inhibitors reactivated p53 and dramatically potentiated the efficacy of cisplatinum in HPV-pos. HNSCC. Taken together, the authors work revealed a novel druggable approach to reactivate p53 in HPV-pos. HNSCC that is expected to translate to other HPV-pos. carcinomas.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 179 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1202788 CAPLUS Full-text

DOCUMENT NUMBER: 161:269285

TITLE: Oligooxopiperazines for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer

INVENTOR(S): Arora, Paramjit S.; Pan, Quintin; Mapp, Anna

PATENT ASSIGNEE(S): New York University, USA; The Ohio State University Research Foundation; The Regents of the University of Michigan

SOURCE: PCT Int. Appl., 95pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014113794	A2	20140724	WO 2014-US12337	20140121
WO 2014113794	A3	20140912		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2898329	A1	20140724	CA 2014-2898329	20140121
US 20140205655	A1	20140724	US 2014-14160037	20140121
AU 2014207311	A1	20150820	AU 2014-207311	20140121
EP 2945631	A2	20151125	EP 2014-741084	20140121
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

PRIORITY APPLN. INFO.: US 2013-61754575 P 20130119
WO 2014-US12337 W 20140121

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 161:269285; MARPAT 161:269285

AB The present invention relates to oligooxopiperazines for reactivating p53. Methods of using the oligooxopiperazines are also disclosed. A first aspect of the present invention relates to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, the method comprising administering to the subject an oligooxopiperazine that substantially mimics helix αB of the C-terminal transactivation domain of Hypoxia-Inducible Factor Iα under conditions effective to treat or prevent the disorder. A second aspect of the present invention relates to a method of inducing apoptosis or decreasing survival and/or proliferation of a cell, the method comprising contacting the cell with an oligooxopiperazine. In this study, the authors took a novel approach and functionally reactivated p53 in Human papillomaviruses (HPV)-pos. head and neck squamous cell carcinoma (HNSCC) by blocking the interaction between E6 and p300. Ectopic expression of the CH1 domain of p300 squelched E6 to disrupt E6-p300 association resulting in an increase in p53 acetylation, accumulation, and activity. CH1 domain inhibitors reactivated p53 and dramatically potentiated the efficacy of cisplatinum in HPV-pos. HNSCC. Taken together, the authors work revealed a novel druggable approach to reactivate p53 in HPV-pos. HNSCC that is expected to translate to other HPV-pos. carcinomas. HMD: helix αB of C-terminal transactivation domain, of HIF-1α, mimics.

L8 ANSWER 180 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1160177 CAPLUS Full-text

DOCUMENT NUMBER: 161:239766

TITLE: Androgen receptor modulator for treatment of prostate cancer and other conditions

INVENTOR(S): Chen, Isan; Hager, Jeffrey H.; Maneval, Edna Chow; Herbert, Mark R.; Smith, Nicholas D.

PATENT ASSIGNEE(S): Aragon Pharmaceuticals, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 46pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

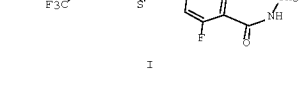
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140199236	A1	20140717	US 2014-14151106	20140109
CA 2898025	A1	20140724	CA 2014-2898025	20140109
WO 2014113260	A1	20140724	WO 2014-US10777	20140109
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014207839	A1	20150723	AU 2014-207839	20140109
IL 239741	A	20150831	IL 2014-239741	20140109
KR 2015105464	A	20150916	KR 2015-7021865	20140109
CN 105007920	A	20151028	CN 2014-80015802	20140109
EP 2945628	A1	20151125	EP 2014-701865	20140109
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CR 20150357	A	20150824	CR 2015-357	20150708

PRIORITY APPLN. INFO.: US 2013-61752842 P 20130115
WO 2014-US10777 W 20140109

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

GI



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AB The invention discloses the androgen receptor modulator I for the treatment of prostate cancer in combination with other therapeutic options and for the treatment of diseases or conditions that are amenable to treatment with the androgen receptor modulator, as well as pharmaceutical compns. and medicaments that include I.

L8 ANSWER 181 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1154296 CAPLUS Full-text

DOCUMENT NUMBER: 161:209516

TITLE: Predictive biomarker and method for combination therapy of EGFR and c-MET inhibitors in non-small cell lung cancer with wild type EGFR

INVENTOR(S): Lee, Mun Ja; Kim, Hyeon Jeong; Kang, Han Na
PATENT ASSIGNEE(S): JEUK Co., Ltd., S. Korea
SOURCE: Repub. Korea, 20pp.
CODEN: KRXXFC
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 1418970	B1	20140711	KR 2013-29977	20130320
PRIORITY APPLN. INFO.:			KR 2013-29977	20130320

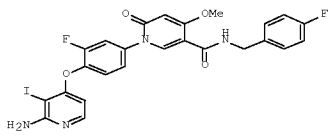
AB The title method comprises the steps of: detg. the p53 genotypes of patients, separating out the patients having cooperation tumor effect probability of combination therapy according to EGFR and c-MET inhibitors. Therefore, the condition of p53 can be used as predicative factor for combination therapy of EGFR and c-MET inhibitors.

L8 ANSWER 182 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1134083 CAPLUS Full-text
DOCUMENT NUMBER: 162:254986
TITLE: A Melanoma Cell State Distinction Influences Sensitivity to MAPK Pathway Inhibitors
AUTHOR(S): Konieczkowski, David J.; Johannessen, Cory M.; Abudayyeh, Omar; Kim, Jong Wook; Cooper, Zachary A.; Piris, Adriano; Frederick, Dennie T.; Barzily-Rokni, Michal; Straussman, Ravid; Haq, Rizwan; Fisher, David E.; Mesirov, Jill P.; Hahn, William C.; Flaherty, Keith T.; Wargo, Jennifer A.; Tamayo, Pablo; Garraway, Levi A.
CORPORATE SOURCE: Broad Institute of Harvard and MIT, Cambridge, MA, USA
SOURCE: Cancer Discovery (2014), 4(7), 816-827
CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID: 10.1158/2159-8290.CD-13-0424
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Most melanomas harbor oncogenic BRAFv600 mutations, which constitutively activate the MAPK pathway. Although MAPK pathway inhibitors show clin. benefit in BRAFV600-mutant melanoma, it remains incompletely understood why 10% to 20% of patients fail to respond. Here, we show that RAF inhibitor-sensitive and inhibitor-resistant BRAFv600-mutant melanomas display distinct transcriptional profiles. Whereas most drug-sensitive cell lines and patient biopsies showed high expression and activity of the melanocytic lineage transcription factor MITF, intrinsically resistant cell lines and biopsies displayed low MITF expression but higher levels of NF-κ signaling and the receptor tyrosine kinase AXL. In vitro, these MITF-low/NF-κβ-high melanomas were resistant to inhibition of RAF and MEK singly or in combination, and ERK. Moreover, in cell lines, NF- activation antagonized MITF expression and induced both resistance marker genes and drug resistance. Thus, distinct cell states characterized by MITF or NF-κβ activity may influence intrinsic resistance to MAPK pathway inhibitors in BRAFv600-mutant melanoma.
OS.CITING REF COUNT: 27 THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (27 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 183 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1064742 CAPLUS Full-text
DOCUMENT NUMBER: 161:455975
TITLE: A targeted next-generation sequencing assay detects a high frequency of therapeutically targetable alterations in primary and metastatic breast cancers: implications for clinical practice
AUTHOR(S): Vasan, Neil; Yelensky, Roman; Wang, Kai; Moulder, Stacy; Dzimitrowicz, Hannah; Avritscher, Rony; Wang, Bauang; Wu, Yun; Cronin, Maureen T.; Palmer, Gary; Symmans, W. Fraser; Miller, Vincent A.; Stephens, Phiup; Pusztai, Lajos
CORPORATE SOURCE: Yale University School of Medicine, Connecticut, New Haven, USA
SOURCE: Oncologist (2014), 19(5), 453-458
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2013-0377
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background. The aim of this study was to assess the frequency of potentially actionable genomic alterations in breast cancer that could be targeted with approved agents or investigational drugs in clin. trials using a next-generation sequencing-based genomic profiling assay performed in a Clin. Laboratory Improvement Amendments-certified and College of American Pathologists-accredited com. laboratory Methods. Fifty-one breast cancers were analyzed, including primary tumor biopsies of 33 stage I-II and 18 stage IV cancers (13 soft tissue, 3 liver, and 2 bone metastases). We assessed 3,230 exons in 182 cancer-related genes and 37 introns in 14 genes often rearranged in cancer for base substitutions, indels, copy number alterations, and gene fusions. The average median sequencing depth was 1,154×. Results. We observed 158 genomic alterations in 55 genes in 48 of 51 (94%) tumors (mean 3.1, range 0-9). The average number of potentially therapeutically relevant alterations was similar in primary (1.6, range 0-4) and in heavily pretreated metastatic cancers (2.0, range 0-4) (p = .24). The most common actionable alterations were in PIK3CA (n = 9, phosphatidylinositol 3-kinase [PI3K]/mammalian target of rapamycin [mTOR] inhibitors), NF1 (n = 7, PI3K/mTOR/mitogen-activated protein kinase inhibitors), v-akt murine thymoma viral oncogene homolog 1-3 (n = 7, PI3K/mTOR/AKT inhibitors), BRCA1/2 (n = 6, poly[ADP-ribose] polymerase inhibitors), and CCND1,2 and CCNE (n = 8)/cycline dependent kinase (CDK)6 (n = 1) (CDK4/6 inhibitors), KIT (n = 1, imatinib/sunitinib), ALK (n = 1, crizotinib), FGFR1,2 (n = 5, fibroblast growth factor receptor inhibitors), and EGFR (n = 2, epidermal growth factor receptor inhibitors). Our sequencing assay also correctly identified all six cases with HER2 (ERBB2) amplification by fluorescence in situ hybridization when tumor content was adequate. In addition, two known activating HER2 mutations were identified, both in unamplified cases. Conclusion. Overall, 84% of cancers harbored at least one genomic alteration linked to potential treatment options. Systematic evaluation of the predictive value of these genomic alterations is critically important for further progress in this field.
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 184 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1049484 CAPLUS Full-text
DOCUMENT NUMBER: 161:246290
TITLE: Design, synthesis and evaluation of highly selective pyridone-based class II MET inhibitors
AUTHOR(S): She, Nengfang; Zhuo, Linsheng; Jiang, Wen; Zhu, Xiaolei; Wang, Jia; Ming, Zhihui; Zhao, Xinge; Cong, Xin; Huang, Wei
CORPORATE SOURCE: Key Laboratory of Pesticide and Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Wuhan, 430079, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2014), 24(15), 3351-3355
CODEN: BMCLE8; ISSN: 0960-894X
DIGITAL OBJECT ID: 10.1016/j.bmcl.2014.05.097
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 161:246290
GI



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AB The high incidence of MET oncogene activation in human malignancies has prompted researchers to develop MET inhibitors. As part of our efforts to developing effective and safe therapeutic agents against MET-dependent tumors, a pyridone-based class II MET inhibitor, namely, 1-(4-((2-amino-3-iodopyridin-4-yl)-oxy)-3-fluorophenyl)-N-(4-fluorobenzyl)- 4-methoxy-6-oxo-1,6-dihydropyridine-3-carboxamide (3s, I), was identified. Knowledge of the binding mode of class II MET inhibitors led to the design of new inhibitors that utilize 2-pyridone to conformationally restrain key pharmacophoric groups within the mol. Integrated mol. docking and SAR studies resulted in the discovery of a novel class of pyridone MET inhibitors with high potency (IC50 of 0.005 μM) and efficient selectivity (>5000 fold) to VEGFR-2, c-Kit and RET kinases.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 185 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1006107 CAPLUS Full-text
DOCUMENT NUMBER: 161:238658
TITLE: Advanced thyroid cancers: new era of treatment
AUTHOR(S): Mohammed, Amrallah A.; El-Shentenawy, Ayman
CORPORATE SOURCE: Oncology Center, King Abdullah Medical City-Holy Capital, Makkah, 21995, Saudi Arabia
SOURCE: Medical Oncology (New York, NY, United States) (2014), 31(7), 1-8
CODEN: MONCEZ; ISSN: 1357-0560
DIGITAL OBJECT ID: 10.1007/s12032-014-0049-x
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Since chemotherapy has been shown to be unsuccessful in case of advanced thyroid carcinomas, the research for new therapies is fundamental. Clin. trials of many tyrosine kinase inhibitors as well as anti-angiogenic inhibitors suggest that patients with thyroid cancer could have an advantage with new target therapy. Recently, Food and Drug Administration approved two targeted therapies, vandetanib and cabozantinib for the treatment of metastatic thyroid carcinomas with acceptable outcome. We summarized the results and the toxic effects associated with these treatments reported in clin. trials. Future trials should aim at combinations of targeted agents with or without other treatment modalities to obtain a more effective result in thyroid carcinoma treatment.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 186 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:969861 CAPLUS Full-text
DOCUMENT NUMBER: 161:455940
TITLE: Role of salvage targeted therapy in differentiated thyroid cancer patients who failed first-line sorafenib
AUTHOR(S): Dadu, Ramona; Devine, Catherine; Hernandez, Mike; Waguespack, Steven G.; Busaidy, Naifa L.; Hu, Mimi I.; Jimenez, Camilo; Habra, Mouhammad A.; Sellin, Rena V.; Ying, Anita K.; Cote, Gilbert J.; Sherman, Steven I.; Cabanillas, Maria E.
CORPORATE SOURCE: Departments of Endocrine Neoplasia and Hormonal Disorders, Baylor College of Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2014), 99(6), 2086-2094
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2013-3588
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Context: Sorafenib, a tyrosine kinase inhibitor, is a common first-line therapy for advanced differentiated thyroid cancer (DTC). However, responses are not durable and drug toxicity remains a problem. Objective: The objective of the study was to determine the efficacy of salvage therapy after first-line sorafenib failure. Design: This was a retrospective review at M. D. Anderson Cancer Center from Jan. 2005 to May 2013. Patients: The study included patients with metastatic DTC who received salvage therapy after their initial sorafenib failure (group 2). Patients who received first-line sorafenib only (group 1) were evaluated for comparison of overall

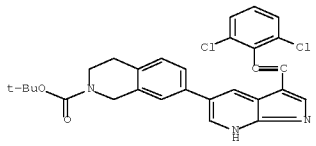
survival (OS). Outcome Measures: Progression-free survival, best response, and median OS were measured. Results: Sixty-four patients with metastatic, radioactive iodine refractory DTC were included; 35 were in group 1 and 25 were in group 2, and the groups were well balanced. Median OS of all 64 patients receiving first line sorafenib was 37 mo; median OS was significantly longer with salvage therapy compared with sorafenib alone (58 vs 28 mo, P = .013). In group 2, 17 patients were evaluable for best response, although two patients had toxicity with sorafenib, which was discontinued before restaging. Best responses with first-line sorafenib were partial response in 2 of 15 (13%), stable disease in 10 of 15 (67%), and progressive disease in 3 of 15 (20%) patients. With salvage therapy, partial responses were seen in 7 of 17 (41%) and stable disease in 10 of 17 (59%) patients. Median progression-free survival was 7.4 mo with first-line sorafenib and 11.4 mo with salvage therapy. Salvage therapy included sunitinib (n = 4), pazopanib (n = 3), cabozantinib (n = 4), lenvatinib (n = 3), and vemurafenib (n = 3). Conclusions: Other targeted agents are effective salvage treatments after sorafenib failure, despite similar mechanisms of action, and should be offered to patients who are able to receive salvage therapy.
OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 187 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:951549 CAPLUS Full-text
DOCUMENT NUMBER: 161:86164
TITLE: Preparation of pyridine compounds as protein tyrosine kinase inhibitors for treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wang, Ruyong; Wang, Liang
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 158pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014089324	A1	20140612	WO 2013-US73367	20131205
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2012-61734903 P 20121207
US 2013-61880184 P 20130920
OTHER SOURCE(S): CASREACT 161:86164; MARPAT 161:86164

GI



AB The present invention provides novel substituted alkynyl compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 189 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:943695 CAPLUS Full-text
DOCUMENT NUMBER: 161:196584
TITLE: Adverse events of targeted therapies
AUTHOR(S): Klastersky, Jean A.
CORPORATE SOURCE: Institut Jules Bordet, Centre des Tumeurs de l'Universite Libre de Bruxelles, Brussels, Belg.
SOURCE: Current Opinion in Oncology (2014), 26(4), 395-402
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0000000000000096
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Purpose of review: There is currently an explosion in the no. of so-called targeted therapies. As new indications for these agents multiply, there is also an increase of new and less new side-effects. Recent findings: Given this rapidly evolving field, any literature on that topic is rapidly obsolete and needs re-evaluation. Summary: Targeted therapies are associated with a wide spectrum of adverse events, which cannot always be easily separated from the complications linked to cancer, its therapy, and comorbidities. A high awareness of these events might improve the patient's quality of life and contribute to the recognition of new syndromes.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 190 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridinyl compds. of general formula I, pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. For I, each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; X is C6-C10 aryl or 5-10 membered heteroaryl that are optionally substituted; and Y is an (un)substituted bicyclic heterocyclyl. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 6-step reaction that culminated in coupling of intermediates III and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-ol. Example compds. of the invention were tested in ALK and c-Met kinase inhibition assays. Pharmacokinetic profiles were also examined in rats, as was compound stability in human and rat liver microsomes.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 188 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:951212 CAPLUS Full-text
DOCUMENT NUMBER: 161:94410
TITLE: Alkynyl compounds and methods of use
INVENTOR(S): Xi, Ning; Li, Xiaobo; Zhou, Shiqing
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014089280	A1	20140612	WO 2013-US73286	20131205
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2012-61734897 P 20121207
OTHER SOURCE(S): CASREACT 161:94410; MARPAT 161:94410

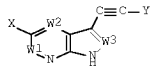
ACCESSION NUMBER: 2014:926742 CAPLUS Full-text
DOCUMENT NUMBER: 161:316322
TITLE: Cabozantinib Suppresses Tumor Growth and Metastasis in Hepatocellular Carcinoma by a Dual Blockade of VEGFR2 and MET
AUTHOR(S): Xiang, Qingfeng; Chen, Weiqiang; Ren, Meng; Wang, Jingnan; Zhang, Hongwu; Deng, David Y. B.; Zhang, Lei; Shang, Changzhen; Chen, Yajin
CORPORATE SOURCE: Departments of Hepatopancreatobiliary Surgery, Sun Yat-sen University, Guangzhou, Peop. Rep. China
SOURCE: Clinical Cancer Research (2014), 20(11), 2959-2970
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-2620
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB MET signaling was suggested a potential role in hepatocellular carcinoma (HCC) and associated with prometastasis during antiangiogenesis therapy. We investigated the potential association between MET expression and therapeutic response to sorafenib in patients with HCC. Antitumor effects of cabozantinib, a dual inhibitor of MET and VEGFR2, were examined in cultured HCC cells as well as in vivo models. Total MET and phosphorylated MET (p-MET) were measured in 29 resected HCC specimens, and correlated with response to sorafenib as postoperative adjuvant therapy. In the second set of expts. using cultured HCC cells, and mouse xenograft and metastatic models, effects of cabozantinib were examined High level of p-MET in resected HCC specimens was associated with resistance to adjuvant sorafenib therapy. In cultured HCC cells that expressed p-MET, cabozantinib inhibited the activity of MET and its downstream effectors, leading to G1-phase arrest. Cabozantinib inhibited tumor growth in p-MET-pos. and p-MET-neg. HCC by decreasing angiogenesis, inhibiting proliferation, and promoting apoptosis, but it exhibited more profound efficacy in p-MET-pos. HCC xenografts. Cabozantinib blocked the hepatocyte growth factor (HGF)-stimulated MET pathway and inhibited the migration and invasion of the HCC cells. Notably, cabozantinib reduced the number of metastatic lesions in the lung and liver in the exptl. metastatic mouse model. Patients with HCC with high level of p-MET are associated with resistance to adjuvant sorafenib treatment. The dual blockade of VEGFR2 and MET by cabozantinib has significant antitumor activities in HCC, and the activation of MET in HCC may be a promising efficacy-predicting biomarker. Clin Cancer Res; 20(11); 2959-70. ©2014 AACR.
OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS 10:402977 CAPLUS HYPERLINK "http://chemport.cas.oREFERENCE COUNT: 38
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 191 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:923002 CAPLUS Full-text
DOCUMENT NUMBER: 161:99226
TITLE: Heterocyclic alkynyl compound, and its use and application as cell proliferation inhibitor and for regulating the activity of protein kinases
INVENTOR(S): Xi, Ning; Li, Xiaobo; Zhou, Shiqing
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 64pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent

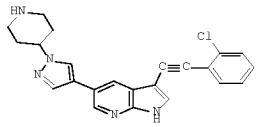
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103833753	A	20140604	CN 2013-10590780	20131121

PRIORITY APPLN. INFO.: CN 2012-10477798 A 20121122
CN 2013-10116694 A 20130403
OTHER SOURCE(S): MARPAT 161:99226
GI



I



II

AB The present invention provides new substituted alkynyl compds. with the formula of I [W1-4 independently = N or CRc, wherein Rc = H, D, F, Cl, Br, etc.; X = Ph, pyridinyl, pyrrolyl, pyrazolyl, etc.; Y = (un)substituted aryl or heteroaryl], pharmaceutically acceptable salts thereof, pharmaceutical formulation thereof, and their use in regulating the activity of protein kinases and regulating the signal response in cells or between cells. Thus, e.g., II was prepared in a multi-step synthesis. Compds. of the invention were tested for their stability and Alk, c-Met kinase inhibitory activity, e.g., II showed IC50 value of 58 nM against Alkaline The present invention also relates to pharmaceutical compns. comprising a compound of the present invention, and using the pharmaceutical composition for treating a mammal, particularly to human hyperproliferative disorders.

L8 ANSWER 192 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:913474 CAPLUS Full-text
DOCUMENT NUMBER: 161:46548
TITLE: Cabozantinib capsule composition and its production method
INVENTOR(S): Wang, Luanqiu; Wang, Xinyao
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103830203	A	20140604	CN 2014-10078549	20140305

PRIORITY APPLN. INFO.: CN 2014-10078549 20140305
AB The invention provides a cabozantinib capsule compn. and its prodn. method. The cabozantinib capsule composition is composed of cabozantinib 10-60wt%, carrier 15-70 wt%, organic solvent 10-30wt%, surfactant 0.5-3.0wt%, micronized silica gel 1.0-3.0wt% and starch 5.0-20wt%. The carrier comprises one or more of glycerol monostearate, polyethylene glycol 6000, cetyl alc. and octyl alc. The organic solvent comprises one or more of ethanol, methanol and acetone. The surfactant comprises one or more of sodium dodecyl sulfate, Tween 80 and lecithin. The production method includes adding carrier into organic solvent, heating to 60℃, adding cabozantinib and surfactant, vacuum drying at 40℃, comminution by gas stream to obtain powder with grain size of 1-8 μm, adding micronized silica gel and starch, mixing, and packaging in. The produced cabozantinib capsule preparation has good oral absorption, high dissoln. rate, high bioavailability, and can remarkably inhibit the growth of tumor volume The invention has simple preparation process, low cost, and applicability for com. process.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 193 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:873778 CAPLUS Full-text
DOCUMENT NUMBER: 161:77594
TITLE: Hydrophilic linkers and their uses for conjugation of drugs to cell binding molecules
INVENTOR(S): Zhao, R. Yongxin
PATENT ASSIGNEE(S): Hangzhou Dac Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 102pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014080251	A1	20140530	WO 2012-IB56700	20121124

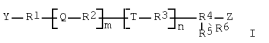
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2891280	A1	20140530	CA 2012-2891280	20121124
AU 2012395148	A1	20150521	AU 2012-395148	20121124
EP 2922818	A1	20150930	EP 2012-888899	20121124

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

US 20150250896	A1	20150910	US 2015-14432073	20150327

PRIORITY APPLN. INFO.: WO 2012-IB56700 W 20121124
OTHER SOURCE(S): CASREACT 161:77594; MARPAT 161:77594
GI



I

AB Prepn. of cell binding agent-drug conjugates comprising hydrophilic linker of formula (I), wherein:Y represents a functional group that enables reaction with a cell-binding agent; Q and T are either -P(=O)(OM)-, or -S(D)-, or -S(O)-;m and n are integer from 0 to 5, but not 0 at the same time; In addition, when m = I, n = 0, Q is not -P(=O)(OM)-; or when n = I, m = 0, T is not -P(=O)(OM)-;Z represents a functional group that enables linkage of a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ether, ester, carbamate, carbonate, amine (secondary, tertiary, or quartary), imine, cycloheteroalkyane, heteroarom., alkoxime or amide bond; R1, R2, R3, R4, R5 and R6, are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl, or 1-6 carbon atoms of esters, ether, amide, or polyethyleneoxy unit of formula (OCH2CH2)p, wherein p is an integer from 0 to about 1000, or combination thereof and methods of using such linkers and conjugates in pharmaceutical dosage forms for combination therapy of cancer, autoimmune and infectious diseases are provided.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 194 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:814874 CAPLUS Full-text
DOCUMENT NUMBER: 161:466864
TITLE: Aerodigestive Fistula Formation as a Rare Side Effect of Antiangiogenic Tyrosine Kinase Inhibitor Therapy for Thyroid Cancer
AUTHOR(S): Blevins, Dean P.; Dadu, Ramona; Hu, Mimi; Baik, Christina; Balachandran, Diwakar; Ross, William; Gunn, Brandon; Cabanillas, Maria E.
CORPORATE SOURCE: Department of Internal Medicine, University of Texas Health Science Center at Houston, Houston, TX, USA
SOURCE: Thyroid (2014), 24(5), 918-922
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2012.0598
PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: In the past decade, targeted therapy with antiangiogenic drugs has become standard of care for most types of metastatic, progressive thyroid cancer. While these drugs were thought initially to be less toxic than traditional chemotherapy, they can have rare but serious and fatal toxicities. Once such toxicity that has been reported in other tumor types is upper airway fistula formation, which can be life-threatening. Summary: Here, we describe three patients treated with antiangiogenic tyrosine kinase inhibitors at two academic institutions who developed aerodigestive fistula. All three patients had risk factors for fistula formation, which included external beam radiation and/or large tumor with invasion of the tracheal wall. Conclusions: Fistula formation is a known but rare side effect of antiangiogenic tyrosine kinase inhibitors. Knowledge of the risk factors that may predispose thyroid cancer patients to this serious adverse event is vital prior to prescribing antiangiogenics. Particular caution should be observed when using these drugs in patients undergoing radiation therapy or surgery, or in patients whose tumor is invading vital structures of the neck, as they may be at higher risk of developing this rare complication. In these patients, antiangiogenic tyrosine kinase inhibitors should be used cautiously, patients should be aware of the risk, and physicians should monitor patients for symptoms of fistula.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 195 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:794981 CAPLUS Full-text
DOCUMENT NUMBER: 160:740120
TITLE: Preparation of heteroaromatic compounds as protein kinase modulators for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 57pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140134133	A1	20140515	US 2013-14076256	20131110
CA 2889346	A1	20140522	CA 2013-2889346	20131110
WO 2014078211	A1	20140522	WO 2013-US69366	20131110

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

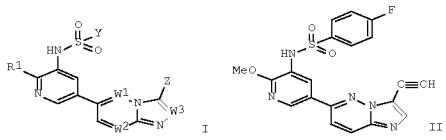
AU 2013345107	A1	20150430	AU 2013-345107	20131110
CN 104755085	A	20150701	CN 2013-80054625	20131110
KR 2015083833	A	20150720	KR 2015-7008264	20131110
EP 2919784	A1	20150923	EP 2013-855522	20131110
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015536994	T	20151224	JP 2015-541973	20131110

PRIORITY APPLN. INFO.: US 2012-61726139 P 20121114
WO 2013-US69366 W 20131110

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 160:740120; MARPAT 160:740120

GI



I

II

AB The invention provides heteroarom. derivs. and pharmaceutically acceptable salts and formulations thereof useful in modulating the protein kinase activity, especially phosphatidylinositol 3-kinases (PI3K) and mTOR kinase, and in modulating inter- and/or intra-cellular signaling activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Compds. of formula I [wherein W1, W2, and W3 are independently N or CRc; Z is D CN, N3, etc.; Y is C1-C6 alkyl, C3-C6 cycloalkyl, C3-C6 heterocyclyl, etc.; R1 is H, C1, C3-C6 cycloalkyl, etc.; each Rc is independently H, D, F, etc.] or stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, prodrugs, or pharmaceutically acceptable salts thereof are claimed and exemplified. For example, II was prepared in five steps (procedure given). Candidate compds. of I were assayed for their stability in liver microsomes, their oral and i.v. bioavailability, and inhibitory activity against PI3K and mTOR kinase (data given).

L8 ANSWER 196 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:718961 CAPLUS Full-text
DOCUMENT NUMBER: 160:630742
TITLE: Replication-competent retroviral vectors for gene therapy using mini-promoters
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Lin, Amy H.; Logg, Christopher R.; Kasahara, Noriyuki
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: PCT Int. Appl., 89pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014066700	A1	20140501	WO 2013-US66709	20131024
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2909324	A1	20150826	EP 2013-849839	20131024
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104884627	A	20150902	CN 2013-80067486	20131024
JP 2015533510	T	20151126	JP 2015-539817	20131024
US 20150273029	A1	20151001	US 2015-14438564	20150424

PRIORITY APPLN. INFO.: US 2012-61718610 P 20121025
WO 2013-US66709 W 20131024

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Compact replicating retroviral vectors using a minimal promoter to express a therapeutic gene with a size of 0.9-1.9 kb are described. An internal ribosome entry sequence may be used for polycistronic expression cassettes. The vectors do not use the prior art SCP1, Ad, or CMV core promoters. Development and optimization of vectors is described.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 197 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:711027 CAPLUS Full-text
DOCUMENT NUMBER: 160:643049
TITLE: Cabozantinib dispersible tablet and preparation method thereof
INVENTOR(S): Peng, Zongyu; Li, Ran; Zheng, Feibo
PATENT ASSIGNEE(S): Qingdao Cancer Hospital, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103751140	A	20140430	CN 2014-10017920	20140115

PRIORITY APPLN. INFO.: CN 2014-10017920 20140115

AB The invention discloses Cabozantinib dispersible tablet and prepn. method and application thereof. The inventive Cabozantinib dispersible tablet consists of the following component according to weight percentage: Cabozantinib 10-60%, filler 10-40%, disintegrant 10-50%, acidulant 10-50%, binder 0.1-10%, and lubricant and glidant 0.1-20%. Compared with the common tablet, the inventive dispersible tablet contains no surfactant, its solubility, dispersivity, and disintegrability are good, and it can be completely disintegrated within 1 min. The prepared Cabozantinib dispersible tablet has high dissoln. rate, high bioavailability, rapid distribution in vivo, stable quality, and good taste. The preparation method is simple, and suitable for industrial production

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 198 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:679549 CAPLUS Full-text
DOCUMENT NUMBER: 161:30896
TITLE: Cabozantinib: a new molecular targeted antitumor drug
AUTHOR(S): Zhang, Xiu-ying; Liu, Yao; Bai, Qiu-jiang; Wang, Nan
CORPORATE SOURCE: Department of Pharmacy, Kailuan General Hospital, Tangshan, Hebei Province, 063000, Peop. Rep. China
SOURCE: Yiyao Daobao (2013), 32(11), 1468-1470
CODEN: YDIAAL; ISSN: 1004-0781
DIGITAL OBJECT ID: 10.3870/yydb.2013.11.021
PUBLISHER: Yiyao Daobao Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review. Cabozantinib, a new mol. targeted antitumor drug, was introduced with several subsections as follow: action mechanisms, pharmacokinetics, adverse reactions, drug interactions, clin. trials, and conclusions.

L8 ANSWER 199 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:653844 CAPLUS Full-text
DOCUMENT NUMBER: 161:257408
TITLE: Preclinical Evaluation of Imaging Biomarkers for Prostate Cancer Bone Metastasis and Response to Cabozantinib
AUTHOR(S): Graham, Timothy J.; Box, Gary; Tunariu, Nina; Crespo, Mateus; Spinks, Terry J.; Miranda, Susana; Attard, Gerhardt; de Bono, Johann; Eccles, Suzanne A.; Davies, Faith E.; Robinson, Simon P.
CORPORATE SOURCE: Division of Radiotherapy and Imaging, Institute of Cancer Research and Royal Marsden NHS Trust, Surrey, SM2 5NG, UK
SOURCE: Journal of the National Cancer Institute (2014), 106(4), ???
CODEN: JNCIEQ; ISSN: 0027-8874
DIGITAL OBJECT ID: 10.1093/jnci/dju033
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background Prostate cancer is incurable once it has metastasized to the bone. Appropriate preclin. models are lacking. The therapeutic efficacy of the multikinase inhibitor cabozantinib was assessed in an orthotopic xenograft model of castration-resistant prostate cancer (CRPC) bone metastasis using noninvasive, multimodality functional imaging. Methods NOD/SCID mice were injected intratibially with luciferase-expressing ERG (v-ets avian erythroblastosis virus E26 oncogene homolog) rearranged VCaP human prostate carcinoma cells. The response of VCaP xenografts (n = 7 per group) to cabozantinib was investigated using bioluminescence imaging and anatomical and diffusion weighted magnetic resonance imaging. This enabled quantitation of tumor volume and apparent diffusion coefficient (ADC). Bone uptake of technetium-methylene diphosphonate (99mTc-MDP) was assessed by single-photon emission computed tomog. Ex vivo micro computed tomog. was used to quantify bone volume and correlated with appropriate histopathol. Statistical significance was determined using the two-sided Mann-Whitney test or Wilcoxon signed rank test. Results VCaP xenografts were predominantly osteosclerotic with some osteolytic activity. Fluorescent in situ hybridization anal. confirmed retention of ERG oncogene rearrangements. Cabozantinib induced a statistically significant 52% reduction in tumor luminance (P = .02) and stasis in tumor volume after 15 days of treatment. Tumor ADC statistically significantly increased with cabozantinib and was associated with extensive necrosis (after 10 days, mean tumor ADC ± SD = 556±43×10-6 mm2/s vs pretreatment ADC = 485±43×10-6 mm2/s; P = .02). Tumor-associated uptake of 99mTc-MDP was statistically significantly reduced after 3 days of treatment (P = .02), sustained over 15 days treatment, and associated with a statistically significant (P = .048) reduction in bone growth on the tibial cortex, yet a highly statistically significant (P = .001) increase in trabecular bone volume Conclusions The intratibial VCaP model faithfully emulates clin. disease. Cabozantinib exerts potent effects on both tumor and tumor-induced bone matrix remodeling, and quantitation of ADC provides a clin. translatable imaging biomarker for early, sensitive assessment of treatment response in CRPC bone metastasis.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 200 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:628215 CAPLUS Full-text
DOCUMENT NUMBER: 160:542029
TITLE: Method for the diagnosis, prognosis and treatment of prostate cancer metastasis
INVENTOR(S): Gomis, Roger; Jean-Mairet, Joel
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 140pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014057357	A2	20140417	WO 2013-IB2866	20131009
WO 2014057357	A3	20140530		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE,				

EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2888122	A1	20140417	CA 2013-2888122		20131009
US 20140105918	A1	20140417	US 2013-14050262		20131009
AU 2013328385	A1	20150507	AU 2013-328385		20131009
EP 2906718	A2	20150819	EP 2013-821939		20131009
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
KR 2015105297	A	20150916	KR 2015-7012297		20131009
CN 104995313	A	20151021	CN 2013-80060218		20131009
US 20150362495	A1	20151217	US 2015-14435128		20150410
PRIORITY APPLN. INFO.:			US 2012-61713318	P	20121012
			WO 2013-IB2866	W	20131009

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to a method for the diagnosis or the prognosis of metastasis in prostate cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for the diagnosis or the prognosis of metastasis in prostate cancer, as well as to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which, comprise determining the c-MAF expression level. Finally, the invention relates to the use of a c-MAF inhibitor as therapeutic target for treating the prostate cancer.

L8 ANSWER 201 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2014:581585 CAPLUS Full-text
DOCUMENT NUMBER:	160:555604
TITLE:	Phage display derived peptides highly specific against Mdm2/Mdm4 and methods for treating cancer
INVENTOR(S):	Joseph, Thomas Leonard; Verma, Chandra Shekhar; Lane, David Phillip; Brown, Christopher John
PATENT ASSIGNEE(S):	Agency for Science, Technology and Research, Singapore
SOURCE:	PCT Int. Appl., 61pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014055039	A1	20140410	WO 2013-SG428	20131001
WO 2014055039	A9	20141106		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2904000	A1	20150812	EP 2013-844064		20131001
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
US 20150246946	A1	20150903	US 2015-14432729		20150331
PRIORITY APPLN. INFO.:			SG 2012-7302	A	20121001
			WO 2013-SG428	W	20131001

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 160:555604

AB By using a phage display derived peptide as an initial template, compds. have been developed that are highly specific against Mdm2/Mdm4. These compds. exhibit greater potency in p53 activation and protein-protein interaction assays than a compound derived from the p53 wild-type sequence. Unlike nutlin, a small mol. inhibitor of Mdm2/Mdm4, the phage derived compds. can arrest cells resistant to p53 induced apoptosis over a wide concentration range without cellular toxicity, suggesting they are highly suitable for cyclo-therapy. In one embodiment, there is disclosed the peptide comprising or consisting o f the amino acid sequence of SEQ ID NO 1 (TSFXaaiEYWXaa3LLXaai), wherein Xaa3 can be N or A and wherein in case Xaa3 is N, Xaai is not A and/or Xaa2 is not S. In one embodiment, Xaa3 can be any type of amino acid other than A and wherein in case Xaa3 is N, Xaaj is not A and/or Xaa2 is not S. Those peptides have been shown to inhibit the p53:Mdm2 interactions with a nanomolar affinity.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 202 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2014:565947 CAPLUS Full-text
DOCUMENT NUMBER:	161:208503
TITLE:	First-, second-, third-line therapy for mRCC: benchmarks for trial design from the IMDC
AUTHOR(S):	Ko, J. J.; Choueiri, T. K.; Rini, B. I.; Lee, J.-L.; Kroeger, N.; Srinivas, S.; Harshman, L. C.; Knox, J. J.; Bjarnason, G. A.; MacKenzie, M. J.; Wood, L.; Vaishampayan, U. N.; Agarwal, N.; Pal, S. K.; Tan, M.-H.; Rha, S. Y.; Yuasa, T.; Donskov, F.; Bamias, A.; Heng, D. Y. C.
CORPORATE SOURCE:	Tom Baker Cancer Center, University of Calgary, Calgary, AB, Can.
SOURCE:	British Journal of Cancer (2014), 110(8), 1917-1922 CODEN: BJCAAI; ISSN: 0007-0920
DIGITAL OBJECT ID:	10.1038/bjc.2014.25
PUBLISHER:	Nature Publishing Group
DOCUMENT TYPE:	Journal; (online computer file)
LANGUAGE:	English

AB Background: Limited data exist on outcomes for metastatic renal cell carcinoma (mRCC) patients treated with multiple lines of therapy. Benchmarks for survival are required for patient counselling and clin. trial design. Methods: Outcomes of mRCC patients from the International mRCC Database Consortium database treated with 1, 2, or 3+ lines of targeted therapy (TT) were compared by proportional hazards regression. Overall survival (OS) and progression-free survival (PFS) were calculated using different population inclusion criteria. Results: In total, 2705 patients were treated with TT of which 57% received only first-line TT, 27% received two lines of TT, and 16% received 3+ lines of TT. Overall survival of patients who received 1, 2, or 3+ lines of TT were 14.9, 21.0, and 39.2 mo, resp., from first-line TT (P<0.0001). On multivariable anal., 2 lines and 3+ lines of therapy were each associated with better OS (HR=0.738 and 0.626, P<0.0001). Survival outcomes for the subgroups were as follows: for all patients, OS 20.9 mo and PFS 7.2 mo; for those similar to eligible patients in the first-line ADAPT trial, OS 14.7 mo and PFS 5.6 mo; for those similar to patients in first-line TIVO-1 trial, OS 24.8 mo and PFS 8.2 mo; for those similar to patients in second-line INTORSECT trial, OS 13.0 mo and PFS 3.9 mo; and for those similar to patients in the third-line GOLD trial, OS 18.0 mo and PFS 4.4 mo. Conclusions: Patients who are able to receive more lines of TT live longer. Survival benchmarks provide context and perspective when interpreting and designing clin. trials.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 203 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2014:542996 CAPLUS Full-text
DOCUMENT NUMBER:	161:267984
TITLE:	Bone-targeted therapies in metastatic castration-resistant prostate cancer: evolving paradigms
AUTHOR(S):	El-Amm, Joelle; Freeman, Ashley; Patel, Nihar; Aragon-Ching, Jeanny B.
CORPORATE SOURCE:	Division of Hematology/Oncology, Department of Medicine, George Washington University Medical Center, Washington, DC, 20037, USA
SOURCE:	Prostate Cancer (2013) 210686/1-210686/11, 11 pp. CODEN: PCRACU; ISSN: 2090-312X
DIGITAL OBJECT ID:	10.1155/2013/210686
PUBLISHER:	Hindawi Publishing Corp.
DOCUMENT TYPE:	Journal; General Review; (online computer file)
LANGUAGE:	English

AB A review. Majority of patients with metastatic castrate resistant prostate cancer (mCRPC) develop bone metastases which results in significant morbidity and mortality as a result of skeletal-related events (SREs). Several bone-targeted agents are either in clin. use or in development for prevention of SREs. Bisphosphonates were the first class of drugs investigated for prevention of SREs and zoledronic acid is the only bisphosphonate that is FDA-approved for this indication. Another bone-targeted agent is denosumab which is a fully humanized monoclonal antibody that binds to the RANK-L thereby inhibiting RANK-L mediated bone resorption.While several radiopharmaceuticals were a approved for pain palliation in mCRPC including strontium and samarium, alpharadin is the first radiopharmaceutical to show significant overall survival benefit. Contemporary therapeutic options including enzalutamide and abiraterone have effects on pain palliation and SREs as well. Other novel bone-targeted agents are currently in development, including the receptor tyrosine kinase inhibitors cabozantinib and dasatinib. Emerging therapeutics in mCRPC has resulted in great strides in preventing one of the most significant sources of complications of bone metastases.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

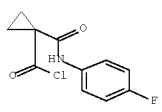
L8 ANSWER 204 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2014:479457 CAPLUS Full-text
DOCUMENT NUMBER:	160:515456
TITLE:	Synthesis method of antitumor therapeutic drug of cabozantinib
INVENTOR(S):	Cai, Jianping; Chen, Zengfei; Zhang, Lifeng; Fang, Ying
PATENT ASSIGNEE(S):	Suzhou Moer Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE:	Faming Zhuanli Shenqing, 9pp. CODEN: CNXXEV
DOCUMENT TYPE:	Patent
LANGUAGE:	Chinese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103664778	A	20140326	CN 2013-10631287	20131127
PRIORITY APPLN. INFO.:			CN 2013-10631287	20131127

OTHER SOURCE(S): CASREACT 160:515456; MARPAT 160:515456

GI



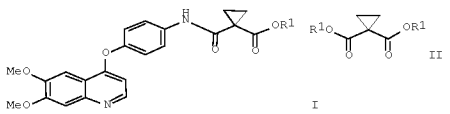
AB The invention discloses a synthesis method of antitumor therapeutic drug of cabozantinib., comprising: using 4-(6, 7- dimethoxy quinoline -4- oxy)-phenylamine to react with 1-((4- fluorophenyl) carbamoyl) cyclopropyl acyl halide, an acid-binding agent in organic solvent at -5~20 ℃ for 0.5~2h to obtain cabozantinib; the inventive method uses cheap raw materials, has mild conditions, simple and convenient operation, stable process, good repeatability, high molar yield, low cost, so invention is an applicable method for com. production of cabozantinib. Cabozantinib was prepared via chlorination of 6,7-dimethoxyquinolin-4-ol; the resulting 4-chloro-6,7-dimethoxyquinoline underwent condensation with 4-aminophenol or 4-nitrophenol to give the corresponding ethers, which underwent redn and/or acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropylcarbonyl halides to give cabozantinib. The said 1-[(4-fluorophenyl)carbamoyl]cyclopropylcarbonyl halides were prepared via

condensation of 1,1-cyclopropanedicarboxylic acid with p-fluoroaniline followed by halogenation. The inventive method uses cheap raw materials, has mild conditions, simple and convenient operation, stable process, good repeatability, high molar yield, low cost, so invention is an applicable method for com. production of cabozantinib.

L8 ANSWER 205 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:478399 CAPLUS Full-text
DOCUMENT NUMBER: 160:501685
TITLE: Process for the preparation of cabozantinib and its intermediate
INVENTOR(S): Shi, Xiangfei; Zhao, Rui; Meng, Qingyi; Zhang, Xiquan
PATENT ASSIGNEE(S): Chia Tai Tianqing Pharmaceutical Group Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 18pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103664776	A	20140326	CN 2012-10374723	20120926
PRIORITY APPLN. INFO.:			CN 2012-10374723	20120926
OTHER SOURCE(S):	MARPAT 160:501685			

GI



I II

AB The invention relates to process for the prepn. of cabozantinib and its intermediate of formula I from 1,1-cyclopropane dicarboxylic acid diester of formula II [R1 = C1-10 alkyl]. For example, cabozantinib was prepared by hydrolysis of compound II [R1 = Et] to afford 1-(ethoxycarbonyl)cyclopropanecarboxylic acid, which underwent amidation reaction with 4-aminophenol followed by arylation with 4-chloro-6,7-dimethoxyquinoline to afford compound I [R1 = Et], which underwent hydrolysis followed by amidation with 4-fluoroaniline to afford cabozantinib.

L8 ANSWER 206 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:448281 CAPLUS Full-text
DOCUMENT NUMBER: 160:480988

EP 2708556	A1	20140319	EP 2013-184072	20130912
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2014035266	A	20140321	KR 2013-108913	20130911
US 20140086926	A1	20140327	US 2013-14025403	20130912
PRIORITY APPLN. INFO.:			KR 2012-101177 A	20120912
			KR 2013-108913 A	20130911

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose combination therapy for prevention or treatment of c-Met-induced or angiogenesis factor-induced diseases. The therapy comprises the co-administration of an angiogenesis inhibitor and an anti-c-Met antibody. In one example, the metastatic potential (migration) of HUVEC cells is shown to be inhibited by the combined effects of an anti-c-Met antibody and an anti-VEGF antibody.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 208 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:431636 CAPLUS Full-text
DOCUMENT NUMBER: 163:325757
TITLE: Effects of Cabozantinib on Pain and Narcotic Use in Patients with Castration-resistant Prostate Cancer: Results from a Phase 2 Nonrandomized Expansion Cohort
AUTHOR(S): Basch, Ethan; Autio, Karen A.; Smith, Matthew R.; Bennett, Antonia V.; Weitzman, Aaron L.; Scheffold, Christian; Sweeney, Christopher; Rathkopf, Dana E.; Smith, David C.; George, Daniel J.; Higano, Celestia S.; Harzstark, Andrea L.; Sartor, A. Oliver; Gordon, Michael S.; Vogelzang, Nicholas J.; de Bono, Johann S.; Haas, Naomi B.; Corn, Paul G.; Schimmoller, Frauke; Scher, Howard I.
CORPORATE SOURCE: Cancer Outcomes Research Program, Lineberger Cancer Center, University of North Carolina, Chapel Hill, NC, USA
SOURCE: European Urology (2015), 67(2), 310-318
CODEN: EUURAV; ISSN: 0302-2838
DIGITAL OBJECT ID: 10.1016/j.eururo.2014.02.013
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Pain neg. affects quality of life for cancer patients. Preliminary data in metastatic castration-resistant prostate cancer (mCRPC) suggested a benefit of the oral tyrosine kinase inhibitor cabozantinib to pain palliation. Prospective evaluation of cabozantinib's benefits on pain and narcotic use in mCRPC.This was a nonrandomized expansion (NRE) cohort (n = 144) of a phase 2 randomized discontinuation trial in docetaxel-refractory mCRPC patients. Pain and interference of symptoms with sleep and general activity were electronically self-reported daily for 7-d intervals at baseline and regularly scheduled throughout the study. Mean per-patient scores were calculated for each interval. Narcotic use was recorded daily during the same intervals.Open-label cabozantinib (100 mg or 40 mg). The following stringent response definition was used: clin. meaningful pain reduction (≥30% improvement in mean scores from baseline) confirmed at a later interval without concomitant increases in narcotics. Only patients with moderate or severe baseline pain were analyzed.Sixty-five patients with moderate or severe baseline pain were evaluable. Of these, 27 (42%) experienced pain palliation according to the stringent response definition. Thirty-seven patients (57%) had clin. meaningful pain relief at two consecutive intervals, reported ≥6 wk apart in the majority. Forty-four patients (68%) had palliation at one or more intervals; 36 (55%) decreased narcotics use during one or more intervals. Clin. meaningful pain reduction was associated with significant ($p \leq 0.001$) improvements in sleep quality and general activity. A limitation of this study was its open-label design. Cabozantinib demonstrated clin. meaningful pain palliation, reduced or eliminated patients' narcotic use, and improved patient functioning, thus meriting prospective validation in phase 3 studies.We evaluated the potential of cabozantinib to improve symptoms in patients with metastatic prostate cancer that no longer responds to standard therapies. We saw a promising reduction in pain and reduced need for narcotic painkillers. Larger, well-controlled trials are necessary to confirm these findings.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TITLE: Inhibition of viral infection-triggered asthma with c-kit inhibitor
INVENTOR(S): Umetsu, Dale T.; Chang, Ya-Jen; De Kruyff, Rosemarie Helena; Baumgarth, Nicole
PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA
SOURCE: PCT Int. Appl., 128pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014043442	A1	20140320	WO 2013-US59609	20130913
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2895170	A1	20150722	EP 2013-836850	20130913
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20150297593	A1	20151022	US 2015-14428272	20150313
PRIORITY APPLN. INFO.:			US 2012-61701296 P	20120914
			WO 2013-US59609 W	20130913

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention provides methods, compns., and kits featuring a c-Kit kinase inhibitor for use in preventing or treating virus-induced respiratory pathol.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

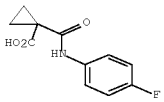
L8 ANSWER 207 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:443739 CAPLUS Full-text
DOCUMENT NUMBER: 160:485576
TITLE: Combination therapy for prevention or treatment of c-met or angiogenesis factor induced diseases
INVENTOR(S): Jeong, Yun Ju; Kim, Kyung Ah; Song, Yun Jeong; Lee, Ji Min; Lee, Hyo Seon; Choi, Jae Hyun; Lee, Saet Byoul
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: Eur. Pat. Appl., 168pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

L8 ANSWER 209 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:410366 CAPLUS Full-text
DOCUMENT NUMBER: 160:451706
TITLE: Inhibitors of Met, VEGFR and Ret for use in the treatment of lung adenocarcinoma
INVENTOR(S): Aftab, Dana T.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014039971	A1	20140313	WO 2013-US58768	20130909
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20140121239	A1	20140501	US 2013-14021614	20130909
CN 104703600	A	20150610	CN 2013-80052164	20130909
EP 2892532	A1	20150715	EP 2013-765886	20130909
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JP 2015530389	T	20151015	JP 2015-531283	20130909
US 20150238477	A1	20150827	US 2015-14426580	20150306

PRIORITY APPLN. INFO.: US 2012-61698143 P 20120907
WO 2013-US58768 W 20130909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:451706; MARPAT 160:451706
GI



AB This invention is directed to the treatment of cancer in a patient, particularly a patient with lung adenocarcinoma, and more particularly a patient with KIF5B-RET fusion-pos. non-small cell lung cancer, with an inhibitor of MET, VEGF, and RET.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 210 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:327215 CAPLUS Full-text
DOCUMENT NUMBER: 160:370140
TITLE: Preparation of substituted azaindole prodrugs, salts, pharmaceutical compositions thereof and methods of use in treating cancer and other proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Tingjin; Tang, Yin; Sun, Mingming; Wang, Qian
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 53pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

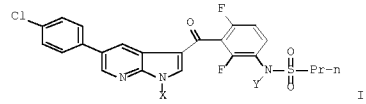
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140056849	A1	20140227	US 2013-13975371	20130826
CA 2882157	A1	20140306	CA 2013-2882157	20130826
WO 2014035846	A2	20140306	WO 2013-US56548	20130826
WO 2014035846	A3	20150625		

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

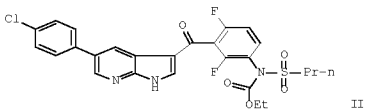
AU 2013309143	A1	20150212	AU 2013-309143	20130826
EP 2888260	A2	20150701	EP 2013-832403	20130826

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PRIORITY APPLN. INFO.: US 2012-61693335 P 20120827
WO 2013-US56548 W 20130826
OTHER SOURCE(S): CASREACT 160:370140; MARPAT 160:370140
GI



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AB The present invention provides substituted azaindole prodrugs of vemurafenib, methods of making said prodrugs, pharmaceutical compns. of said prodrugs and methods of using said prodrugs and pharmaceutical compns. thereof to treat or prevent diseases or disorders such as cancer. The prodrugs have general formula I, wherein each of X and Y is independently H, -C(:O)R3, -C(:O)OR4, -C(R1R2)OC(:O)R3, -C(R1R2)OC(:O)OR4 or -C(R1R2)OP(:O)(OR4)(OR4a), with the proviso that when Y is H, X is not -C(:O)CH3 or H; each R1 and R2 is independently H, D, C1-6alkyl, etc.; each R3 is independently H, D, C1-10alkyl, etc.; and each R4 and R4a is independently H, C1-10alkyl, C3-8cycloalkyl, etc. Example compound II was prepared by reacting vemurafenib with Et chloroformate. Various prodrugs of the invention were studied for their stability in liver microsomes, their oral and i.v. bioavailability, and their antitumor properties.

L8 ANSWER 211 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:211024 CAPLUS Full-text
DOCUMENT NUMBER: 161:316285
TITLE: Cabozantinib Inhibits Prostate Cancer Growth and Prevents Tumor-Induced Bone Lesions
AUTHOR(S): Dai, Jinlu; Zhang, Honglai; Karatsinides, Andreas; Keller, Jill M.; Kozloff, Kenneth M.; Aftab, Dana T.; Schimmoller, Frauke; Keller, Evan T.
CORPORATE SOURCE: Departments of Urology and Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA
SOURCE: Clinical Cancer Research (2014), 20(3), 617-630
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-0839
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Cabozantinib, an orally available multityrosine kinase inhibitor with activity against mesenchymal epithelial transition factor (MET) and VEGF receptor 2 (VEGFR2), induces resolution of bone scan lesions in men with castration-resistant prostate cancer bone metastases. The purpose of this study was to determine whether cabozantinib elicited a direct antitumor effect, an indirect effect through modulating bone, or both. Exptl. Design: Using human prostate cancer xenograft studies in mice, we determined the impact of cabozantinib on tumor growth in soft tissue and bone. In vitro studies with cabozantinib were performed using (i) prostate cancer cell lines to evaluate its impact on cell growth, invasive ability, and MET and (ii) osteoblast cell lines to evaluate its impact on viability and differentiation and VEGFR2. Results: Cabozantinib inhibited progression of multiple prostate cancer cell lines (Ace-1, C4-2B, and LuCaP 35) in bone metastatic and soft tissue murine models of prostate cancer, except for PC-3 prostate cancer cells in which it inhibited only s.c. growth. Cabozantinib directly inhibited prostate cancer cell viability and induced apoptosis in vitro and in vivo and inhibited cell invasion in vitro. Cabozantinib had a dose-dependent biphasic effect on osteoblast activity and inhibitory effect on osteoclast production in vitro that was reflected in vivo. It blocked MET and VEGFR2 phosphorylation in prostate cancer cells and osteoblast-like cells, resp. Conclusion: These data indicate that cabozantinib has direct antitumor activity, and that its ability to modulate osteoblast activity may contribute to its antitumor efficacy. Clin Cancer Res; 20(3); 617-30. ©2013 AACR.
OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 212 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:211001 CAPLUS Full-text
DOCUMENT NUMBER: 161:316087
TITLE: Cabozantinib and Prostate Cancer: Inhibiting Seed and Disrupting Soil?
AUTHOR(S): Lee, Richard J.; Smith, Matthew R.
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA
SOURCE: Clinical Cancer Research (2014), 20(3), 525-527
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-2636
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Treatment with cabozantinib, an inhibitor of MET and VEGFR2 signaling, has demonstrated clin. benefit in early trials in men with metastatic prostate cancer. Preclin. evidence suggests that cabozantinib can kill cancer cell seeds while disrupting angiogenesis and stromal cells in the metastatic soil.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 213 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:175942 CAPLUS Full-text
DOCUMENT NUMBER: 160:310859
TITLE: Preparation of substituted pyrazolone compounds as protein tyrosine kinase modulators useful in treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022117	A1	20140206	WO 2013-US51175	20130719

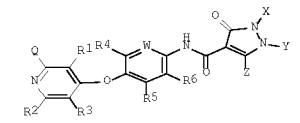
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20150050239	A1	20150219	US 2013-13945925	20130719
US 8969388	B2	20150303		
EP 2879676	A1	20150610	EP 2013-825325	20130719

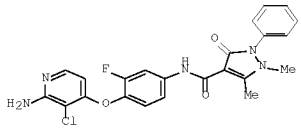
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JP 2015523390	T	20150813	JP 2015-524334	20130719

PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
WO 2013-US51175 W 20130719
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:310859; MARPAT 160:310859
GI



I



II

AB The invention provides substituted pyrazolone compds.of formula I, stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, and pharmaceutical preparation for regulating the activity of protein kinases and adjusting the signal response in the cell or between cells. The invention also relates to pharmaceutical compns. comprising the compds. and a method for treating hyperproliferative disorder of mammal, particularly human using the compns. Compds. of formula I [wherein Q is H, NH2 and derivative, OH and derivs., -NHCOR, etc.; W is (un)substituted CH or N; X, Y, and Z are independently H, D, C1-6 alkyl, C3-8 cycloalkyl-C1-4 alkylene, etc.; R1-R6 are independently H, D, F, Cl, Br, CN, etc.; R is H, C1-6 alkyl, C3-8 cycloalkyl-C1-4 alkylene, C3-7 heterocycloalkyl, etc.] and their stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, are claimed and exemplified. For example, II was prepared in a multistep process (procedure given). I were evaluated for stability in liver microsomes and pharmacokinetic properties in mice, rats, dogs, and monkeys (data given). Binding of I to receptor tyrosine kinases was determined using KINOMEscan where II exhibited binding constant (Kd) values of 23 nM for KDR tyrosine kinase and 4.4 nM for c-Met tyrosine kinase.

L8 ANSWER 214 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2014:175941 CAPLUS Full-text
DOCUMENT NUMBER:	160:310858
TITLE:	Preparation of substituted pyrazolone compounds as protein tyrosine kinase modulators for treatment of proliferative disease
INVENTOR(S):	Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S):	Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE:	PCT Int. Appl., 110pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

PATENT INFORMATION:

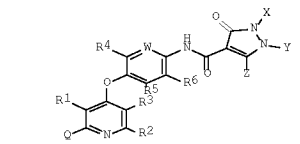
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022116	A2	20140206	WO 2013-US51174	20130719
WO 2014022116	A3	20150716		
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CA 2876246	A1	20140206	CA 2013-2876246	20130719
AU 2013296897	A1	20141218	AU 2013-296897	20130719
AU 2013296897	B2	20150917		
US 20150050239	A1	20150219	US 2013-13945925	20130719
US 8969388	B2	20150303		
EP 2879677	A2	20150610	EP 2013-826459	20130719
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JP 2015530975	T	20151029	JP 2015-524333	20130719

PRIORITY APPLN. INFO.:	US 2012-61676944	P	20120728
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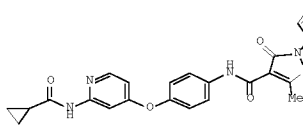
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 160:310858; MARPAT 160:310858

GI



I



II

AB The invention provides substituted pyrazolone compds.of formula I, stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, and pharmaceutical preparation for regulating the activity of protein kinases and adjusting the signal response in the cell or between cells. The invention also relates to pharmaceutical compns. comprising the compds. and a method for treating hyperproliferative disorder of mammal, particularly human using the compns. Compds. of formula I [wherein Q is D, NH2 and derivs., -NHCOR, etc.; W is (un)substituted CH or N; each X, Y, and Z is independently H, D, C1-6 alkyl, C3-8 cycloalkyl, etc.; each R1-R6 is independently H, D, F, Cl, Br, CN, etc.; R is D, C3-8 cycloalkyl, -C1-4 alkylene -C6-10 aryl, etc.] and their stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, are claimed and exemplified. For example, II was prepared in a multistep process (procedure given). Candidate compds. of I were evaluated for stability in liver microsomes and pharmacokinetic properties in mice, rats, dogs, and monkeys (data given). Binding of I to receptor tyrosine kinases was determined using KINOMEscan where II exhibited binding constant (Kd) values of 2.9 nM for KDR tyrosine kinase and 0.21 nM for c-Met tyrosine kinase.

L8 ANSWER 215 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2014:173876 CAPLUS Full-text
DOCUMENT NUMBER:	160:294980
TITLE:	Preparation of N-[3-(quinolin-6-yl)pyridin-5-yl] benzenesulfonamides as PI3 kinase modulators
INVENTOR(S):	Xi, Ning; Li, Zhuo; Wang, Tingjin; Wu, Zuping; Wen, Qiuling
PATENT ASSIGNEE(S):	Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE:	PCT Int. Appl., 88pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

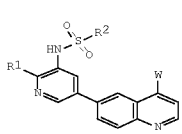
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022128	A1	20140206	WO 2013-US51405	20130719
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

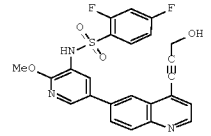
PRIORITY APPLN. INFO.:	US 2012-61676966	P	20120729

OTHER SOURCE(S): CASREACT 160:294980; MARPAT 160:294980

GI



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II

AB This invention relates to the field of lipid kinases and modulators thereof. In particular, the invention relates to compds. I [W = D, CN, N3, (un)substituted C5-12 spirobicyclyl or C≡CX; X = H, D, alkyl, cycloalkyl, etc.; R1 = H, D, Cl, alkyl, etc.; R2 = alkyl, cycloalkyl, aryl, etc.] as modulators of phosphatidylinositol 3-kinases (PI3 kinases or PBKs) signaling pathways, and methods of their use. Twenty-nine compds. I were prepared and disclosed. E.g., a multi-step synthesis of II, starting from 5-bromo-2-chloro-3-nitropyridine, was described. Exemplified compds. I exhibited potent activities in the PI3Kα(h) and mTOR(h) assays (data given for representative compds. I). The invention also provides pharmaceutically acceptable compns. comprising compds. I and methods of using the compns. in modulating of PI3K signaling pathways and their related disorders in mammals, especially humans.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 216 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:151402 CAPLUS Full-text
DOCUMENT NUMBER: 160:242457
TITLE: In-frame fusion of genes CEP55 and RET associated with diffuse-type gastric cancer and their use in drug discovery and cancer therapy
INVENTOR(S): Shibata, Tatsuhiro; Hosoda, Fumie
PATENT ASSIGNEE(S): National Cancer Center, Japan
SOURCE: PCT Int. Appl., 53pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014017491	A1	20140130	WO 2013-JP69929	20130723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 104619841	A	20150513	CN 2013-80039589	20130723
EP 2878672	A1	20150603	EP 2013-822713	20130723
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20150177246	A1	20150625	US 2015-14417052	20150123
PRIORITY APPLN. INFO.:			JP 2012-165694 A	20120726
			WO 2013-JP69929 W	20130723

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Through transcriptome an in-frame fusion of 2 genes (CEP55 and RET) of human chromosome 10 was found in patients with diffuse-type gastric cancer. The fused genes can be used for evaluation of the effectiveness of an antitumor agent such as RET tyrosine kinase inhibitors. Antibody to CEP55 or RET protein is also claimed.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 217 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:146206 CAPLUS Full-text
DOCUMENT NUMBER: 160:225648
TITLE: Efflux inhibitor compositions and methods of treatment using the same
INVENTOR(S): Bunt, Antonius Martinus Gustave; Van Tellingen, Olaf
PATENT ASSIGNEE(S): Neth.
SOURCE: PCT Int. Appl., 74pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014018932	A2	20140130	WO 2013-US52402	20130726
WO 2014018932	A3	20140320		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2880236	A1	20140130	CA 2013-2880236	20130726
AU 2013295549	A1	20150319	AU 2013-295549	20130726
EP 2877159	A2	20150603	EP 2013-745549	20130726
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104736144	A	20150624	CN 2013-80050643	20130726
JP 2015523400	T	20150813	JP 2015-524485	20130726
IN 2015MN00408	A	20150904	IN 2015-MN408	20150225
PRIORITY APPLN. INFO.:			US 2012-61676689 P	20120727
			WO 2013-US52402 W	20130726

AB The present invention relates to efflux inhibitor compns. and methods of using these agents for treating conditions where the activity of efflux transporter proteins (e.g., Breast Cancer Resistance Protein (BCRP) and P-Glycoprotein (P-GP)) inhibit effective delivery of a therapeutic agent to a target tissue (e.g., brain, spinal cord, nerves, cerebrospinal fluid, testis, eyeballs, retina, inner ear, placenta, mammary gland, liver, biliary tract, kidney, intestines, lung, adrenal cortex, endometrium, hematopoietic cells, and/or stem cells).

L8 ANSWER 218 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:127915 CAPLUS Full-text
DOCUMENT NUMBER: 160:362955
TITLE: Novel tyrosine kinase inhibitors for renal cell carcinoma
AUTHOR(S): Dorff, Tanya B.; Pal, Sumanta K.; Quinn, David I.
CORPORATE SOURCE: Department of Medicine, USC Norris Comprehensive Cancer Center, USC Keck School of Medicine, Los Angeles, CA, 90033, USA
SOURCE: Expert Review of Clinical Pharmacology (2014), 7(1), 67-73
CODEN: ERCPAG; ISSN: 1751-2433
DIGITAL OBJECT ID: 10.1586/17512433.2014.862496
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Although targeted therapy against VEGF and mTOR have revolutionized the treatment of advanced renal cell carcinoma (RCC), addnl. agents are required due to toxicity and resistance to currently available drugs. Some next-generation tyrosine kinase inhibitors have focused on VEGF, narrowing the spectrum of receptors which are inhibited and enhancing binding affinity. However, targeting novel receptors with tyrosine kinase inhibition of addnl. receptor targets has also emerged as an important future therapeutic strategy for RCC, both clear cell and variant histol. New pathways being targeted include FGF, angiopoietin and MET. In this review, we highlight five novel tyrosine kinase inhibitors in development for RCC: tivozanib; dovitinib; regorafenib; cabozantinib; and tivantinib.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 219 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:93138 CAPLUS Full-text
DOCUMENT NUMBER: 160:289739
TITLE: c-MET kinase inhibitors: a patent review (2011 - 2013)
AUTHOR(S): Zhu, Kongkai; Kong, Xiangqian; Zhao, Dan; Liang, Zhongjie; Luo, Cheng
CORPORATE SOURCE: Center for Systems Biology, Soochow University, Jiangsu, 215006, Peop. Rep. China
SOURCE: Expert Opinion on Therapeutic Patents (2014), 24(2), 217-230
CODEN: EOTPEG; ISSN: 1354-3776
DIGITAL OBJECT ID: 10.1517/13543776.2014.864279
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Introduction: The receptor tyrosine kinase c-MET displays aberrant activation in the malignant phenotype of various tumors, and thus, has drawn considerable attention as drug target for cancer therapy. Many c-MET inhibitors are now under clin. investment, and one of them - Cabozantinib - has been approved by US FDA in 2012 for the treatment of medullary thyroid cancer, which further proved the feasibility of c-MET inhibition method in cancer therapy. Areas covered: This article briefly outlines the role of c-MET in oncogenesis and provides a broad overview of the assays used to characterize new inhibitors. Then, a series of representative small-mol. inhibitors of c-MET, especially from the published patent literature from 2011 to 2013, are recorded. Herein, the challenges in the kinase inhibitor design, such as the inhibitor selectivity and resistance mutations, are also discussed. Expert opinion: Up to now, at least 17 inhibitors of c-MET are under clin. evaluation, and several agents exhibit encouraging results. Thus, inhibiting c-MET signaling has major therapeutic value in cancer therapy. Focus on the selectivity of both types of inhibitors, with potent selectivity or multi-targets, have demonstrated antitumor efficacy. The network pharmacol. and clin. trials integrated would provide powerful tools to further evaluate the superiority of both inhibitors in continued efficacy and toxicity.
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 220 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:2007812 CAPLUS Full-text
DOCUMENT NUMBER: 160:380536
TITLE: Newly approved antitumor drugs by FDA in 2012
AUTHOR(S): Yang, Minglun
CORPORATE SOURCE: Department of Pharmacy, Linqu County People's Hospital, Linqu, Shandong Province, 262600, Peop. Rep. China
SOURCE: Yaoxue Fuwu Yu Yanjiu (2013), 13(4), 304-306
CODEN: YFYYAH; ISSN: 1671-2838
DIGITAL OBJECT ID: 10.5428/pcar20130420
PUBLISHER: Yaoxue Fuwu Yu Yanjiu Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Newly approved antitumor drugs by FDA in 2012 were introduced.

L8 ANSWER 221 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:2006727 CAPLUS Full-text
DOCUMENT NUMBER: 160:380516
TITLE: Pharmacological and clinical studies of cabozantinib
AUTHOR(S): Zheng, Xi-yuan; Jiang, Han-jie; Pu, Xiao-ping
CORPORATE SOURCE: Department of Molecular and Cellular Pharmacology, School of Pharmaceutical Sciences, Peking University, Beijing, 100191, Peop. Rep. China
SOURCE: Zhongguo Xinyao Zazhi (2013), 22(17), 1990-1993
CODEN: ZXZHA6; ISSN: 1003-3734
PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Cabozantinib, a new drug for medullary thyroid cancer treatment, is a potent inhibitor of MET, RET, and vascular endothelial factor receptor 2 (VEGFR2) as well as other tyrosine kinases that have been implicated in tumor development and progression. The mechanism, pharmacokinetics, drug interaction, clin. evaluation, and safety of cabozantinib were reviewed.

L8 ANSWER 222 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1965166 CAPLUS Full-text
DOCUMENT NUMBER: 160:155703
TITLE: Metastatic castration-resistant prostate cancer reveals intrapatient similarity and interpatient heterogeneity of therapeutic kinase targets
AUTHOR(S): Drake, Justin M.; Graham, Nicholas A.; Lee, John K.; Stoyanova, Tanya; Faltermeier, Claire M.; Sud, Sudha; Titz, Bjorn; Huang, Jiaoti; Pienta, Kenneth J.; Graeber, Thomas G.; Witte, Owen N.
CORPORATE SOURCE: Department of Microbiology, Immunology, and Molecular Genetics, David Geffen School of Medicine, University of California, Los Angeles, CA, 90095, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2013), 110(49), E4762-E4769, SE4762/1-SE4762/23
CODEN: PNASA6; ISSN: 0027-8424
DIGITAL OBJECT ID: 10.1073/pnas.1319948110
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB In prostate cancer, multiple metastases from the same patient share similar copy number, mutational status, erythroblast transformation specific (ETS) rearrangements, and methylation patterns supporting their clonal origins. Whether actionable targets such as tyrosine kinases are also similarly expressed and activated in anatomically distinct metastatic lesions of the same patient is not known. We evaluated active kinases using phosphotyrosine peptide enrichment and quant. mass spectrometry to identify druggable targets in metastatic castration-resistant prostate cancer obtained at rapid autopsy. We identified distinct phosphopeptide patterns in metastatic tissues compared with treatment-naive primary prostate tissue and prostate cancer cell line-derived xenografts. Evaluation of metastatic castration-resistant prostate cancer samples for tyrosine phosphorylation and upstream kinase targets revealed SRC, epidermal growth factor receptor (EGFR), rearranged during transfection (RET), anaplastic lymphoma kinase (ALK), and MAPK1/3 and other activities while exhibiting intrapatient similarity and interpatient heterogeneity. Phosphoproteomic analyses and identification of kinase activation states in metastatic castration-resistant prostate cancer patients have allowed for the prioritization of kinases for further clin. evaluation.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

L8 ANSWER 223 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1898455 CAPLUS Full-text
DOCUMENT NUMBER: 160:555100
TITLE: In Vitro and In Vivo Activity of Cabozantinib (XL184), an Inhibitor of RET, MET, and VEGFR2, in a Model of Medullary Thyroid Cancer
AUTHOR(S): Bentzien, Frauke; Zuzow, Marcus; Heald, Nathan; Gibson, Anna; Shi, Yongchang; Goon, Leanne; Yu, Peiwen; Engst, Stefan; Zhang, Wentao; Huang, Donghui; Zhao, Lora; Vysotskaia, Valentina; Chu, Felix; Bautista, Rajana; Cancilla, Belinda; Lamb, Peter; Joly, Alison H.; Yakes, F. Michael
CORPORATE SOURCE: ., Exelixis, Inc., South San Francisco, CA, USA
SOURCE: Thyroid (2013), 23(12), 1569-1577
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2013.0137
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background: A limited no. of approved therapeutic options are available to metastatic medullary thyroid cancer (MTC) patients, and the response to conventional chemotherapy and/or radiotherapy strategies is inadequate. Sporadic and inherited mutations in the tyrosine kinase RET result in oncogenic activation that is associated with the pathogenesis of MTC. Cabozantinib is a potent inhibitor of MET, RET, and vascular endothelial factor receptor 2 (VEGFR2), as well as other tyrosine kinases that have been implicated in tumor development and progression. The object of this study was to determine the in vitro biochem. and cellular inhibitory profile of cabozantinib against RET, and in vivo antitumor efficacy using a xenograft model of MTC.Methods: Cabozantinib was evaluated in biochem. and cell-based assays that determined the potency of the compound against wild type and activating mutant forms of RET. Addnl., the pharmacodynamic modulation of RET and MET and in vivo antitumor activity of cabozantinib was examined in a MTC tumor model following subchronic oral administration.Results: In biochem. assays, cabozantinib inhibited multiple forms of oncogenic RET kinase activity, including M918T and Y791F mutants. Addnl., it inhibited proliferation of TT tumor cells that harbor a C634W activating mutation of RET that is most often associated with MEN2A and familial MTC. In these same cells grown as xenograft tumors in nude mice, oral administration of cabozantinib resulted in dose-dependent tumor growth inhibition that correlated with a reduction in circulating plasma calcitonin levels. Moreover, immunohistochem. analyses of tumors revealed that cabozantinib reduced levels of phosphorylated MET and RET, and decreased tumor cellularity, proliferation, and vascularization.Conclusions: Cabozantinib is a potent inhibitor of RET and prevalent mutationally activated forms of RET known to be associated with MTC, and effectively inhibits the growth of a MTC tumor cell model in vitro and in vivo.

OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

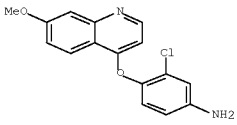
L8 ANSWER 224 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1873443 CAPLUS Full-text
DOCUMENT NUMBER: 160:50465
TITLE: Substituted quinoline compounds and use as Antitumor agents
INVENTOR(S): Xi, Ning; Wang, Tingjin; Zeng, Shan; Sun, Mingming; Wang, Kunrui
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013180949	A1	20131205	WO 2013-US41036	20130515

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61652210 P 20120527
OTHER SOURCE(S): CASREACT 160:50465; MARPAT 160:50465
GI



AB The present invention provides novel substituted quinoline compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

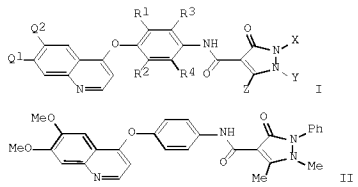
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 225 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1866363 CAPLUS Full-text
DOCUMENT NUMBER: 160:33885
TITLE: Substituted quinoline compound useful in treatment of hyperproliferative diseases and its preparation
INVENTOR(S): Xi, Ning; Wang, Tingjin; Zeng, Shan; Sun, Mingming; Wang, Kunrui
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 57pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103420986	A	20131204	CN 2013-10179608	20130515
PRIORITY APPLN. INFO.:			CN 2012-10154478 A	20120518
			CN 2013-10118880 A	20130403

OTHER SOURCE(S): CASREACT 160:33885; MARPAT 160:33885
GI



AB The invention relates to substituted quinoline compds. of formula I as protein kinase regulator useful in treatment of proliferative diseases and their preparation Compound I, wherein R1, R2, R3, and R4 are independently H, D, F, Cl, or Br; Q1 and Q2 are independently H, D, C1-6 alkyl, etc.; X and Z are independently H, D, C1-6 alkyl, etc.; Y is H, D, C2-6 alkynyl, etc.; their stereoisomers, N-oxides, solvates, pharmaceutically acceptable salts, are claimed. Compound II was prepared by multi-step procedure (procedure given). The present invention also relates to the pharmaceutical compns. containing the inventive compds., and method of application of the pharmaceutical composition for treatment of a mammal, especially hyperproliferative disease.

L8 ANSWER 226 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1864045 CAPLUS Full-text
DOCUMENT NUMBER: 161:30833
TITLE: An update on clinical trials of targeted therapies in thyroid cancer
AUTHOR(S): Haraldsdottir, Sigurdis; Shah, Manisha H.
CORPORATE SOURCE: The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA
SOURCE: Current Opinion in Oncology (2014), 26(1), 36-44
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0000000000000029
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB Purpose of review: Several new targeted therapies with multikinase inhibitors targeting vascular endothelial growth factor (VEGF), rearranged during transfection and v-raf murine sarcoma viral oncogene homolog B1 pathways have been tested in clin. trials for radioiodine-refractory differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC) in the past 10 years. Recent findings: Results of the first phase III trial of VEGF-targeted therapy (sorafenib) in DTC were presented in June 2013, and two phase III trials with VEGF and rearranged during transfection-targeted therapies (vandetanib and cabozantinib) in MTC have led to approval by US Food and Drug Administration in the past 2 years. Whereas such therapies increase median progression-free survival compared to placebo, there is no therapy proven to improve overall survival yet. Significant potential adverse event risks associated with such therapies need to be recognized.

Dissemination of knowledge about targeted therapies is critical for various medical specialists as patient care for thyroid cancers is best delivered in a multidisciplinary setting. Summary: Successful development of targeted systemic therapies in DTC and MTC in the past 5 years is incredibly exciting in the field and patients with advanced DTC/MTC now have new standard-of-care therapy options.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 227 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1837363 CAPLUS Full-text

DOCUMENT NUMBER: 160:28188

TITLE: Substituted alkynyl pyridine compounds and methods of use

INVENTOR(S): Xi, Ning; Yin, Lihua; Li, Xiaobo; Yu, Na; Wu, Yanjun

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China

SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013177092	A1	20131128	WO 2013-US41918	20130521

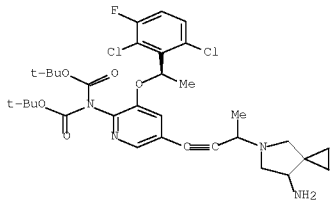
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61650513 P 20120523

OTHER SOURCE(S): CASREACT 160:28188; MARPAT 160:28188

GI



AB The present invention provides novel substituted alkynyl pyridine compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 228 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1836624 CAPLUS Full-text

DOCUMENT NUMBER: 160:28252

TITLE: Compounds and methods of use thereof for treating neurodegenerative disorders

INVENTOR(S): Zack, Donald J.; Welsbie, Derek Stuart; Yang, Zhiyong

PATENT ASSIGNEE(S): The Johns Hopkins University, USA

SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013177367	A2	20131128	WO 2013-US42367	20130523

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

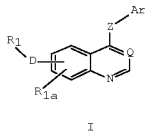
EP 2852388	A2	20150401	EP 2013-793466	20130523

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

US 20150164906	A1	20150618	US 2014-14403523	20141124

PRIORITY APPLN. INFO.:
US 2012-61650613 P 20120523
US 2012-61680931 P 20120808
WO 2013-US42367 W 20130523

GI



I

AB When using molecularly targeted agents (MTAs), oncologists and patients face new and sometimes unexpected toxicities. Though ocular adverse events (OAEs) are not uncommon with chemotherapy, they are rarely severe or dose limiting. Ocular toxicity profile may differ with MTAs, indeed severe and dose limiting toxicities have been described with targeted therapies currently under investigation. Our study aimed to review OAEs experienced with MTAs approved in solid tumors. This review revealed that many OAEs, frequent and potentially severe, exist and concern most MTAs. The suggestion is prompt referral of patients with severe pain and/or visual impairment to the ophthalmologist since these symptoms can be associated with potentially severe OAE and need ophthalmic assessment. Oncologists must be aware of such events and their potential severity for better treatment and better diagnosis in daily practice as well as in clin. trials.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 229 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1823382 CAPLUS Full-text

DOCUMENT NUMBER: 161:178446

TITLE: Ocular adverse events of molecularly targeted agents approved in solid tumours: A systematic review

AUTHOR(S): Huillard, Olivier; Bakalian, Silvin; Levy, Christine; Desjardins, Laurence; Lumbroso-Le Rouic, Livia; Pop, Simona; Sablin, Marie-Paule; Le Tourneau, Christophe

CORPORATE SOURCE: Department of Medical Oncology, Clinical Trial Unit, Institut Curie, Paris, Fr.

SOURCE: European Journal of Cancer (2014), 50(3), 638-648
CODEN: EJCAEL; ISSN: 0959-8049

DIGITAL OBJECT ID: 10.1016/j.ejca.2013.10.016

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB In some embodiments, the presently disclosed subject matter provides a method for treating or preventing a neurodegenerative disease, disorder, or condition in a subject in need thereof, the method comprising administering to the subject a 15 therapeutically effective amount of a compound of Formula I (wherein D is selected from the group consisting of O, S(O)0-2, and NR1b; R1a is selected from the group consisting of H, substituted or unsubstituted alkyl, halogen, OR1b, NO2, NR1bR1c; wherein: R1b and R1c are each independently selected from the group consisting of H or substituted or unsubstituted alkyl, aryl, etc.; R1 is H, substituted alkyl, aryl, etc.; Q is CR2a or N wherein R2a is H, alkyl or cyano; Z is O, NR1b and S(O)0-2; and Ar is substituted aryl or substituted heteroaryl), or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, thereby treating or preventing the neurodegenerative disease, disorder, or condition.

L8 ANSWER 230 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1802363 CAPLUS Full-text

DOCUMENT NUMBER: 160:509021

TITLE: Multivoxel 1H MR spectroscopy is superior to contrast-enhanced MRI for response assessment after anti-angiogenic treatment of orthotopic human glioma xenografts and provides handles for metabolic targeting

AUTHOR(S): Hamans, Bob; Navis, Anna Catharina; Wright, Alan; Wesseling, Pieter; Heerschap, Arend; Leenders, William

CORPORATE SOURCE: Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.

SOURCE: Neuro-Oncology (Cary, NC, United States) (2013), 15(12), 1615-1624
CODEN: NEURJR; ISSN: 1522-8517

DIGITAL OBJECT ID: 10.1093/neuonc/not129

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Background Anti-angiogenic treatment of glioblastoma characteristically results in therapy resistance and tumor progression via diffuse infiltration. Monitoring tumor progression in these patients is thwarted because therapy results in tumor invisibility in contrast-enhanced (CE) MRI. To address this problem, we examined whether tumor progression could be monitored by metabolic mapping using 1H MR spectroscopic imaging (MRSI). Methods We treated groups of BALB/c nu/nu mice carrying different orthotopic diffuse-infiltrative glioblastoma xenografts with bevacizumab (anti-vascular endothelial growth factor [VEGF] antibody, n = 13), cabozantinib (combined VEGF receptor 2/c-Met tyrosine kinase inhibitor, n = 11), or placebo (n = 15) and compared CE-MRI with MRS-derived metabolic maps before, during, and after treatment. Metabolic maps and CE-MRIs were subsequently correlated to histol. and immunohistochem. Results In vivo imaging of choline/n-acetyl aspartate ratios via multivoxel MRS is better able to evaluate response to therapy than CE-MRI. Lactate imaging revealed that diffuse infiltrative areas in glioblastoma xenografts did not present with excessive glycolysis. In contrast, glycolysis was observed in hypoxic areas in angiogenesis-dependent compact regions of glioma only, especially after anti-angiogenic treatment. Conclusion Our data present MRSI as a powerful and feasible approach that is superior to CE-MRI and may provide

handles for optimizing treatment of glioma. Furthermore, we show that glycolysis is more prominent in hypoxic areas than in areas of diffuse infiltrative growth. The Warburg hypothesis of persisting glycolysis in tumors under normoxic conditions may thus not be valid for diffuse glioma.
OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 231 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1792084 CAPLUS Full-text
DOCUMENT NUMBER: 159:737215
TITLE: Cabozantinib in progressive medullary thyroid cancer
AUTHOR(S): Elisei, Rossella; Schlumberger, Martin J.; Mueller, Stefan P.; Schoffski, Patrick; Brose, Marcia S.; Shah, Manisha H.; Licitra, Lisa; Jarzab, Barbara; Medvedev, Viktor; Kreissl, Michael C.; Niederle, Bruno; Cohen, Ezra E. W.; Wirth, Lori J.; Ali, Haythem; Hessel, Colin; Yaron, Yifah; Ball, Douglas; Nelkin, Barry; Sherman, Steven I.
CORPORATE SOURCE: University of Pisa, Pisa, Italy
SOURCE: Journal of Clinical Oncology (2013), 31(29), 3639-3646
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.48.4659
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Cabozantinib, a tyrosine kinase inhibitor (TKI) of hepatocyte growth factor receptor (MET), vascular endothelial growth factor receptor 2, and rearranged during transfection (RET), demonstrated clin. activity in patients with medullary thyroid cancer (MTC) in phase I. Patients and Methods: We conducted a double-blind, phase III trial comparing cabozantinib with placebo in 330 patients with documented radiog. progression of metastatic MTC. Patients were randomly assigned (2:1) to cabozantinib (140 mg per day) or placebo. The primary end point was progression-free survival (PFS). Addnl. outcome measures included tumor response rate, overall survival, and safety. Results: The estimated median PFS was 11.2 mo for cabozantinib vs. 4.0 mo for placebo (hazard ratio, 0.28; 95% CI, 0.19 to 0.40; P < .001). Prolonged PFS with cabozantinib was observed across all subgroups including by age, prior TKI treatment, and RET mutation status (hereditary or sporadic). Response rate was 28% for cabozantinib and 0% for placebo; responses were seen regardless of RET mutation status. Kaplan-Meier ests. of patients alive and progression-free at 1 yr are 47.3% for cabozantinib and 7.2% for placebo. Common cabozantinib-associated adverse events included diarrhea, palmar-plantar erythrodysesthesia, decreased weight and appetite, nausea, and fatigue and resulted in dose redns. in 79% and holds in 65% of patients. Adverse events led to treatment discontinuation in 16% of cabozantinib-treated patients and in 8% of placebo-treated patients. Conclusion: Cabozantinib (140 mg per day) achieved a statistically significant improvement of PFS in patients with progressive metastatic MTC and represents an important new treatment option for patients with this rare disease. This dose of cabozantinib was associated with significant but manageable toxicity.
OS.CITING REF COUNT: 94 THERE ARE 94 CAPLUS RECORDS THAT CITE THIS RECORD (96 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 232 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1772555 CAPLUS Full-text
DOCUMENT NUMBER: 159:738209
TITLE: Methods for determining nucleotide sequence
INVENTOR(S): Iafrate, Anthony John; Le, Long Phi; Zheng, Zongli
PATENT ASSIGNEE(S): The General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

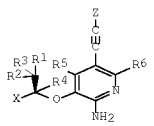
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013169339	A1	20131114	WO 2013-US30201	20130311
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2873176	A1	20131114	CA 2013-2873176	20130311
US 20130303461	A1	20131114	US 2013-13793564	20130311
EP 2847353	A1	20150318	EP 2013-787745	20130311
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104603287	A	20150506	CN 2013-80037100	20130311
JP 2015517307	T	20150622	JP 2015-511444	20130311

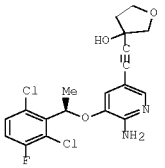
PRIORITY APPLN. INFO.: US 2012-61645364 P 20120510
US 2012-61679302 P 20120803
WO 2013-US30201 W 20130311
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The technol. described herein is directed to methods of detg. oligonucleotide sequences, e.g. by enriching target sequences prior to sequencing the sequences. The invention provides the sequences of the DNA primers used for sequencing anal. The target sequence may be genomic DNA, RNA or cDNA with or without gene rearrangement.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 233 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1771791 CAPLUS Full-text
DOCUMENT NUMBER: 159:742705
TITLE: Substituted alkynyl pyridine compounds as protein kinase regulator useful in treatment various diseases and their preparation
INVENTOR(S): Xi, Ning; Yin, Lihua; Li, Xiaobo; Yu, Na; Wu, Yanjun
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 65pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103387535	A	20131113	CN 2013-10173770	20130510

PRIORITY APPLN. INFO.: CN 2012-10141993 A 20120510
CN 2013-10116652 A 20130403
OTHER SOURCE(S): CASREACT 159:742705; MARPAT 159:742705
GI


I


II

AB The invention relates to substituted alkynyl pyridine compds. of formula I as protein kinase regulator useful in treatment of various diseases and their preparation Compds. I, wherein R1, R2, R3, R4, R5 and R6 are independently H, D or F; X is C6-10 aryl or heteroaryl containing 5-10 atoms; Z is C1-6 alkyl, C3-6 cycloalkyl, C3-6 heterocyclic radical, etc.; their stereoisomers, solvates, N-oxidants, pharmaceutically acceptable salts, are claimed. Compound II was prepared by multi-step reaction (procedure given). The invention compds. were evaluated for their ALK(h) kinase activity. From assay, it was determined that II exhibited the IC50 value of 52 nM against ALK(h).

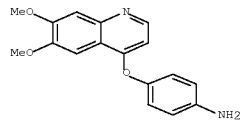
L8 ANSWER 234 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1746648 CAPLUS Full-text
DOCUMENT NUMBER: 160:200751
TITLE: Cabozantinib: a novel agent with a dual mechanism of action for castration-resistant prostate carcinoma
AUTHOR(S): Pinto, Alvaro
CORPORATE SOURCE: Medical Oncology Department, University Hospital La Paz-IdiPAZ, Madrid, Spain
SOURCE: Cancer Chemotherapy and Pharmacology (2014), 73(2), 219-222
CODEN: CCPHDZ; ISSN: 0344-5704
DIGITAL OBJECT ID: 10.1007/s00280-013-2343-2
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The landscape of castration-resistant prostate carcinoma has changed completely in the last few years, with the approval of four new agents with proven benefit in overall survival. Abiraterone, cabazitaxel, enzalutamide and radium-223 dichloride have been added to the armamentarium of available agents for the treatment of these patients. We still lack information about which agent works best in an individual patient and how to optimally use them in a sequential strategy. Cabozantinib, a targeted agent against MET and vascular endothelial growth factor receptor-2, has shown promising results and could become the first targeted therapy to be approved for castration-resistant prostate carcinoma. This paper reviews the clin. development of cabozantinib in prostate cancer and future research possibilities for this drug.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 235 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1734775 CAPLUS Full-text
DOCUMENT NUMBER: 159:691817
TITLE: A dual MET-VEGF modulator for treating osteolytic bone metastases
INVENTOR(S): Aftab, Dana T.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013166296	A1	20131107	WO 2013-US39284	20130502
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2844254	A1	20150311	EP 2013-722238	20130502
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015515988	T	20150604	JP 2015-510456	20130502
US 20150133494	A1	20150514	US 2014-14398188	20141031

PRIORITY APPLN. INFO.: US 2012-61641837 P 20120502
WO 2013-US39284 W 20130502
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 159:691817; MARPAT 159:691817

GI



AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and osteolytic bone metastases, with a dual inhibitor of MET and VEGF.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 236 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1717033 CAPLUS Full-text
DOCUMENT NUMBER: 160:363229
TITLE: Cabozantinib inhibits growth of androgen-sensitive and castration-resistant prostate cancer and affects bone remodeling
AUTHOR(S): Nguyen, Holly M.; Ruppender, Nazanin; Zhang, Xiaotun; Brown, Lisha G.; Gross, Ted S.; Morrissey, Colm; Gulati, Roman; Vessella, Robert L.; Schimmoller, Frauke; Aftab, Dana T.; Corey, Eva
CORPORATE SOURCE: Department of Urology, University of Washington, Seattle, WA, USA
SOURCE: PLoS One (2013), 8(10), e78881
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0078881
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is an inhibitor of multiple receptor tyrosine kinases, including MET and VEGFR2. In a phase II clin. trial in advanced prostate cancer (PCa), cabozantinib treatment improved bone scans in 68% of evaluable patients. Our studies aimed to determine the expression of cabozantinib targets during PCa progression and to evaluate its efficacy in hormone-sensitive and castration-resistant PCa in preclin. models while delineating its effects on tumor and bone. Using immunohistochem. and tissue microarrays containing normal prostate, primary PCa, and soft tissue and bone metastases, our data show that levels of MET, P-MET, and VEGFR2 are increasing during PCa progression. Our data also show that the expression of cabozantinib targets are particularly pronounced in bone metastases. To evaluate cabozantinib efficacy on PCa growth in the bone environment and in soft tissues we used androgen-sensitive LuCaP 23.1 and castration-resistant C4-2B PCa tumors. In vivo, cabozantinib inhibited the growth of PCa in bone as well as growth of s.c. tumors. Furthermore, cabozantinib treatment attenuated the bone response to the tumor and resulted in increased normal bone volume In summary, the expression pattern of cabozantinib targets in primary and castration-resistant metastatic PCa, and its efficacy in two different models of PCa suggest that this agent has a strong potential for the effective treatment of PCa at different stages of the disease.
OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 237 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1698309 CAPLUS Full-text
DOCUMENT NUMBER: 159:662217
TITLE: Detection of RET fusions in cancer
INVENTOR(S): Doebele, Robert; Garcia, Marileila Varella; Le, Anh T.; Xu, Liangguo
PATENT ASSIGNEE(S): University of Colorado, USA
SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013163428	A1	20131031	WO 2013-US38215	20130425

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61638452 P 20120425
AB Disclosed are methods and assay systems for the identification of chromosomal rearrangements involving the RET kinase gene in cellular samples. Further described are methods for identifying cancer patients who are predicted to respond, or not respond to the therapeutic administration of a chemotherapeutic regimen including one or more kinase inhibitor(s), to treat cancer in the patient.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 238 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1679191 CAPLUS Full-text
DOCUMENT NUMBER: 160:82446
TITLE: Commentary on "Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial." Smith DC, Smith MR, Sweeney C, Elfiky AA, Logothetis C, Corn PG, Vogelzang NJ, Small EJ, Harzstark AL, Gordon MS, Vaishampayan UN, Haas NB, Spira AI, Lara PN Jr, Lin CC, Srinivas S, Sella A, SchoffskiSchoeffski P, Scheffold C, Weitzman AL, Hussain M, University of Michigan, Ann Arbor, MI
AUTHOR(S): Trump, Donald L.
CORPORATE SOURCE: Neth.
SOURCE: Urologic Oncology: Seminars and Original Investigations (2013), 31(8), 1848
CODEN: UOSOAA; ISSN: 1078-1439
DIGITAL OBJECT ID: 10.1016/j.urolonc.2013.07.012
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (XL184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. Patients received 100 mg of cabozantinib daily. Those with stable disease per RECIST at 12 wk were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 wk and progression-free survival (PFS) after random assignment. One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 wk was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 wk (95% CI, 10.7 to 62.4 wk) with cabozantinib and 5.9 wk (95% CI, 5.4 to 6.6 wk) with placebo (hazard ratio, 0.12; P<.001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by≥50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot syndrome (8%). Cabozantinib has clin. activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and redns. in bone turnover markers, pain, and narcotic use.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 239 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1655693 CAPLUS Full-text
DOCUMENT NUMBER: 159:632725
TITLE: Menainv and cancer invasion and metastasis diagnosis and antitumor screening
INVENTOR(S): Gertler, Frank B.; Hughes-Alford, Shannon K.; Lauffenburger, Douglas A.; Neil, Jason; White, Forest; Condeelis, John S.; Oudin, Madeleine J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA; Albert Einstein College of Medicine of Yeshiva University
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013158485	A1	20131024	WO 2013-US36336	20130412

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20150044234	A1	20150212	US 2014-14390113	20141002

PRIORITY APPLN. INFO.: US 2012-61625985 P 20120418
US 2013-61778767 P 20130313
WO 2013-US36336 W 20130412
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Methods and compns. are provided for diagnosing or inhibiting invasion or metastasis of a cancer in a subject based on MenaINV. A method is provided of identifying an agent as an inhibitor of sarcoma or carcinoma cell invasion or as an inhibitor of metastasis of a carcinoma or sarcoma, comprising contacting a preparation comprising a growth factor receptor and a protein tyrosine phosphatase 1b (PTP1b) in the presence of an amount of MenaINV and an amount of Mena and quantifying the association of the growth factor receptor and PTP1b in the presence of the agent and in the absence of the agent. An agent that increases the association of growth factor receptor and PTP1b in the presence of the agent as compared to in the absence of the agent is identified as an inhibitor of sarcoma or carcinoma cell invasion or of metastasis, and an agent that does not increase, or decreases, the association of growth factor receptor and PTP1b in the presence of the agent as compared to in the absence of the agent is not identified as an inhibitor of sarcoma or carcinoma cell invasion or metastasis. A further method is provided of identifying an agent as an inhibitor of sarcoma or carcinoma cell invasion or of metastasis of a carcinoma or sarcoma, the method comprising contacting a preparation comprising an amount of MenaINV, an amount of Mena, and a protein, wherein the protein is phosphorylated, with the agent and PTP1b and quantifying phosphorylation of the protein at the site or sites. A decrease in phosphorylation in (a) the presence of the agent and PTP1b as compared to (b) in the absence of the agent and presence of PTP1b identifies the agent as an inhibitor of sarcoma or carcinoma cell invasion or metastasis, and wherein an increase in, or no change in, phosphorylation in (i) the presence of the agent and PTP1b as compared to (ii) in the absence of the agent and presence of PTP1b does not identify the agent as an inhibitor of sarcoma or carcinoma cell invasion or metastasis.
OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 240 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1629334 CAPLUS Full-text
DOCUMENT NUMBER: 159:602931
TITLE: Method for the prognosis and treatment of cancer metastasis

INVENTOR(S): Arnal, Anna; Tarragona, Maria; Pavlovic, Milica; Planet, Evarist; Gomis, Roger
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 150pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013153458	A2	20131017	WO 2013-IB1204	20130315
WO 2013153458	A3	20140227		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2650682	A1	20131016	EP 2012-382139	20120409
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CA 2891609	A1	20131017	CA 2013-2891609	20130315
AU 2013246618	A1	20141106	AU 2013-246618	20130315
KR 2015014919	A	20150209	KR 2014-7031148	20130315
EP 2836837	A2	20150218	EP 2013-731875	20130315
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104797935	A	20150722	CN 2013-80027292	20130315
JP 2015520606	T	20150723	JP 2015-505034	20130315
US 20150293100	A1	20151015	US 2014-14391085	20141007
MX 2014012233	A	20150617	MX 2014-12233	20141009

PRIORITY APPLN. INFO.:

EP 2012-382139	A	20120409
US 2012-61621949	P	20120409
US 2012-61724807	P	20121109
US 2012-61732175	P	20121130
US 2012-61732174	P	20121130
WO 2013-IB1204	W	20130315

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to a method for the prognosis of bone metastasis in triple neg. (including basal-like) breast cancer or, alternatively, ER+ breast cancer (including luminal A and β) which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of triple neg. (including basal-like) breast cancer metastasis or, alternatively, ER+ breast cancer (including luminal A and B) metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.

L8 ANSWER 241 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1622779 CAPLUS Full-text
DOCUMENT NUMBER: 160:260019
TITLE: Novel Modeling of Cancer Cell Signaling Pathways Enables Systematic Drug Repositioning for Distinct Breast Cancer Metastases
AUTHOR(S): Zhao, Hong; Jin, Guangxu; Cui, Kemi; Ren, Ding; Liu, Timothy; Chen, Peikai; Wong, Solomon; Li, Fuhai; Fan, Yubo; Rodriguez, Angel; Chang, Jenny; Wong, Stephen T. C.
CORPORATE SOURCE: Department of Systems Medicine and Bioengineering; NCI Center for Modeling Cancer Development, The Methodist Hospital Research Institute, Weill Cornell Medical College; Methodist Cancer Center, The Methodist Hospital, Dan L. Duncan Cancer Center, Baylor College of Medicine, Houston, TX, USA
SOURCE: Cancer Research (2013), 73(20), 6149-6163
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-12-4617
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new type of signaling network element, called cancer signaling bridges (CSB), has been shown to have the potential for systematic and fast-tracked drug repositioning. On the basis of CSBs, we developed a computational model to derive specific downstream signaling pathways that reveal previously unknown target-disease connections and new mechanisms for specific cancer subtypes. The model enables us to reposition drugs based on available patient gene expression data. We applied this model to repurpose known or shelved drugs for brain, lung, and bone metastases of breast cancer with the hypothesis that cancer subtypes have their own specific signaling mechanisms. To test the hypothesis, we addressed specific CSBs for each metastasis that satisfy (i) CSB proteins are activated by the maximal number of enriched signaling pathways specific to a given metastasis, and (ii) CSB proteins are involved in the most differential expressed coding genes specific to each breast cancer metastasis. The identified signaling networks for the three types of breast cancer metastases contain 31, 15, and 18 proteins and are used to reposition 15, 9, and 2 drug candidates for the brain, lung, and bone metastases. We conducted both in vitro and in vivo preclin. expts. as well as anal. on patient tumor specimens to evaluate the targets and repositioned drugs. Of special note, we found that the Food and Drug Administration-approved drugs, sunitinib and dasatinib, prohibit brain metastases derived from breast cancer, addressing one particularly challenging aspect of this disease.
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 242 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1619978 CAPLUS Full-text
DOCUMENT NUMBER: 159:634400
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis Cabre, Roger; Planet, Evarist; Pavlovic, M. Milica
PATENT ASSIGNEE(S): Fundacio Privada Institut de Recerca Biomedica, Spain; Fundacio Privada Institucio Catalana de Recerca i Estudis Avancats
SOURCE: Eur. Pat. Appl., 51pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2650682	A1	20131016	EP 2012-382139	20120409
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CA 2891609	A1	20131017	CA 2013-2891609	20130315
WO 2013153458	A2	20131017	WO 2013-IB1204	20130315
WO 2013153458	A3	20140227		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2013246618	A1	20141106	AU 2013-246618	20130315
KR 2015014919	A	20150209	KR 2014-7031148	20130315
EP 2836837	A2	20150218	EP 2013-731875	20130315
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104797935	A	20150722	CN 2013-80027292	20130315
JP 2015520606	T	20150723	JP 2015-505034	20130315
US 20150293100	A1	20151015	US 2014-14391085	20141007
MX 2014012233	A	20150617	MX 2014-12233	20141009

PRIORITY APPLN. INFO.:

EP 2012-382139	A	20120409
US 2012-61621949	P	20120409
US 2012-61724807	P	20121109
US 2012-61732174	P	20121130
US 2012-61732175	P	20121130
WO 2013-IB1204	W	20130315

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to a method for the prognosis of bone metastasis in triple neg. (including basal-like) breast cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level. The invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of triple neg. (including basal-like) breast cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 243 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1549396 CAPLUS Full-text
DOCUMENT NUMBER: 159:577130
TITLE: Preparation of spirobicyclyl substituted pyrazolyl pyridinamine compounds as tyrosine kinase inhibitors for treating hyperproliferative disorders
INVENTOR(S): Xi, Ning; Li, Minxiong; Zhou, Xuan; Wu, Yanjun
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 90pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013148537	A1	20131003	WO 2013-US33633	20130325
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2012-61617626 P 20120329
OTHER SOURCE(S): CASREACT 159:577130; MARPAT 159:577130
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides spirobicyclic compds. of general formula I (wherein R1-R6 are independently H, D, or F; each X and Y is independently (un)substituted C6-10aryl or (un)substituted 5-10 membered heteroaryl; Z is (un)substituted C5-12spirobicyclyl or (un)substituted -(C1-4alkylene)-(C5-12spirobicyclyl)-, with provisos), pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Synthetic procedures for preparing I are exemplified. For example, II was prepared in a 12-step synthesis that culminated in reaction of intermediates III and IV. II inhibited ALK kinase and c-Met kinase with IC50 values of 15 and 9 nM, resp.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 244 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1459937 CAPLUS Full-text
DOCUMENT NUMBER: 159:472093
TITLE: Preparation of substituted pyrazolylpyridinamine compounds as protein tyrosine kinase modulators for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning; Wang, Tingjin; Yi, Lei
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 141pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013138210	A1	20130919	WO 2013-US30096	20130311

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61610473 P 20120314
US 2012-61617626 P 20120329
OTHER SOURCE(S): CASREACT 159:472093; MARPAT 159:472093
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides substituted pyrazolylpyridinamine compds. of formula I as protein tyrosine kinase modulators capable of regulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion for use in the treatment of hyperproliferative disorders. Compds. of formula I [wherein each R1, R2, R3, R4, R5, and R6 are independently H, D, or F; Z is substituted C3-7 heterocyclyl, substituted (C1-4 alkylene)-(C3-7 heterocyclyl), (un)substituted C5-12 fused bicyclyl, etc.;] stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, or pharmaceutically acceptable salts or prodrugs thereof are claimed and prepared For example, II was prepared by the reaction of 4-iodo-1-(4-((tetrahydro-2H-pyran-2-yl)oxy)tetrahydrofuran-3-yl)-1H-pyrazole with III followed by removal of the tetrahydro-2H-pyran and deprotection of the amine group to afford II in 80% yield. Pharmacodynamic and pharmacokinetic assays were performed on II. II inhibited ALK kinase and c-Met kinase with IC50 of 5 nM and 4 nM resp., demonstrated 82% inhibition of glioblastoma tumor growth when dosed orally at 60 mg/kg to mice, and exhibited a half-life of 35.37 min in human microsomes.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 245 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1270627 CAPLUS Full-text
DOCUMENT NUMBER: 159:384885
TITLE: Epithelial membrane protein 2 (EMP2) regulates angiogenesis in cancer cells through induction of VEGF
INVENTOR(S): Wadehra, Madhuri; Braun, Jonathan; Gordon, Lynn K.
PATENT ASSIGNEE(S): University of California, USA; United States Dept. of Veterans Affairs
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013119693	A1	20130815	WO 2013-US24968	20130206

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2863986	A1	20130815	CA 2013-2863986	20130206
AU 2013203424	A1	20130822	AU 2013-203424	20130206
EP 2812354	A1	20141217	EP 2013-747090	20130206

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2015508066	T	20150316	JP 2014-555854	20130206
US 20150079089	A1	20150319	US 2014-14376724	20140805

PRIORITY APPLN. INFO.: US 2012-61595617 P 20120206
WO 2013-US24968 W 20130206
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose the targeting of epithelial membrane protein 2 (EMP2) for the treatment and prevention of endometrial cancer. In one example, EMP2 expression directly correlated with VEGF protein levels as well as with secreted protein expression by endometrial adenocarcinoma cells. Ribozyme-mediated reduction of EMP2 resulted in undetectable levels of VEGF.
OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 246 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1255893 CAPLUS Full-text
DOCUMENT NUMBER: 159:660795
TITLE: Ponatinib is a potent inhibitor of wild-type and drug-resistant gatekeeper mutant RET kinase
AUTHOR(S): Mologni, Luca; Redaelli, Sara; Morandi, Andrea; Plaza-Menacho, Ivan; Gambacorti-Passerini, Carlo
CORPORATE SOURCE: Dept. of Health Sciences, University of Milano-Bicoccavia Cadore, Monza, 20900, Italy
SOURCE: Molecular and Cellular Endocrinology (2013), 377(1-2), 1-6
CODEN: MCEND6; ISSN: 0303-7207
DIGITAL OBJECT ID: 10.1016/j.mce.2013.06.025
PUBLISHER: Elsevier Ireland Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB RET kinase is aberrantly activated in thyroid cancers and in rare cases of lung and colon cancer, and has been validated as a mol. target in these tumors. Vandetanib was recently approved for the treatment of medullary thyroid cancer. However, vandetanib is ineffective in vitro against RET mutants carrying bulky aminoacids at position 804, the gatekeeper residue, similarly to drug-resistant BCR-ABL mutants in chronic myeloid leukemia. Ponatinib is a multi-target kinase inhibitor that was recently approved for treatment-refractory Philadelphia-pos. leukemia. We show here potent inhibition of oncogenic RET by ponatinib, including the drug-insensitive V804M/L mutants. Ponatinib inhibited the growth of RET+ and BCR-ABL+ cells with similar potency, while not affecting RET-neg. cells. Both in biochem. and in cellular assays ponatinib compared favorably with known RET inhibitors, such as vandetanib, cabozantinib, sorafenib, sunitinib and motesanib, used as reference compds. We suggest that ponatinib should be considered for the treatment of RET+ tumors, in particular those expressing vandetanib-resistant V804M/L mutations.
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 247 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1254595 CAPLUS Full-text
DOCUMENT NUMBER: 159:353569
TITLE: Combination therapy comprising selective VEGFR-2 inhibitors and MEK inhibitors
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 106pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2626066	A1	20130814	EP 2012-154880	20120210

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

PRIORITY APPLN. INFO.: EP 2012-154880 20120210
AB The present invention relates to a combination therapy comprising selective inhibitors of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase and inhibitors of MAP kinase kinase (MEK). Accordingly, a pharmaceutical composition is provided that comprises a selective inhibitor of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase or a pharmaceutically acceptable salt, solvate and/or hydrate thereof, and an inhibitor or a pharmaceutically acceptable salt, solvate and/or hydrate thereof, for use in medicine, especially in the treatment of cancer, like lung cancer, such as non-small cell lung cancer, lung adenocarcinoma or small cell lung cancer. Also a method for identifying patients that are particularly susceptible to such a combination therapy is subject of the present invention. The method comprises the evaluation of the expression level of VEGFR-2 and/or VEGF. An increase in said expression level indicates susceptibility to the combination therapy.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 248 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1227139 CAPLUS Full-text
DOCUMENT NUMBER: 159:329544
TITLE: Methods for predicting tumor response to targeted therapies with signal transduction pathway inhibitors using biomarkers
INVENTOR(S): Cohen, Jonathan M.; Derrien-Colemyn, Alexandrine Josephe; Gillespie, John Williams; Park, Soon Sik
PATENT ASSIGNEE(S): 20/20 Gene Systems, Inc., USA
SOURCE: PCT Int. Appl., 146pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013116735	A1	20130808	WO 2013-US24456	20130201

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,

VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140378500	A1	20141225	US 2014-14375827	20140731
PRIORITY APPLN. INFO.:			US 2012-61593688	P 20120201
			US 2012-61654400	P 20120601
			US 2012-61660305	P 20120615
			US 2012-61660692	P 20120616
			US 2012-61665943	P 20120629
			US 2012-61699760	P 20120911
			US 2012-61699874	P 20120912
			WO 2013-US24456	W 20130201

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A method for identifying cancer patients that are likely to be responders or non-responders to a signal transduction pathway inhibitor is described. The present invention is directed to methods and tests that help predict the likelihood that a tumor will respond to a targeted therapy so that those cancer patients most likely to benefit can receive that drug in a timely manner and those patients unlikely to benefit from a particular drug can instead be prescribed alternative therapies. The test comprises a panel of two or more biomarkers that are part of a signal transduction pathway. The biomarkers included in the panel, in combination, express differently in tumors that respond the drug from those that do not respond. The drugs to which these tests predict response may be designed or determined to target the signal transduction pathway of which the biomarker panel is associated Examples of such drugs are those that target angiogenesis pathways like VEGF or cellular growth pathways like mTOR. Alternatively, the drugs might target something other than the pathway with which the biomarkers are associated but activation of that pathway might otherwise limit or defeat the effectiveness of that drug. Examples of such drugs are those that block cellular receptors but for which activation of downstream signaling pathways nevertheless maintains cellular growth.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 249 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2013:1191423 CAPLUS Full-text
DOCUMENT NUMBER:	159:508181
TITLE:	Cabozantinib (XL184) for the treatment of locally advanced or metastatic progressive medullary thyroid cancer
AUTHOR(S):	Viola, David; Cappagli, Virginia; Elisei, Rossella
CORPORATE SOURCE:	Endocrinology Unit, Department of Clinical & Experimental Medicine, WHO Collaborating Center for the Study & Treatment of Thyroid Diseases & other Endocrine & Metabolic Disorders, University of Pisa, Via Paradisa 2, Pisa, 56124, Italy
SOURCE:	Future Oncology (2013), 9(8), 1083-1092 CODEN: FOUNBN; ISSN: 1479-6694
DIGITAL OBJECT ID:	10.2217/fon.13.128
PUBLISHER:	Future Medicine Ltd.
DOCUMENT TYPE:	Journal; General Review; (online computer file)
LANGUAGE:	English

AB A review. Cabozantinib (XL184) is an oral multiple receptor tyrosine kinase inhibitor manufactured by Exelixis Inc., CA, USA. It mainly inhibits three tyrosine kinase receptors: MET, VEGFR2 and RET. In both preclin. and clin. studies it has been shown to inhibit tumor angiogenesis, invasiveness and metastases. The most frequent side effects are fatigue, diarrhea, decreased appetite, nausea, weight loss and palmar-plantar erythrodysesthesia. A Phase III clin. trial (EXAM study) of XL184 vs. placebo in advanced and progressive medullary thyroid cancer showed a 28 vs. 0% overall response rate and a progression-free survival of 11.2 vs. 4.0 mo (hazard ratio: 0.28; 95% CI: 0.19-0.40; $p < 0.0001$) in patients treated with cabozantinib and placebo, resp. The drug has been approved by the US FDA for the treatment of advanced/progressive metastatic medullary thyroid cancer in the USA. The EMA is now evaluating its approval in Europe.

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 250 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2013:1087476 CAPLUS Full-text
DOCUMENT NUMBER:	159:649618
TITLE:	The novel c-Met inhibitor cabozantinib overcomes gemcitabine resistance and stem cell signaling in pancreatic cancer
AUTHOR(S):	Hage, C.; Rausch, V.; Giese, N.; Giese, T.; Schoensiegel, F.; Labsch, S.; Nwaeburu, C.; Mattern, J.; Gladkich, J.; Herr, I.
CORPORATE SOURCE:	Department of Experimental Medicine, Molecular OncoSurgery Group, University of Heidelberg and German Cancer Research Center, Heidelberg, Germany
SOURCE:	Cell Death & Disease (2013), 4(May), e627 CODEN: CDDEA4; ISSN: 2041-4889
DIGITAL OBJECT ID:	10.1038/cddis.2013.158
PUBLISHER:	Nature Publishing Group
DOCUMENT TYPE:	Journal; (online computer file)
LANGUAGE:	English

AB Pancreatic ductal adenocarcinoma (PDA) is one of the most lethal malignancies. Cancer stem cells (CSCs), which are not targeted by current therapies, may be the reason for pronounced therapy resistance. A new treatment option in phase II trials is cabozantinib that inhibits the pancreatic CSC surface marker and tyrosine kinase receptor c-Met. The purpose of this study was to evaluate the effect of cabozantinib to stem-like features and therapy resistance. Established PDA cell lines, a gemcitabine-resistant subclone, non-malignant pancreatic ductal cells and primary spheroidal cultures from patient tumors were analyzed by MTT-assay, flow cytometry, colony and spheroid formation assays, western blotting, qRT-PCR, antibody protein array, immunohistochem. and morphol. features. Cabozantinib inhibited viability and spheroid formation and induced apoptosis in malignant cells with minor effects in non-malignant cells. After long-term cabozantinib treatment, PDA cells had altered anti- and pro-apoptotic signaling, but still responded to cabozantinib, as apoptosis only slightly decreased and viability only slightly increased suggesting a low resistance-inducing potential of cabozantinib. In parallel, c-Met expression and the pluripotency transcription factor SOX2 were downregulated, which might counteract development of full therapy resistance in long-term treated subclones. In single-treatment studies, cabozantinib increased efficacy of gemcitabine. Most importantly, cabozantinib strongly induced apoptosis and reduced viability in PDA cell lines, which are completely resistant toward gemcitabine. In primary, CSC-enriched spheroidal cultures cabozantinib downregulated CSC markers SOX2, c-Met and CD133 and induced apoptosis. These findings suggest that the clin. use of cabozantinib may be more effective than current chemotherapeutics.

OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 251 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2013:948019 CAPLUS Full-text
DOCUMENT NUMBER:	159:312293
TITLE:	Drug monographs: cabozantanib and omacetaxine
AUTHOR(S):	Solimando, Dominic A., Jr.; Ho, Kristin V.; Waddell, J. Aubrey
CORPORATE SOURCE:	Walter Reed National Military Medical Center, Bethesda, MD, USA
SOURCE:	Hospital Pharmacy (2013), 48(5), 373-377 CODEN: HOPHAZ; ISSN: 0018-5787
DIGITAL OBJECT ID:	10.1310/hpj4805-373
PUBLISHER:	Thomas Land Publishers, Inc.
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB A review. The complexity of cancer chemotherapy requires pharmacists be familiar with the complicated regimens and highly toxic agents used. This column reviews various issues related to preparation, dispensing, and administration of antineoplastic therapy, and the agents, both com. available and investigational, used to treat malignant diseases. Questions or suggestions for topics should be addressed to Dominic A. Solimando, Jr, President, Oncol. Pharmacy Services, Inc, 4201 Wilson Blvd #110-545, Arlington, VA 22203, e-mail: OncRxSvc@aol.com; or J. Aubrey Waddell, Professor, University of Tennessee College of Pharmacy; Oncol. Pharmacist, Pharmacy Department, Blount Memorial Hospital, 907 E. Lamar Alexander Parkway, Maryville, TN 37804, e-mail: waddfour@charter.net.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 252 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2013:909480 CAPLUS Full-text
DOCUMENT NUMBER:	159:736844
TITLE:	Prostate cancer progression after androgen deprivation therapy: mechanisms of castrate resistance and novel therapeutic approaches
AUTHOR(S):	Karantanos, T.; Corn, P. G.; Thompson, T. C.
CORPORATE SOURCE:	Department of Genitourinary Medical Oncology-Research, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
SOURCE:	Oncogene (2013), 32(49), 5501-5511 CODEN: ONCNES; ISSN: 0950-9232
DIGITAL OBJECT ID:	10.1038/onc.2013.206
PUBLISHER:	Nature Publishing Group
DOCUMENT TYPE:	Journal; General Review; (online computer file)
LANGUAGE:	English

AB A review. Prostate cancer is the second-leading cause of cancer-related mortality in men in Western societies. Androgen receptor (AR) signaling is a critical survival pathway for prostate cancer cells, and androgen-deprivation therapy (ADT) remains the principal treatment for patients with locally advanced and metastatic disease. Although a majority of patients initially respond to ADT, most will eventually develop castrate resistance, defined as disease progression despite serum testosterone levels of <20 ng/dL. The recent discovery that AR signaling persists during systemic castration via intratumoral production of androgens led to the development of novel anti-androgen therapies including abiraterone acetate and enzalutamide. Although these agents effectively palliate symptoms and prolong life, metastatic castration-resistant prostate cancer remains incurable. An increased understanding of the mechanisms that underlie the pathogenesis of castrate resistance is therefore needed to develop novel therapeutic approaches for this disease. The aim of this review is to summarize the current literature on the biol. and treatment of castrate-resistant prostate cancer.

OS.CITING REF COUNT: 57 THERE ARE 57 CAPLUS RECORDS THAT CITE THIS RECORD (57 CITINGS)

REFERENCE COUNT: 158 THERE ARE 158 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 253 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2013:907853 CAPLUS Full-text
DOCUMENT NUMBER:	160:94029
TITLE:	Response to Cabozantinib in Patients with RET Fusion-Positive Lung Adenocarcinomas
AUTHOR(S):	Drilon, Alexander; Wang, Lu; Hasanovic, Adnan; Suehara, Yoshiyuki; Lipson, Doron; Stephens, Phil; Ross, Jeffrey; Miller, Vincent; Ginsberg, Michelle; Zakowski, Maureen F.; Kris, Mark G.; Ladanyi, Marc; Rizvi, Naiyer
CORPORATE SOURCE:	Department of Medicine Thoracic Oncology Service, Lenox Hill Hospital, New York, NY, USA
SOURCE:	Cancer Discovery (2013), 3(6), 630-635 CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID:	10.1158/2159-8290.CD-13-0035
PUBLISHER:	American Association for Cancer Research
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The discovery of RET fusions in lung cancers has uncovered a new therapeutic target for patients whose tumors harbor these changes. In an unselected population of non-small cell lung carcinomas (NSCLCs), RET fusions are present in 1%to2% of cases. This incidence increases substantially, however, in never-smokers with lung adenocarcinomas that lack other known driver oncogenes. Although preclin. data provide exptl. support for the use of RET inhibitors in the treatment of RET fusion-pos. tumors, clin. data on response are lacking. We report preliminary data for the first three patients treated with the RET inhibitor cabozantinib on a prospective phase II trial for patients with RET fusion-pos. NSCLCs (NCT01639508). Confirmed partial responses were observed in 2 patients, including one harboring a novel TRIM33-RET fusion. A third patient with a KIF5B-RET fusion has had prolonged stable disease approaching 8 mo (31 wk). All three patients remain progression-free on treatment.

OS.CITING REF COUNT: 77 THERE ARE 77 CAPLUS RECORDS THAT CITE THIS RECORD (79 CITINGS)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 254 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:884114 CAPLUS Full-text
DOCUMENT NUMBER: 161:430953
TITLE: Tumour angiogenesis: an elusive target in castration-resistant prostate cancer
AUTHOR(S): Galsky, Matthew D.; Oh, William K.
CORPORATE SOURCE: The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA
SOURCE: Lancet Oncology (2013), 14(8), 681-682
CODEN: LOANBN; ISSN: 1470-2045
DIGITAL OBJECT ID: 10.1016/S1470-2045(13)70239-0
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In this article, tumor angiogenesis an attractive target in castration-resistant prostate cancer is studied. Indeed, impressive single-agent activity has been reported with cabozantinib, a small mol. inhibitor of the tyrosine kinases MET and VEGFR2. The author reports on randomly allocated 1050 patients with castration-resistant prostate cancer to treatment with docetaxel plus prednisone with or without bevacizumab-the median overall survival for patients receiving bevacizumab was 22.6 mo compared with 21.5 mo for patients treated with placebo (hazard ratio 0.91, 95% CI 0.78-1.05; stratified log-rank p=0.181).
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 255 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:882495 CAPLUS Full-text
DOCUMENT NUMBER: 159:68803
TITLE: Targeting microRNA's miR-409-5p, miR-379 and miR-154* to treat prostate cancer bone metastasis and drug resistant lung cancer
INVENTOR(S): Chung, Leland W. K.; Josson, Sajni; Gururajan, Murali; Jain, Anjali
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 79pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013082499	A1	20130606	WO 2012-US67403	20121130

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

AU 2012345666	A1	20140619	AU 2012-345666	20121130
CN 104080461	A	20141001	CN 2012-80067969	20121130
EP 2785355	A1	20141008	EP 2012-854115	20121130

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2015504847	T	20150216	JP 2014-544946	20121130
US 20140323551	A1	20141030	US 2014-14360489	20140523

PRIORITY APPLN. INFO.: US 2011-61565226 P 20111130
WO 2012-US67403 W 20121130
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention describes methods of treating cancer, cancer metastasis, and drug resistant cancers using miRNA inhibitors; for example, inhibitors of miR-409-5p. Also described are methods of using the miRNA as biomarkers; for example, to predict responsiveness to a cancer drug, to detect a disease state of cancer.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 256 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:873882 CAPLUS Full-text
DOCUMENT NUMBER: 159:100783
TITLE: Medical combination containing hepatocyte growth factor receptor inhibitor and Bcl-2 inhibitor for treating cancer
INVENTOR(S): Zhao, Lei; Wang, Limei
PATENT ASSIGNEE(S): Beijing Tianhe Ruitong Technology Development Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 25pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103127510	A	20130605	CN 2011-10389330	20111130
CN 103127510	B	20150325		

PRIORITY APPLN. INFO.: CN 2011-10389330 20111130
AB The title medical combination comprises a hepatocyte growth factor receptor (cMet) inhibitor and a Bcl-2 inhibitor. The medical combination can be used for preparing a drug for treating colon cancer, liver cancer, lung cancer, renal cancer, gastric cancer, brain tumor, sarcoma, neurospongioma, pancreas cancer, ovarian cancer or prostatic cancer. The medical combination has the advantages of good synergistic effects, high effects, low administration dosage and low side effects.

L8 ANSWER 257 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:869127 CAPLUS Full-text
DOCUMENT NUMBER: 159:436784
TITLE: A Dose-Ranging Study of Cabozantinib in Men with Castration-Resistant Prostate Cancer and Bone Metastases
AUTHOR(S): Lee, Richard J.; Saylor, Philip J.; Dror Michaelson, M.; Michael Rothenberg, S.; Smas, Malgorzata E.; Miyamoto, David T.; Gurski, Carol A.; Xie, Wanling; Maheswaran, Shyamala; Haber, Daniel A.; Goldin, Jonathan G.; Smith, Matthew R.
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Boston, MA, USA
SOURCE: Clinical Cancer Research (2013), 19(11), 3088-3094
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-0319
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Cabozantinib is an oral MET/VEGFR2 inhibitor. A recent phase II study of cabozantinib (100 mg daily) showed improved bone scans in subjects with metastatic castration-resistant prostate cancer (mCRPC), but adverse events (AE) caused frequent dose redns. This study was designed to determine the efficacy and tolerability of cabozantinib at lower starting doses. Exptl. Design: An adaptive design was used to determine the lowest active daily dose among 60, 40, and 20 mg. The primary endpoint was week 6 bone scan response, defined as ≥30% decrease in bone scan lesion area. The secondary endpoint was change in circulating tumor cells (CTC). Results: Among 11 evaluable subjects enrolled at 40 mg, there were 9 partial responses (PR), 1 complete response, and 1 stable disease (SD). Of 10 subjects subsequently enrolled at 20 mg, there were 1 PR, 5 SDs, and 4 with progressive disease. Among 13 subjects enrolled on the 40 mg expansion cohort, there were 6 PRs and 7 SDs. No subjects required dose reduction or treatment interruption at 6 or 12 wk; 3 subjects at dose level 0 discontinued due to AEs by 12 wk. At 40 mg, median treatment duration was 27 wk. 58% of subjects with ≥5 CTCs/7.5mL at baseline converted to <5. Conclusions: Cabozantinib 40 mg daily was associated with a high rate of bone scan response. Cabozantinib 40 mg daily was associated with better tolerability than previously reported for cabozantinib 100 mg daily. These observations informed the design of phase III studies of cabozantinib in mCRPC. Clin Cancer Res; 19(11); 3088-94. ©2013 AACR.
OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 258 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:847461 CAPLUS Full-text
DOCUMENT NUMBER: 159:357745
TITLE: The antiangiogenic ceiling in hepatocellular carcinoma: does it exist and has it been reached?
AUTHOR(S): Abou-Alfa, Ghassan K.; Venook, Alan P.
CORPORATE SOURCE: Section of Gastrointestinal Oncology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
SOURCE: Lancet Oncology (2013), 14(7), e283-e288
CODEN: LOANBN; ISSN: 1470-2045
DIGITAL OBJECT ID: 10.1016/S1470-2045(13)70161-X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The recommendation of sorafenib as std. of care in advanced hepatocellular carcinoma has lent support to the increased use of antiangiogenic therapies. However, in three phase 3 randomised trials that compared other antiangiogenics with sorafenib, results did not show superiority or non-inferiority of the new therapies. The 10-mo median overall survival shown in these studies for patients given sorafenib might be a ceiling for single-agent antiangiogenic therapy. Strategies to increase survival time include combination therapies that pair antiangiogenic treatment with biol. therapy or chemotherapy. The combination of sorafenib and erlotinib was not superior to sorafenib alone, which suggests no pos. interaction between antiangiogenics and tyrosine kinase inhibitors in the treatment of advanced hepatocellular carcinoma. A combination of sorafenib and doxorubicin is being assessed in a randomised phase 3 trial. Differences in patient outcome with sorafenib because of disease cause and the ethnic origin of patients suggest that sorafenib's multitarget capacity, including RAF kinase inhibition, might be important. MET inhibitors cabozantinib and tivantinib are drugs that might also bypass the so-called antiangiogenic ceiling and have led to selective treatment of patients that overexpress MET with these drugs. Although this intense period of research activity has not yet resulted in significant improvements in survival for patients with advanced hepatocellular carcinoma, we are certainly closer to a customised treatment, which should increase the antiangiogenic survival ceiling.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 259 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:761990 CAPLUS Full-text
DOCUMENT NUMBER: 158:704608
TITLE: Method of quantifying cancer treatment
INVENTOR(S): Holland, Jaymes
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 50pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013070903	A1	20130516	WO 2012-US64134	20121108

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2854664	A1	20130516	CA 2012-2854664	20121108
AU 2012335750	A1	20140605	AU 2012-335750	20121108
AR 88813	A1	20140710	AR 2012-104223	20121108

CN 104039226 A 20140910 CN 2012-80066413 20121108
EP 2775921 A1 20140917 EP 2012-795939 20121108
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
JP 2015505360 T 20150219 JP 2014-541261 20121108
IN 2014CN03674 A 20150703 IN 2014-CN3674 20140515
PRIORITY APPLN. INFO.: US 2011-61557362 P 20111108
WO 2012-US64134 W 20121108
OTHER SOURCE(S): CASREACT 158:704608
AB This invention is directed to a method for quantifying cancer treatment response in patients with bone metastases using computer aided bone scan assessment, comprising: (a) obtaining a bone scan image; (b) normalizing the obtained bone scan image to identify normalized bone scan lesions; and (c) quant. assessing the normalized bone scan lesions using bone scan lesion area, bone scan intensity, or bone scan lesion count.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 260 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:761969 CAPLUS Full-text
DOCUMENT NUMBER: 158:704607
TITLE: Dual inhibitor of Met and VEGF for treating cancer
INVENTOR(S): Aftab, Dana T.; Schimmoller, Frauke
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013070890	A1	20130516	WO 2012-US64116	20121108

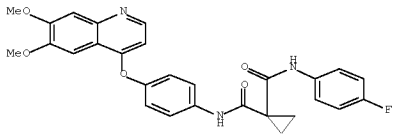
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2854336	A1	20130516	CA 2012-2854336	20121108
AU 2012335737	A1	20140605	AU 2012-335737	20121108
IL 232421	A	20140630	IL 2012-232421	20121108
KR 2014088610	A	20140710	KR 2014-7015127	20121108
EP 2776033	A1	20140917	EP 2012-787328	20121108

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

CN 104159585	A	20141119	CN 2012-80066410	20121108
JP 2014532766	T	20141208	JP 2014-541256	20121108
MX 2014005458	A	20150416	MX 2014-5458	20140506
US 20140323522	A1	20141030	US 2014-14356927	20140508
IN 2014CN04067	A	20151023	IN 2014-CN4067	20140530

PRIORITY APPLN. INFO.: US 2011-61557358 P 20111108
WO 2012-US64116 W 20121108
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:704607; MARPAT 158:704607
GI



AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and bone metastases, with a dual inhibitor of MET and VEGF.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 261 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:729332 CAPLUS full-text
DOCUMENT NUMBER: 158:676742
TITLE: Fusion proteins with a C-terminal domain of the gene ret receptor and their use in cancer diagnosis
INVENTOR(S): Ju, Young-Seok; Seo, Jeong-Sun; Kim, Kun-Hee
PATENT ASSIGNEE(S): Macrogen Inc., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 61pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20130116280	A1	20130509	US 2012-13663565	20121030
WO 2013066047	A1	20130510	WO 2012-KR9056	20121031

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS,

SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

KR 2014092846	A	20140724	KR 2014-7013826	20121031
EP 2773673	A1	20140910	EP 2012-845116	20121031

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

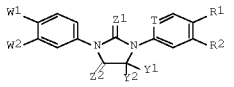
JP 2015504299 T 20150212 JP 2014-538724 20121031
PRIORITY APPLN. INFO.: US 2011-61553483 P 20111031
US 2012-13663565 A 20121030
WO 2012-KR9056 W 20121031
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A fusion protein including N-terminal domain of a fusion partner at N-terminal and C-terminal domain of RET protein at C-terminal and the gene encoding are identified as diagnostic markers for cancers, especially lung cancers. The somatic mutation forming the chimeric gene was identified in a poorly differentiated lung adenocarcinoma. The adenocarcinoma did not show any of the most common lung cancer-associated mutations, but several discordant reads, indicating transposition events, were identified. Expression of the chimeric KIF5B-RET gene in NIH-3T3 resulted in a neoplastic phenotype. Growth of these cells could be inhibited by the ret kinase inhibitor cabozantinib.

L8 ANSWER 262 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:728614 CAPLUS Full-text
DOCUMENT NUMBER: 158:672026
TITLE: Methods using heteroaryl compounds for treatment of disorders involving androgen-, estrogen- and progesterone-receptors
INVENTOR(S): Protter, Andrew A.; Hung, David T.; Chakravarty, Sarvajit; Bernales, Sebastian
PATENT ASSIGNEE(S): Medivation Technologies, Inc., USA
SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013067131	A1	20130510	WO 2012-US62980	20121101

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2011-61554919 P 20111102
OTHER SOURCE(S): MARPAT 158:672026
GI



I

AB The disclosure describes compds. of formula I [W1 = CN, NO2, SO2R4; W2 = alkyl, alkenyl, alkynyl, halo; Z1 = S, O; Z2 = S, O, NR4; R4 = independently H, alkyl, aryl; Y1, Y2 = independently H, alkyl, alkenyl, aryl, arylalkyl, heterocyclic etc.; R1 = alkyl, cycloalkyl, heterocyclic etc.; R2 = independently H, halo, CN, alkyl etc.], or pharmaceutically acceptable salts thereof, useful for treating disorders involving androgen, estrogen, and/or progesterone receptors. In another embodiment of the invention the disorder is selected from the group consisting of neurodegenerative disorders, cancer, polyglutamate disease, rheumatoid arthritis, systemic hyperandrogenism, seborrhea, hirsutism, precocious puberty, polycystic ovary syndrome, acne, alopecia, benign prostatic hyperplasia, intrauterine fibroids, endometriosis, glaucoma, meningiomas, Kennedy's disease (KD) or X-linked spinal and bulbar muscular atrophy.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 263 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:725439 CAPLUS Full-text
DOCUMENT NUMBER: 158:676739
TITLE: Fusion proteins with a C-terminal domain of the gene ret receptor and their use in cancer diagnosis
INVENTOR(S): Ju, Young-Seok; Seo, Jeong-Sun; Kim, Eun-Hee
PATENT ASSIGNEE(S): Macrogen Inc., S. Korea
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013066047	A1	20130510	WO 2012-KR9056	20121031

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,

MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20130116280	A1	20130509	US 2012-13663565	20121030
KR 2014092846	A	20140724	KR 2014-7013826	20121031
EP 2773673	A1	20140910	EP 2012-845116	20121031
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2015504299	T	20150212	JP 2014-538724	20121031
PRIORITY APPLN. INFO.:			US 2011-61553483 P	20111031
			US 2012-13663565 A	20121030
			WO 2012-KR9056 W	20121031

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A fusion protein including N-terminal domain of a fusion partner at N-terminal and C-terminal domain of RET protein at C-terminal and the gene encoding are identified as diagnostic markers for cancers, especially lung cancers. The somatic mutation forming the chimeric gene was identified in a poorly differentiated lung adenocarcinoma. The adenocarcinoma did not show any of the most common lung cancer-associated mutations, but several discordant reads, indicating transposition events, were identified. Expression of the chimeric KIF5B-RET gene in NIH-3T3 resulted in a neoplastic phenotype. Growth of these cells could be inhibited by the ret kinase inhibitor cabozantinib.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 264 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:684015 CAPLUS Full-text

DOCUMENT NUMBER: 158:649640

TITLE: Free prostate specific antigen (PSA) antibodies as diagnostics, prognostics and therapeutics for prostate cancer

INVENTOR(S): Sawyers, Charles; Ulmert, David; Lewis, Jason; Evans, Michael; Lija, Hans

PATENT ASSIGNEE(S): Memorial Sloan-Kettering Cancer Center, USA

SOURCE: PCT Int. Appl., 103pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013063312	A1	20130502	WO 2012-US61982	20121025
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,				

identification of novel markers of response and resistance to these therapies may better individualize treatment for patients with CRPC.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 266 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:644308 CAPLUS Full-text

DOCUMENT NUMBER: 158:620790

TITLE: Process for preparing quinoline derivatives

INVENTOR(S): Wilson, Jo Ann; Naganathan, Sriram; Pfeiffer, Matthew; Andersen, Neil G.

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

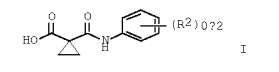
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013059788	A1	20130425	WO 2012-US61320	20121022
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2852771	A1	20130425	CA 2012-2852771	20121022
AU 2012325768	A1	20140522	AU 2012-325768	20121022
IL 232139	A	20140528	IL 2012-232139	20121022
AR 88483	A1	20140611	AR 2012-103944	20121022
KR 2014088874	A	20140711	KR 2014-7012435	20121022
EP 2768796	A1	20140827	EP 2012-783763	20121022
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2014530880	T	20141120	JP 2014-537359	20121022
CN 104395284	A	20150304	CN 2012-80054241	20121022
ZA 2014002579	A	20150325	ZA 2014-2579	20140409
MX 2014004583	A	20141006	MX 2014-4583	20140415
US 20140256938	A1	20140911	US 2014-14353251	20140421
IN 2014CN02971	A	20150703	IN 2014-CN2971	20140421
PRIORITY APPLN. INFO.:			US 2011-61549312 P	20111020
			WO 2012-US61320 W	20121022

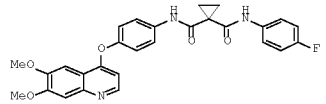
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 158:620790; MARPAT 158:620790

GI



I



II

AB The invention is directed to processes for prepg. compds. of formula I (R2 is H, F, Cl and Br) by activation of 1,1-cyclopropanedicarboxylic acid with thionyl chloride followed by amidation with substituted aniline derivative Example compound II L-malate was prepared by chlorination of 6,7-dimethoxyquinolin-4-ol followed by etherification of 4-chloro-6,7-dimethoxyquinoline with 4-aminophenol; the resulting 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine underwent acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropanecarbonyl chloride to give compound II, which underwent addition of L-malic acid to give the desired product.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 267 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:564369 CAPLUS Full-text

DOCUMENT NUMBER: 159:419448

TITLE: Lessons learned and questions unanswered from use of multitargeted kinase inhibitors in medullary thyroid cancer

AUTHOR(S): Sherman, Steven I.

CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Oral Oncology (2013), 49(7), 707-710
CODEN: EJCCER; ISSN: 1368-8375

DIGITAL OBJECT ID: 10.1016/j.oraloncology.2013.03.442

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB To review studies of novel multitargeted kinase inhibitors studied in patients with medullary thyroid cancer (MTC). Search of relevant refs. in PubMed and Google Scholar on "chemotherapy" and "medullary thyroid cancer". Multitargeted kinase inhibitors have revolutionized the role of chemotherapy for progressive MTC, providing for the first time tolerable therapeutic

MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2853705	A1	20130502	CA 2012-2853705	20121025
AU 2012328679	A1	20140612	AU 2012-328679	20121025
EP 2771688	A1	20140903	EP 2012-844178	20121025
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
CN 104040341	A	20140910	CN 2012-80063852	20121025
JP 2015502339	T	20150122	JP 2014-539018	20121025
US 20140308204	A1	20141016	US 2014-14353989	20140424
PRIORITY APPLN. INFO.:			US 2011-61551195 P	20111025
			WO 2012-US61982 W	20121025

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The authors disclose the use of antibodies to free prostate-specific antigen (fPSA) in the diagnosis, prognosis, and therapeutic monitoring of prostate cancer. In one example, tumor localization of labeled anti-fPSA antibody is shown to be reduced by the antiandrogen MDV3100.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 265 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:647172 CAPLUS Full-text

DOCUMENT NUMBER: 159:188392

TITLE: Emerging targeted therapies for castration-resistant prostate cancer

AUTHOR(S): Adamo, Vincenzo; Noto, Laura; Franchina, Tindara; Chiofalo, Giuseppe; Picciotto, Maria; Toscano, Giuseppe; Caristi, Nicola

CORPORATE SOURCE: Integrated Therapies in Oncology Unit, Department of Human Pathology, University of Messina, Messina, 98125, Italy

SOURCE: Frontiers in Cancer Endocrinology (2012), 3(May), 73
CODEN: FCERD9

DIGITAL OBJECT ID: 10.3389/fendo.2012.00073

PUBLISHER: Frontiers Media S.A.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. Until recently, few therapeutic options were available for patients with castration-resistant prostate cancer (CRPC). Since 2010, four new mols. with a demonstrated benefit (sipuleucel-T, cabazitaxel, abiraterone and denosumab) have been approved in this setting and to-date several other agents are under investigation in clin. trials. The purpose of this review is to present an update of targeted therapies for CRPC. Presented data are obtained from literature and congress reports updated until Dec. 2011. Targeted therapies in advanced phases of clin. development include novel androgen signaling inhibitors, inhibitors of alternative signaling pathways, anti-angiogenic agents, inhibitors that target the bone microenvironment and immunotherapeutic agents. Radium-223 and MDV3100 demonstrated a survival advantage in phase III trials and the road for their introduction in clin. practice is rapidly ongoing. Results are also awaited for phase III studies currently underway or planned with new drugs given as monotherapy (TAK-700, cabozantinib, tasquinimod, PROSTVAC-VF, ipilimumab) or in combination with docetaxel (custirsen, aflibercept, dasatinib, zibotentan). The optimal timing, combination and sequencing of emerging therapies remain unknown and require further investigation. Addnl., the

options that can improve outcomes in patients with progressive disease. Drugs thought to inhibit the RET kinase have advanced the furthest for this disease, but these agents also target the VEGF receptor along with other kinases that may be relevant to both beneficial and adverse effects. Vandetanib improved progression-free survival from 19.3 to 30.5 mo compared with placebo in patients with metastatic disease, whereas cabozantinib improved progression-free survival from 4.0 mo to 11.2 mo in a population with more aggressive disease. However, "cure" remains elusive, adverse events frequent, and exactly how such "targeted" agents actually function within MTC remains unclear. New approaches to clin. trial design and the preclin. development of targeted agents may be required to optimize the combination of maximum efficacy with minimal toxicity for patients with metastatic MTC.

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 268 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:522453 CAPLUS Full-text
DOCUMENT NUMBER: 159:125821
TITLE: Emerging therapies in metastatic castration-sensitive and castration-resistant prostate cancer
AUTHOR(S): MacVicar, Gary R.; Hussain, Maha H.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Internal Medicine, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
SOURCE: Current Opinion in Oncology (2013), 25(3), 252-260
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e32835ff161
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB Purpose of review: Therapeutic options for men with metastatic prostate cancer are expanding. Here we discuss the scientific progress in this disease that led to approval of several agents in the last decade and highlight ongoing clin. investigation. Recent findings: In androgen-sensitive disease, trials are evaluating the role of intermittent androgen-deprivation therapy, early chemotherapy, and novel targeted and hormonal therapies. For chemotherapy-naive, metastatic castration-resistant prostate cancer (mCRPC), abiraterone is effective. Trials with addnl. agents targeting androgen receptor (AR) signaling, such as TAK-700 and enzalutamide, are ongoing. Other agents in development target the endothelin pathway, angiogenesis, AR chaperones, and immune mechanisms. Docetaxel with prednisone remains the standard first-line chemotherapeutic regimen as trials incorporating novel agents with docetaxel have been neg. Postdocetaxel, enzalutamide improves survival. Early results with cabozantinib are encouraging, and phase III studies are ongoing. Denosumab and radium-223 reduce the risk of skeletal-related events (SREs), but only radium-223 improves survival. Summary: Progress in understanding the disease biol. and mechanisms of castration resistance led to significant therapeutic advancements, particularly in the setting of mCRPC in which several phase III trials, each incorporating agents with different mechanisms of action, have improved survival. As a result, new options exist, and the standard of care has changed significantly. Further advances are anticipated.

ACCESSION NUMBER: 2013:522110 CAPLUS Full-text
DOCUMENT NUMBER: 159:125815
TITLE: Targeting MET and Vascular Endothelial Growth Factor Receptor Signaling in Castration-Resistant Prostate Cancer
AUTHOR(S): Lee, Richard J.; Smith, Matthew R.
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA
SOURCE: Cancer Journal (Philadelphia, PA, United States) (2013), 19(1), 90-98
CODEN: CAJOCB; ISSN: 1528-9117
DIGITAL OBJECT ID: 10.1097/PPO.0b013e318281e280
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Effective management of bone metastases in men with castration-resistant prostate cancer (CRPC) remains an important unmet medical need. MET and vascular endothelial growth factor receptor (VEGFR) are rational targets for intervention in CRPC. Clin. trials involving agents that inhibit one but not both pathways have reported modest activity and no improvement in overall survival. Cabozantinib is an oral multitargeted tyrosine kinase inhibitor that inhibits both MET and VEGFR-2. A phase II randomized discontinuation study involving subjects with CRPC demonstrated that cabozantinib therapy is associated with improvement in bone scans, bone turnover markers, and pain response, but with significant adverse events leading to dose reduction and treatment discontinuation. Lower doses of cabozantinib retain high levels of activity with less toxicity. Ongoing phase III clin. trials will define the role of cabozantinib in CRPC. We summarize the rationale for targeting MET and VEGFR pathways in CRPC and the clin. data available to date.

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 271 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:470327 CAPLUS Full-text
DOCUMENT NUMBER: 158:493976
TITLE: Combinations comprising c-Met antagonists and B-raf antagonists for treatment of cancer
INVENTOR(S): Wilson, Timothy R.; Koeppen, Hartmut; Merchant, Mark; Settleman, Jeffrey
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 148pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013043715	A1	20130328	WO 2012-US56106	20120919
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
CA 2846630	A1	20130328	CA 2012-2846630	20120919
US 20130078252	A1	20130328	US 2012-13622878	20120919
AU 2012312515	A1	20140313	AU 2012-312515	20120919
IL 231056	A	20140331	IL 2012-231056	20120919
AR 87918	A1	20140423	AR 2012-103446	20120919
KR 2014064971	A	20140528	KR 2014-7010162	20120919
CN 103930111	A	20140716	CN 2012-80055708	20120919
EP 2758055	A1	20140730	EP 2012-768982	20120919
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2014534949	T	20141225	JP 2014-530956	20120919
ZA 2014001370	A	20150930	ZA 2014-1370	20120919
MX 2014002990	A	20140521	MX 2014-2990	20140313
US 20150125452	A1	20150507	US 2014-14535071	20141106
PRIORITY APPLN. INFO.:			US 2011-61536436 P	20110919
			US 2011-61551328 P	20111025
			US 2012-61598783 P	20120214
			US 2012-61641139 P	20120501
			US 2012-13622878 B1	20120919
			WO 2012-US56106 W	20120919

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides combination therapies for treating a pathol. condition, such as cancer, wherein a c-met antagonist (e.g. crizotinib, tivantinib, anti-HGF antibody, onartuzumab) is combined with a B-raf antagonist (e.g. vemurafenib), thereby providing significant antitumor activity. C-met expression was inversely correlated with sensitivity to vemurafenib treatment. In one aspect, provided are methods for treating a cancer patient who has increased likelihood of developing resistance to B-raf antagonist comprising administering an effective amount (in combination) of B-raf antagonist and c-met antagonist. In addition, patients with B-raf mutant melanoma who had higher levels of circulating hepatocyte growth factor (HGF) showed substantially reduced progression free survival and overall survival when treated with B-raf antagonist, relative to patients with lower circulating HGF levels treated with B-raf antagonist.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 272 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:466384 CAPLUS Full-text
DOCUMENT NUMBER: 158:494085
TITLE: Method for treating osteoporosis
INVENTOR(S): Aftab, Dana T.; Clary, Douglas
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 73pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 269 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:522113 CAPLUS Full-text
DOCUMENT NUMBER: 159:125816
TITLE: From Bevacizumab to Tasquinimod: Angiogenesis as a Therapeutic Target in Prostate Cancer
AUTHOR(S): Schweizer, Michael T.; Carducci, Michael A.
CORPORATE SOURCE: Prostate Cancer Research Program, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins, Baltimore, MD, USA
SOURCE: Cancer Journal (Philadelphia, PA, United States) (2013), 19(1), 99-106
CODEN: CAJOCB; ISSN: 1528-9117
DIGITAL OBJECT ID: 10.1097/PPO.0b013e31827e0b86
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. It was first posited in the 1970s that angiogenesis may prove to be a useful target for anticancer therapies. Since then, a number of agents have been developed and tested across a range of tumor types; however, to date, there have unfortunately been more failures than successes. Prostate cancer (PCa) is no exception in this regard, and despite a strong preclin. rationale for targeting angiogenesis in men with PCa, there has yet to be an antiangiogenic therapy proven to prolong survival in this group of patients. Drugs have been developed to target a host of angiogenesis mediators. These include vascular endothelial growth factor (VEGF), the VEGF receptors, antiangiogenic factors (e.g., thrombospondin-1), and downstream mediators of angiogenesis (e.g., hypoxia-inducible factor-1α and MET). At present, there are 2 drugs being tested in the phase III setting for men with PCa: cabozantinib and tasquinimod. Cabozantinib, a dual VEGF receptor-2/MET inhibitor, has shown dramatic beneficial effects on radiog. evident bone metastases and pain in the phase II setting. There are currently 2 large phase III trials underway to further investigate cabozantinib's role in treating men with PCa. Both trials randomize subjects to cabozantinib vs. mitoxantrone: one is designed to evaluate overall survival, and the other, pain response durability. The other drug, tasquinimod, has a somewhat poorly understood mechanism of action. It is thought to exert an antiangiogenic effect through the inhibition of myeloid-derived suppressor cells, key to the support of an angiogenic environment, and down-regulation of hypoxia-inducible factor-1α. A phase II trial randomizing men to tasquinimod vs. placebo revealed a median progression-free survival advantage in the exptl. arm (7.6 vs. 3.3 mo with placebo; P = 0.0042). Based on these encouraging phase II results, a randomized, double-blind, placebo-controlled trial in men with metastatic castration-resistant PCa was launched. That trial is powered for a primary endpoint of progression-free survival and is expected to enroll 1200 men.

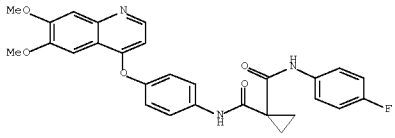
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 270 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013043840	A1	20130328	WO 2012-US56281	20120920
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2848512	A1	20130328	CA 2012-2848512	20120920
AU 2012312364	A1	20140410	AU 2012-312364	20120920
IL 231495	A	20140430	IL 2012-231495	20120920
KR 2014069133	A	20140609	KR 2014-7009534	20120920
CN 103957915	A	20140730	CN 2012-80051094	20120920
EP 2758057	A1	20140730	EP 2012-770368	20120920
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2014527984	T	20141023	JP 2014-531955	20120920
AR 87995	A1	20140430	AR 2012-103501	20120921
MX 2014003027	A	20141024	MX 2014-3027	20140313
IN 2014CN02093	A	20141010	IN 2014-CN2093	20140319
US 20140228401	A1	20140814	US 2014-14346570	20140321
PRIORITY APPLN. INFO.:			US 2011-61538039 P	20110922
			WO 2012-US56281 W	20120920

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:494085; MARPAT 158:494085
GI



PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Anti-angiogenic treatment of glioblastoma with Vascular Endothelial Growth Factor (VEGF)- or VEGF Receptor 2 (VEGFR2) inhibitors normalizes tumor vessels, resulting in a profound radiol. response and improved quality of life. This approach however does not halt tumor progression by diffuse infiltration, as this phenotype is less angiogenesis dependent. Combined inhibition of angiogenesis and diffuse infiltrative growth would therefore be a more effective treatment approach in these tumors. The HGF/c-MET axis is important in both angiogenesis and cell migration in several tumor types including glioma. We therefore analyzed the effects of the c-MET- and VEGFR2 tyrosine kinase inhibitor cabozantinib (XL184, Exelixis) on c-MET pos. orthotopic E98 glioblastoma xenografts, which routinely present with angiogenesis-dependent areas of tumor growth, as well as diffuse infiltrative growth. In in vitro cultures of E98 cells, cabozantinib effectively inhibited c-MET phosphorylation, concomitant with inhibitory effects on AKT and ERK1/2 phosphorylation, and cell proliferation and migration. VEGFR2 activation in endothelial cells was also effectively inhibited in vitro. Treatment of BALB/c nu/nu mice carrying orthotopic E98 xenografts resulted in a significant increase in overall survival. Cabozantinib effectively inhibited angiogenesis, resulting in increased hypoxia in angiogenesis-dependent tumor areas, and induced vessel normalization. Yet, tumors ultimately escaped cabozantinib therapy by diffuse infiltrative outgrowth via vessel co-option. Of importance, in contrast to the results from in vitro expts., in vivo blockade of c-MET activation was incomplete, possibly due to multiple factors including restoration of the blood-brain barrier resulting from cabozantinib-induced VEGFR2 inhibition. In conclusion, cabozantinib is a promising therapy for c-MET pos. glioma, but improving delivery of the drug to the tumor and/or the surrounding tissue may be needed for full activity.
OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 275 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:378985 CAPLUS Full-text
DOCUMENT NUMBER: 159:193339
TITLE: Cellular signaling pathway alterations and potential targeted therapies for medullary thyroid carcinoma
AUTHOR(S): Giunti, Serena; Antonelli, Alessandro; Amorosi, Andrea; Santarpia, Libero
CORPORATE SOURCE: Department of Pathology, Centro Oncologico Fiorentino, Sesto Fiorentino, 50019, Italy
SOURCE: International Journal of Endocrinology (2013) 803171, 16 pp.
CODEN: IJENIG; ISSN: 1687-8345
DIGITAL OBJECT ID: 10.1155/2013/803171
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Parafollicular C-cell-derived medullary thyroid cancer (MTC) comprises 3% to 4% of all thyroid cancers. While cytotoxic treatments have been shown to have limited efficacy, targeted mol. therapies that inhibit rearranged during transfection (RET) and other tyrosine kinase receptors that are mainly involved in angiogenesis have shown great promise in the treatment of metastatic or locally advanced MTC. Multi-tyrosine kinase inhibitors such as vandetanib, which is already approved for the treatment of progressive MTC, and cabozantinib have shown distinct advantages with regard to rates of disease response and control. However, these types of tyrosine kinase inhibitor compds. are able to concurrently block several types of targets, which limits the understanding of RET as a specific target. Moreover, important resistances to tyrosine kinase inhibitors can occur, which limit the long-term efficacy of these treatments. Deregulated cellular signaling pathways and genetic alterations in MTC, particularly the activationof the RAS/mammalian target of rapamycin (mTOR) cascades and RET crosstalk signaling, are now emerging as novel and potentially promising therapeutic treatments for aggressive MTC.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 276 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:377358 CAPLUS Full-text
DOCUMENT NUMBER: 159:86211
TITLE: Cabozantinib as a Novel Therapy for Renal Cell Carcinoma
AUTHOR(S): Vaishampayan, Ulka
CORPORATE SOURCE: Wayne State University, Detroit, MI, 48201, USA
SOURCE: Current Oncology Reports (2013), 15(2), 76-82
CODEN: CORUAT; ISSN: 1534-6269
DIGITAL OBJECT ID: 10.1007/s11912-012-0289-x
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib/XL184 (Exelexis, Inc.) has demonstrated remarkable responses in kidney cancer. Preclin. results revealed VEGF, KIT and MET inhibition in a variety of solid tumors such as thyroid, ovarian, renal, lung, liver and prostate cancers. A phase II trial demonstrated efficacy in renal cancer with a 28 % objective response rate, stable disease rate of 62 % and median progression free survival of 14.7 mo. Predominant toxicities of fatigue and diarrhea were noted. Dramatic responses in bone metastases (three of four patients) make the agent especially valuable for palliation in a disease, where presence of bone metastases is a predictor of worse survival. Cabozantinib is an emerging novel agent with promising activity in advanced kidney cancer. Randomized trials are planned in comparison with standard VEGF inhibitor therapy. Defining the role of MET overexpression would help patient selection and enrich and enhance the future evaluation of this targeted novel agent.
OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 277 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:359822 CAPLUS Full-text
DOCUMENT NUMBER: 159:33929
TITLE: Treatment directed to signalling molecules in patients with advanced differentiated thyroid cancer
AUTHOR(S): Saez, Jose M. G.
CORPORATE SOURCE: Endocrinology and Nutrition Service, L'Hospitalet of

L8 ANSWER 273 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:417299 CAPLUS Full-text
DOCUMENT NUMBER: 159:86304
TITLE: Pharmacokinetic evaluation of
AUTHOR(S): Karras, Spyridon; Pontikides, Nikolaos; Krassas, Gerasimos E.
CORPORATE SOURCE: Department of Endocrinology, Diabetes and Metabolism, Panagia General Hospital, Thessaloniki, Greece
SOURCE: Expert Opinion on Drug Metabolism & Toxicology (2013), 9(4), 507-515
CODEN: EODMAP; ISSN: 1742-5255
DIGITAL OBJECT ID: 10.1517/17425255.2013.780028
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Introduction: Conventional treatment modalities for thyroid cancer lead to complete remission in only one-third of patients with distant metastases. On the other hand, medullary thyroid cancer (MTC) and anaplastic thyroid cancer (ATC), although rare, are responsible for a significant percentage of thyroid cancer-related deaths. New treatments are needed to treat such patientsAreas covered: The aim of this review is to provide the latest information on , a new tyrosine kinase inhibitor (TKI) that is currently used mainly as a treatment of MTC. The authors collated data that were retrieved from a PubMed literature search.Expert opinion: CBZ targets multiple cell-signaling pathways involved in the mol. pathogenesis of thyroid cancer. These are namely VEGF receptor-2, hepatocyte growth factor receptor and rearranged during transfection receptor. Furthermore, it is a drug which may be used in cases where conventional therapies (mainly for MTC) are proved ineffective or have shown poor results with a good outcome. CBZ may also be administered alone or in combination with other drugs of the same family.
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 274 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:414621 CAPLUS Full-text
DOCUMENT NUMBER: 159:53852
TITLE: Effects of dual targeting of tumor cells and stroma in human glioblastoma xenografts with a tyrosine kinase inhibitor against c-MET and VEGFR2
AUTHOR(S): Navis, Anna C.; Bourgonje, Annika; Wesseling, Pieter; Wright, Alan; Hendriks, Wiljan; Verrijp, Kiek; van der Laak, Jeroen A. W. M.; Heerschap, Arend; Leenders, William P. J.
CORPORATE SOURCE: Department of Pathology, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.
SOURCE: PLoS One (2013), 8(3), e58262
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0058262
AB This invention is directed to the treatment of osteoporosis using N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Llobregat, Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (CIBERDEM), University Hospital of Bellvitge, Barcelona, Spain
SOURCE: Anti-Cancer Agents in Medicinal Chemistry (2013), 13(3), 483-495
CODEN: AAMCE4; ISSN: 1871-5206
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Mutation detection in samples from thyroid cancer with the addition of BRAF mutation, and also the detection of RAS, RET/PTC, and PAX8/PPARγ mutations, may also contribute to cancer diagnosis. On the other hand, the MAPK/ERK (mitogen-activated protein kinase/extracellular signal-regulated kinase signaling pathway) and PI3K/Akt (lipid kinase phoshoinositid-3-kinase signaling pathway) play an important role in the transmission of cell signals. The genes, coding the signaling cascade proteins (RET, RAS, BRAF, PI3K, PTEN, AKT), are mutated or aberrantly expressed in thyroid cancer derived from follicular thyroid cells. Genetic and epigenetic alternations, concerning MAPK/ERK and PI3K/Akt signaling pathways, contribute to their activation and interaction as a consequence of malignant follicular cell transformation. The understanding of this mol. mechanism provides access to novel mol. prognostic and therapeutic strategies for inhibiting the oncogenic activity of the signaling pathways. This ability to investigate tumor biol. allows for the selection of different drugs. Nowadays the most relevant are treatments directed to tyrosine kinase receptors that bind for a wide variety of ligands and are frequently mutated and induce a constitutive activation such that a chimerical protein expression takes place in follicular cells in the domain of RET, as well as in other receptors. Many mols. such as: motesanib, sorafenib, vandetanib, sunitinib, XL-184, imatinib, axitinib, pazopanib, lenvatinib, combretastatin, gefitinib, cetuximab, bortezomib and thiazoldonedione have been developed. Some of them also can act in receptors of vascular endothelial growth factor and epidermal growth factor receptors. Information obtained through cytol. or biopsy samples permits the study of complex metabolic or genetic pathways, thus providing researchers with a high throughput tool for elucidating changes in the global expression patterns seen in tumor cells and allowing for different therapeutic strategies in thyroid cancer which take into account the predominant altered pathways observed in these samples.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 278 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:260769 CAPLUS Full-text
DOCUMENT NUMBER: 158:690611
TITLE: Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial
AUTHOR(S): Smith, David C.; Smith, Matthew R.; Sweeney, Christopher; Elfiky, Aymen A.; Logothetis, Christopher; Corn, Paul G.; Vogelzang, Nicholas J.; Small, Eric J.; Harzstark, Andrea L.; Gordon, Michael S.; Vaishampayan, Ulka N.; Haas, Naomi B.; Spira, Alexander I.; Lara, Primo N., Jr.; Lin, Chia-Chi; Srinivas, Sandy; Sella, Avishay; Schoffski, Patrick; Scheffold, Christian; Weitzman, Aaron L.; Hussain, Maha
CORPORATE SOURCE: University of Michigan, Ann Arbor, USA
SOURCE: Journal of Clinical Oncology (2013), 31(4), 412-419
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.45.0494
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Cabozantinib (XL 184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. Patients and Methods: Patients received 100 mg of cabozantinib daily. Those with stable disease per RECIST at 12 wk were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 wk and progression-free survival (PFS) after random assignment. Results: One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 wk was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 wk (95% CI, 10.7 to 62.4 wk) with cabozantinib and 5.9 wk (95% CI, 5.4 to 6.6 wk) with placebo (hazard ratio, 0.12; P < .001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by ≥ 50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot syndrome (8%). Conclusion: Cabozantinib has clin. activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and redns. in bone turnover markers, pain, and narcotic use.
OS.CITING REF COUNT: 130 THERE ARE 130 CAPLUS RECORDS THAT CITE THIS RECORD (130 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 279 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:260767 CAPLUS Full-text
DOCUMENT NUMBER: 160:42366
TITLE: Cabozantinib in prostate cancer: the beginning of a precision paradigm?
AUTHOR(S): Goodin, Susan; DiPaola, Robert S.
CORPORATE SOURCE: The Cancer Institute of New Jersey, University of Medicine and Dentistry of New Jersey Robert Wood Johnson Medical School, New Brunswick, NJ, USA
SOURCE: Journal of Clinical Oncology (2013), 31(4), 401-403
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.46.6185
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The research of Smith et al. (2013) entitled, 'Cabozantinib in patients with advanced prostate cancer: Results of a phase II randomized discontinuation trial' is reviewed with commentary and refs. The authors presented data on a novel orally bioavailable tyrosine kinase inhibitor (TKI), cabozantinib, with activity against multiple targets including mesenchymal-epithelial transition factor (MET), also known as hepatocyte growth factor receptor, and the vascular endothelial growth factor receptor 2 (VEGFR2). They reported a reduction in uptake on bone scan with improvement in 68% of men (79 of 116) with bone metastasis and complete resolution in 14 patients.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 280 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:187940 CAPLUS Full-text
DOCUMENT NUMBER: 159:33573
TITLE: Profile of cabozantinib and its potential in the treatment of advanced medullary thyroid cancer
AUTHOR(S): Hart, Christopher D.; De Boer, Richard H.
CORPORATE SOURCE: Department of Oncology, Royal Melbourne Hospital, Parkville, Victoria, 3050, Australia
SOURCE: OncoTargets and Therapy (2013), 6, 1-7
CODEN: OTNHAZ; ISSN: 1178-6930
DIGITAL OBJECT ID: 10.2147/OTT.S27671
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Medullary thyroid cancer is an uncommon malignancy for which until recently little effective treatment existed. It is often characterized by mutation and overexpression of the receptor tyrosine kinases RET (rearranged during transfection), VEGFR2 (vascular endothelial growth factor receptor 2) and MET (mesenchymal-epithelial transition factor), which make attractive targets for drug development. Cabozantinib is an orally bioavailable tyrosine kinase inhibitor which blocks MET, VEGFR2 and RET, and has shown considerable activity in medullary thyroid cancer in a Phase III trial, including in heavily pretreated patients. Its novel combination of vascular endothelial growth factor and MET inhibition is believed to address the MET escape pathway, which is thought to be the cause of nonsustained tumor responses resulting from inhibition of vascular endothelial growth factor alone.
OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 281 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1893113 CAPLUS Full-text
DOCUMENT NUMBER: 158:123654
TITLE: Methods of treating cancer using a chemotherapeutic agent with an agent that blocks the activity of hepatocyte growth factor or its cognate receptor c-MET.
INVENTOR(S): Golub, Todd; Straussman, Ravid
PATENT ASSIGNEE(S): The Broad Institute, Inc., USA; Dana-Farber Cancer Institute, Inc.
SOURCE: PCT Int. Appl., 104pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012178038	A1	20121227	WO 2012-US43788	20120622
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20140348819	A1	20141127	US 2014-14128916	20140819
PRIORITY APPLN. INFO.:			US 2011-61501091 P1	20110624
			WO 2012-US43788 W	20120622

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention provides methods of treating cancer by preventing or reducing chemoresistance in a tumor by administering a chemotherapeutic agent together with another agent that blocks the activity of hepatocyte growth factor or its cognate receptor c-MET.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 282 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1845709 CAPLUS Full-text
DOCUMENT NUMBER: 158:644003
TITLE: New agents in metastatic prostate cancer
AUTHOR(S): Choudhury, Atish D.; Kantoff, Philip W.
CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE: Journal of the National Comprehensive Cancer Network (2012), 10(11), 1403-1409
CODEN: JNCCA4; ISSN: 1540-1405
PUBLISHER: Harborside Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Discoveries of mol. mechanisms and therapeutic targets in metastatic castration-resistant prostate cancer (CRPC) have led to significant advancements in the development of effective agents in this setting, with diverse mechanisms of action. Within the past 2 years, 5 agents have been approved for the treatment of patients with metastatic CRPC (cabazitaxel, abiraterone, sipuleucel-T, denosumab, and enzalutamide), and another (Alpharadin) has shown overall survival benefit in a phase III trial. This article summarizes the phase III data showing clin. benefit from these agents, highlights other promising therapies in phase III studies as single agents (PROSTVAC-VF, ipilimumab, cabozantinib), discusses important

unanswered questions regarding these therapies, and provides a schema for their use based on current regulatory approval and how this is likely to evolve as data from ongoing studies are reported. Although curative interventions in metastatic CRPC still do not exist, the hope is that optimization of therapeutic strategies can reduce the morbidity and mortality associated with this disease.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 283 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1765841 CAPLUS Full-text

DOCUMENT NUMBER: 158:670189

TITLE: Cabozantinib for the Treatment of Advanced Medullary Thyroid Cancer

AUTHOR(S): Nagilla, Madhavi; Brown, Rebecca L.; Cohen, Ezra E. W.

CORPORATE SOURCE: Section of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Chicago, Chicago, IL, 60645, USA

SOURCE: Advances in Therapy (2012), 29(11), 925-934
CODEN: ADTHE7; ISSN: 0741-238X

DIGITAL OBJECT ID: 10.1007/s12325-012-0060-6

PUBLISHER: Springer Healthcare Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. Introduction Patients with advanced medullary thyroid cancer (MTC) have poor prognoses and limited treatment options. Improved knowledge about mol. aberrations associated with MTC and the availability of novel targeted tyrosine kinase inhibitors (TKIs) have led to new potential treatment modalities. Cabozantinib is an oral multitargeted TKI with activity against multiple receptors including RET, vascular endothelial growth factor receptor type 2 (VEGFR2), and MET that has been evaluated in MTC in the preclin. and clin. arenas. Methods This article reviews unmet clin. needs in advanced MTC. The authors consider novel agents that have been studied in MTC, with a focus on the investigational agent cabozantinib. Up-to-date clin. data of cabozantinib in MTC are discussed. Results Recent clin. evaluation suggests that cabozantinib is the first agent to prolong progression-free survival in patients with progressive MTC. These findings indicate that cabozantinib may be an effective therapy in advanced MTC. No improvement in overall survival has been demonstrated but data are not mature. Conclusion Cabozantinib may be an effective treatment option for patients with advanced MTC and is worthy of further evaluation.

OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 284 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1630842 CAPLUS Full-text

DOCUMENT NUMBER: 157:699601

TITLE: Method of treating cancer and bone cancer pain

INVENTOR(S): Schwab, Gisela; Aftab, Dana T.

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

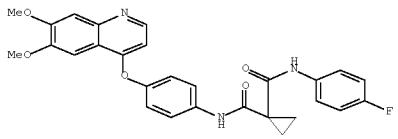
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012151326	A1	20121108	WO 2012-US36191	20120502
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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CA 2834778	A1	20121108	CA 2012-2834778	20120502
AR 86242	A1	20131127	AR 2012-101544	20120502
AU 2012250759	A1	20131128	AU 2012-250759	20120502
IL 229094	A	20131231	IL 2012-229094	20120502
KR 2014025496	A	20140304	KR 2013-7031635	20120502
EP 2704717	A1	20140312	EP 2012-720754	20120502
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 103717221	A	20140409	CN 2012-80026424	20120502
JP 2014513129	T	20140529	JP 2014-509417	20120502
BR 212013028314	U2	20151103	BR 2013-212013028314	20120502
MX 2013012695	A	20140327	MX 2013-12695	20131030
ZA 2013008206	A	20140730	ZA 2013-8206	20131101
IN 2013KN03259	A	20140221	IN 2013-KN3259	20131105
US 20140179736	A1	20140626	US 2014-14115236	20140228
PRIORITY APPLN. INFO.:			US 2011-61481682 P	20110502
			US 2011-61557366 P	20111108
			WO 2012-US36191 W	20120502

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 157:699601; MARPAT 157:699601

GI



AB This invention is directed to the treatment of cancer, particularly lung cancer, breast cancer, melanoma, renal cell carcinoma, thyroid cancer that has metastasized to the bone. The invention is also directed to a method for treating bone cancer pain in an individual in need of such treatment comprising administering to the individual an effective amount of a compound of Formula I.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 285 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1563334 CAPLUS Full-text

DOCUMENT NUMBER: 158:492390

TITLE: New developments in castrate-resistant prostate cancer

AUTHOR(S): Shore, N.; Mason, M.; de Reijke, Th. M.

CORPORATE SOURCE: Carolina Urologic Research Center, Atlantic Urology Clinics, Myrtle Beach, SC, USA

SOURCE: BJU International (2012), 109(Suppl. 6), 22-32
CODEN: BJINFO; ISSN: 1464-4096

DIGITAL OBJECT ID: 10.1111/j.1464-410X.2012.11217.x

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Castrate-resistant prostate cancer (CRPC) occurs when disease progresses in the presence of castrate levels of androgens and remains sensitive to further hormonal manipulation. For many years the treatment of CRPC was limited to the use of docetaxel for metastatic disease. However, this has recently changed with the approval of several new agents. Sipuleucel-T, an immunotherapeutic vaccine, is now available in the US for patients with non-metastatic CRPC and abiraterone, an oral enzyme inhibitor of androgen biosynthesis, as well as cabazitaxel, a cytotoxic chemotherapeutic, have been approved for the treatment of metastatic CRPC. Also, denosumab, a s.c. antibody, is now an option for the treatment of patients with CRPC with bone metastases, in addition to zoledronic acid, an i.v. bisphosphonate. Further treatment advances for metastatic CRPC therapeutics are in late stage phase III development. These include therapies affecting the androgen receptor (MDV3100) as well as addnl. immune-based therapeutics, PROSTVAC and ipilimumab. A broad range of agents is also emerging under the term targeted therapies. The endothelin-A receptor antagonist zibotentan, the tyrosine kinase inhibitors dasatinib, sorafenib and cabozantinib, the anti-angiogenic agent aflibercept, and the clusterin inhibitor custirsen, are all currently being tested for efficacy in metastatic CRPC. The mechanism of action of these and other promising agents are discussed alongside current therapeutic options and their potential place in the treatment landscape for CRPC is considered.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 286 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1483426 CAPLUS Full-text

DOCUMENT NUMBER: 157:573884

TITLE: Methods for predicting and improving the survival of gastric cancer patients

INVENTOR(S): Kim, Phillip; Singh, Sharat

PATENT ASSIGNEE(S): Nestec SA, Switz.

SOURCE: PCT Int. Appl., 147pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012138785	A1	20121011	WO 2012-US32206	20120404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2831468	A1	20121011	CA 2012-2831468	20120404
AU 2012240242	A1	20131010	AU 2012-240242	20120404
IL 228579	A	20131128	IL 2012-228579	20120404
EP 2694972	A1	20140212	EP 2012-716858	20120404
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2014020318	A	20140218	KR 2013-7029113	20120404
CN 103597354	A	20140219	CN 2012-80027365	20120404
JP 2014517259	T	20140717	JP 2014-503964	20120404
MX 2013011431	A	20140606	MX 2013-11431	20130930
US 20140099300	A1	20140410	US 2013-14044792	20131002
PRIORITY APPLN. INFO.:			US 2011-61471678 P	20110404
			US 2012-61590787 P	20120125
			WO 2012-US32206 W	20120404

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides assays and methods for predicting the post-operative survival of a subject having an early stage gastric cancer after tumor surgery. The present invention also provides methods for treating a subject having an early stage gastric cancer by administering a combination therapy tailored to the signal transduction biomarkers that are activated in the cancer. In particular embodiments, the methods of the invention rely on the detection of the activation state or level of a specific combination of signal transducer analytes in a cancer cell obtained from the subject. Thus, the methods of the invention are particularly useful for predicting the survival or prognosis of a subject having an early stage gastric cancer and for guiding both pre- and post-operative treatment decisions by identifying subjects who would benefit from combination therapy as opposed to monotherapy.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 287 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1450760 CAPLUS Full-text

DOCUMENT NUMBER: 157:567006
TITLE: Method of treating cancer
INVENTOR(S): Aftab, Dana T.; Schimmoller, Frauke
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 17pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

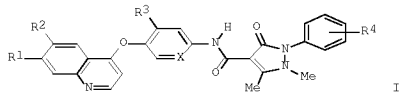
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120252840	A1	20121004	US 2012-13438964	20120404
US 20150196545	A1	20150716	US 2015-14668312	20150325
PRIORITY APPLN. INFO.:			US 2011-61471367 P	20110404
			US 2012-13438964 A1	20120404

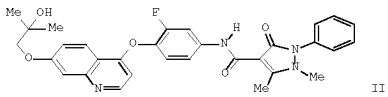
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:567006
AB This invention is directed to the treatment of cancer, particularly ocular melanoma, with a dual inhibitor of MET and VEGF such as Compound 1.

L8 ANSWER 288 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1270117 CAPLUS Full-text
DOCUMENT NUMBER: 157:438359
TITLE: Preparation of substituted quinoline compounds as protein tyrosine kinase modulators
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., USA; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120219522	A1	20120830	US 2012-13400586	20120221
US 9133162	B2	20150915		
CA 2820709	A1	20120907	CA 2012-2820709	20120221
WO 2012118632	A1	20120907	WO 2012-US25834	20120221
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
KR 2013095806	A	20130828	KR 2013-7015842	20120221
KR 1546693	B1	20150824		
EP 2680886	A1	20140108	EP 2012-752321	20120221
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JP 2014506925	T	20140320	JP 2013-556713	20120221
JP 5707518	B2	20150430		
ZA 2013003793	A	20140730	ZA 2013-3793	20120221
AU 2012223639	B2	20150319	AU 2012-223639	20120221
RU 2568258	C2	20151120	RU 2013-135662	20120221
MX 2013007278	A	20130913	MX 2013-7278	20130621
US 20150342945	A1	20151203	US 2015-14824096	20150812
PRIORITY APPLN. INFO.:			US 2011-61447104 P	20110228
			US 2012-13400586 A3	20120221
			WO 2012-US25834 W	20120221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:438359; MARPAT 157:438359
GI


I


II

AB The present invention provides novel substituted quinoline compds. I [R1, R2 = H, alkoxy, hydroxyalkoxy; R3 = H, F; R4 = H, F, Cl, Br, I, etc.; X = CH or N, wherein at least one of R1 and R2 = hydroxyalkoxy], pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. Syntheses of exemplified compds. I were described. E.g., a multi-step synthesis of the pyrazolecarboxamide II, starting from 3-benzyloxybenzenamine, was provided. Exemplified compds. I were tested for their efficacy as inhibitors of receptor tyrosine kinases such as c-Met, VEGFR and Axl, and as antitumor agents (data given). The invention also provides pharmaceutically acceptable compns. comprising compds. I and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 289 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1269771 CAPLUS Full-text
DOCUMENT NUMBER: 157:431629
TITLE: Methods for detecting cancer and/or determining response to therapeutic agent, and numerous circulating markers (including proteins, nucleic acids and vesicles) used in said methods
INVENTOR(S): Spetzler, David; Holterman, Daniel A.; Pawlowski, Traci; Tasinato, Andrea
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, S.A.R.L., Luxembourg
SOURCE: PCT Int. Appl., 695pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

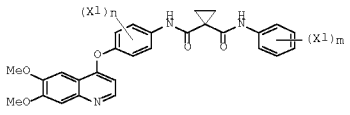
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012115885	A1	20120830	WO 2012-US25741	20120217
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2827894	A1	20120830	CA 2012-2827894	20120217
AU 2012220872	A1	20130912	AU 2012-220872	20120217
CN 103492590	A	20140101	CN 2012-80019718	20120217
EP 2678448	A1	20140101	EP 2012-749642	20120217
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2014507160	T	20140327	JP 2013-555467	20120217
US 20140141986	A1	20140522	US 2014-14001016	20140207
PRIORITY APPLN. INFO.:			US 2011-61445273 P	20110222
			US 2011-61446313 P	20110224
			US 2011-61471417 P	20110404
			US 2011-61501680 P	20110627
			US 2011-61523763 P	20110815
			WO 2012-US25741 W	20120217

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention provides methods for detecting cancer, for detg. whether a cancer is responding to treatment, and /or for determining whether a cancer is likely to respond to treatment that involve detecting of circulating biomarkers. The invention relates that said circulating biomarkers can includie nucleic acids, proteins, vesicles and/or microRNAs. The invention also relates that said biol. samples used in the disclosed methods include isolated extracellular microvesicle populations. The invention also provides kits comprising all reagents used in the disclosed methods. In the examples, the invention disclosed that specific biomarkers are elevated in specific types of cancer, which can used in diagnosis and in determining treatments.
OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

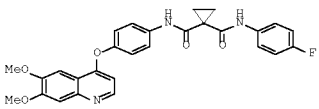
L8 ANSWER 290 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1201570 CAPLUS Full-text
DOCUMENT NUMBER: 157:382704
TITLE: Processes for preparing quinoline compounds and pharmaceutical compositions containing such compounds
INVENTOR(S): Wilson, Jo Ann
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012109510	A1	20120816	WO 2012-US24591	20120210
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2826751	A1	20120816	CA 2012-2826751	20120210
AU 2012214322	A1	20130829	AU 2012-214322	20120210
AR 85155	A1	20130911	AR 2012-100446	20120210
IL 227848	A	20130930	IL 2012-227848	20120210
CN 103459373	A	20131218	CN 2012-80017723	20120210
EP 2673262	A1	20131218	EP 2012-704492	20120210
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JP 2014505109	T	20140227	JP 2013-553580	20120210
KR 2014044782	A	20140415	KR 2013-7023174	20120210
MX 2013009116	A	20140131	MX 2013-9116	20130807
ZA 2013006072	A	20140430	ZA 2013-6072	20130813
IN 2013KN02666	A	20140103	IN 2013-KN2666	20130903
US 20140200242	A1	20140717	US 2014-13984559	20140320
PRIORITY APPLN. INFO.:			US 2011-61441520 P	20110210
			US 2011-61441527 P	20110210
			WO 2012-US24591 W	20120210

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:382704; MARPAT 157:382704
GI



I



II

AB The invention is directed to processes for prepg. quinoline compds. of formula I wherein X1 is H, Br, Cl and F; X2 is H, Br, Cl and F; n is 1-2 and m is 1-2; and pharmaceutically acceptable salts thereof. Example compound II L-malate was prepared by chlorination of 6,7-dimethoxyquinolin-4-ol followed by etherification of 4-chloro-6,7-dimethoxyquinoline with 4-aminophenol; the resulting 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine underwent acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropanecarbonyl chloride to give compound II, which underwent addition of L-malic acid to give the desired product.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 291 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1051547 CAPLUS Full-text
DOCUMENT NUMBER: 157:218520
TITLE: Molecular diagnostic methods for predicting brain metastasis of breast cancer
INVENTOR(S): Wong, Stephen T. C.; Zhao, Hong
PATENT ASSIGNEE(S): The Methodist Hospital Research Institute, USA
SOURCE: U.S. Pat. Appl. Publ., 53pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120184560	A1	20120719	US 2011-13245706	20110926
PRIORITY APPLN. INFO.:			US 2010-61386186 P	20100924

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed are mol. diagnostic compns. and methods for predicting brain metastasis of breast cancer, as well as methods for drug repositioning to identify existing and new therapeutics for use in developing individualized, patient-specific treatment regimens for improving diagnoses and patient outcomes in individuals at risk for brain metastasis of breast cancer.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 292 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1042874 CAPLUS Full-text
DOCUMENT NUMBER: 157:221701
TITLE: Bcl-2-like protein 11 (BIM) SRM/MRM assay
INVENTOR(S): Krizman, David B.; Hembrough, Todd; Thyparambil, Sheeno; Liao, Wei-Li
PATENT ASSIGNEE(S): Expression Pathology, Inc., USA
SOURCE: PCT Int. Appl., 28pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012097276	A2	20120719	WO 2012-US21283	20120113
WO 2012097276	A3	20121129		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2824752	A1	20120719	CA 2012-2824752	20120113
AU 2012205337	A1	20130801	AU 2012-205337	20120113
IL 227471	A	20130829	IL 2012-227471	20120113
EP 2663863	A2	20131120	EP 2012-734572	20120113
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JP 2014505251	T	20140227	JP 2013-549580	20120113
US 20130302334	A1	20131114	US 2013-13942574	20130715
PRIORITY APPLN. INFO.:			US 2011-61432462 P	20110113
			WO 2012-US21283 W	20120113

AB Specific peptides, and derived ionization characteristics of those peptides, from the Bcl-2-like protein 11 (BIM) are provided that are particularly advantageous for quantifying the BIM protein directly in biol. samples that have been fixed in formalin by the method of Selected Reaction Monitoring (SRM) mass spectrometry, or what can also be termed as Multiple Reaction Monitoring (MRM). Such biol. samples are chemical preserved and fixed where the biol. sample is selected from tissues and cells treated with formaldehyde containing agents/fixatives including formalin-fixed tissue/cells, formalin- fixed/paraffin embedded (FFPE) tissue/cells, FFPE tissue blocks and cells from those blocks, and tissue culture cells that have been formalin fixed and or paraffin embedded. A protein sample is prepared from the biol. sample using the Liquid Tissue reagents and protocol, and the BIM protein is quantitated in the Liquid Tissue sample by the method of SRM/MRM mass spectrometry by quantitating in the protein sample at least one or more of the peptides described. These peptides can be quantitated if they reside in a modified or an unmodified form. An example of a modified form of a BIM peptide is phosphorylation of a tyrosine, threonine, serine, and/or other amino acid residues within the peptide sequence. Samples were prepared with Liquid Tissue and digested with trypsin. Three peptides from BIM were found to be suitable for SRM/MRM assay.

L8 ANSWER 293 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:924299 CAPLUS Full-text
DOCUMENT NUMBER: 157:122897
TITLE: Drug selection for therapy for malignancies involving c-Met signaling using antibody-based arrays
INVENTOR(S): Singh, Sharat; Hoe, Nicholas; Princen, Fred; Liu, Xinjun
PATENT ASSIGNEE(S): Prometheus Laboratories Inc., USA
SOURCE: PCT Int. Appl., 140pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012088337	A1	20120628	WO 2011-US66624	20111221
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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CA 2822283	A1	20120628	CA 2011-2822283	20111221
AU 2011348256	A1	20130711	AU 2011-348256	20111221
IL 227009	A	20130829	IL 2011-227009	20111221
EP 2656077	A1	20131030	EP 2011-805738	20111221
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 103384828	A	20131106	CN 2011-80068269	20111221
KR 2014002711	A	20140108	KR 2013-7019356	20111221
JP 2014503821	T	20140213	JP 2013-546392	20111221
NZ 612483	A	20150327	NZ 2011-612483	20111221
US 20140024548	A1	20140123	US 2013-13923316	20130620
MX 2013007429	A	20140131	MX 2013-7429	20130621
PRIORITY APPLN. INFO.:			US 2010-61426948 P	20101223
			US 2011-61438904 P	20110202
			WO 2011-US66624 W	20111221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods for selecting a suitable anticancer drug therapy, and for identifying and predicting response, for the treatment of a malignant cancer involving aberrant c-Met signaling. The present invention also provides methods for monitoring the status of a malignant cancer involving aberrant c-Met signaling and monitoring how a patient with the malignant cancer is responding to anticancer drug therapy. Information on the expression and/or activation states of components of signal transduction pathways (e.g., HER3 and/or c-Met signal transduction pathway components) derived from practice of the present invention can be used for malignant cancer diagnosis, prognosis, and in the design of cancer treatments for malignancies involving aberrant c-Met signaling. Certain embodiments comprise administering a cMet inhibitor alone or a cMet inhibitor in combination with a pathway-directed therapy based upon the differences between the expression and/or activation levels of cMet protein and/or HER3 protein in the sample compared to the control protein and/or control sample.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 294 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:706472 CAPLUS Full-text
DOCUMENT NUMBER: 156:628365
TITLE: Cancer cell-derived receptor activator of the NF-KB ligand drives bone and soft tissue metastases
INVENTOR(S): Chu, Gina C. Y.; Chung, Leland W. K.; Zhau, Haiyen E.; Wang, Ruoxiang
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012064967	A2	20120518	WO 2011-US60204	20111110
WO 2012064967	A3	20120705		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20130263297	A1	20131003	US 2013-13889135	20130507
PRIORITY APPLN. INFO.:			US 2010-61412360 P	20101110

US 2011-61442679 P 20110214
WO 2011-US60204 A2 20111110
US 2012-61718626 P 20121025
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention relates to metastases. More specifically, the invention relates to compns. and methods for the inhibition of metastases of cancer cells, such as prostate cancer cells, to bones and soft tissue. The present invention also relates to the treatment of cancer, including but not limited to prostate cancer. Also provided are animal models for studying cancer metastasis; particularly, prostate cancer metastasis.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 295 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:560657 CAPLUS Full-text
DOCUMENT NUMBER: 158:122090
TITLE: Recent advances in the molecular pathogenesis and targeted therapies of medullary thyroid carcinoma
AUTHOR(S): Almeida, Madson Q.; Hoff, Ana O.
CORPORATE SOURCE: Instituto do Cancer da Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil
SOURCE: Current Opinion in Oncology (2012), 24(3), 229-234
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e328351c71a
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: This review will focus on the recent advances in mol. pathogenesis and targeted therapies for medullary thyroid carcinoma (MTC). Unlike hereditary MTC in which rearranged during transfection (RET) mutations are the most important precipitating events, in sporadic MTC the genetic or mol. biomarkers are yet to be established. Recent findings: Targeted mol. therapies that inhibit RET and other tyrosine kinase receptors involved in angiogenesis have shown great promise in the treatment of metastatic or locally advanced MTC and are under investigation. In addition, the recent findings of H-RAS mutations in 56% of RET-neg. sporadic MTC and the activation of the mammalian target of rapamycin (mTOR) intracellular signaling pathway in hereditary MTC suggests that addnl. or alternative genetic events are important for MTC pathogenesis. Summary: Recently, vandetanib (ZD6474), an inhibitor of vascular endothelial growth factor receptor (VEGFR) 2 and VEGFR 3, RET, and epidermal growth factor receptor (EGFR), was approved for the treatment of adults with symptomatic or progressive MTC. Significant advantages for vandetanib over placebo were seen in terms of response rate, disease control rate, and biochem. response in a phase III study. Furthermore, cabozantinib (XL184), an inhibitor of VEGFR 1 and VEGFR 2, hepatocyte growth factor receptor (MET), and RET, was associated with partial response and stable disease in 29 and 41%, resp.
OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 296 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:508891 CAPLUS Full-text
DOCUMENT NUMBER: 158:93453
TITLE: Novel Molecular Targets for the Therapy of Castration-Resistant Prostate Cancer
AUTHOR(S): Agarwal, Neeraj; Sonpavde, Guru; Sternberg, Cora N.
CORPORATE SOURCE: Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA
SOURCE: European Urology (2012), 61(5), 950-960
CODEN: EUURAV; ISSN: 0302-2838
DIGITAL OBJECT ID: 10.1016/j.eururo.2011.12.028
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Improved understanding of mechanisms underlying metastatic castration-resistant prostate cancer (mCRPC) progression has led to the recognition of multiple mol. targets and advances in the therapeutic landscape. The addition of abiraterone acetate, sipuleucel-T, cabazitaxel, and denosumab to the therapeutic armamentarium and the impending addition of MDV-3100 and radium-223 underscore the importance of androgen pathway inhibition, immunotherapy, tubulin antagonism, and pathophysiol. of bone metastasis. Review the next generation of mol. targets in mCRPC. Medline databases were searched for >100 original articles published as of Oct. 18, 2011, with the search terms metastatic castration-resistant prostate cancer, targeted therapy, biol. agents, and immunotherapy. Proceedings from the last 5 yr of conferences of the American Society of Clin. Oncol., American Urol. Association, European Society of Medical Oncol., and the European Association of Urol. were also searched. We included novel and promising drugs that have reached clin. trial evaluation. The major findings were addressed in an evidence-based fashion. Prospective trials and important preclin. data were analyzed.mCRPC is a disease with multiple mol. drivers. Mol. pathways being targeted in ongoing phase 3 trials are androgen signaling (MDV3100, TAK700), immunoregulatory pathways (ipilimumab, Prostvac-VF-TRICOM), Src (dasatinib), Met (cabozantinib), clusterin (custirsen), and angiogenesis (aflibercept, tasquinimod). The strides made in identifying multiple other novel mol. targets offer potential opportunities for further improving outcomes.
OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (25 CITINGS)
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 297 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:495814 CAPLUS Full-text
DOCUMENT NUMBER: 156:469436
TITLE: Dual inhibitors of Met and VEGF for the treatment of castration- resistant prostate cancer and osteoblastic bone metastases
INVENTOR(S): Smith, David; Hussain, Maha
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012044572	A1	20120405	WO 2011-US53233	20110926

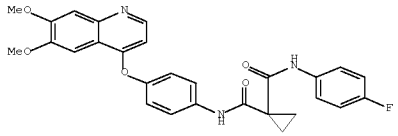
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2812750	A1	20120405	CA 2011-2812750	20110926
AU 2011307304	A1	20130502	AU 2011-307304	20110926
IL 225507	A	20130530	IL 2011-225507	20110926
EP 2621481	A1	20130807	EP 2011-764655	20110926

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JP 2013537916	T	20131007	JP 2013-530386	20110926
CN 103402505	A	20131120	CN 2011-80056580	20110926
KR 2014025304	A	20140304	KR 2013-7010372	20110926
MX 2013003594	A	20130801	MX 2013-3594	20130327
ZA 2013002422	A	20131223	ZA 2013-2422	20130404
IN 2013KN00998	A	20130906	IN 2013-KN998	20130409
US 20140057943	A1	20140227	US 2013-13876290	20131105

PRIORITY APPLN. INFO.: US 2010-61386959 P 20100927
US 2011-61481671 P 20110502
WO 2011-US53233 W 20110926
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:469436; MARPAT 156:469436
GI



AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and osteoblastic bone metastases, with a dual inhibitor of MET and VEGF.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 298 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:495788 CAPLUS Full-text
DOCUMENT NUMBER: 156:469435
TITLE: Dual inhibitors of Met and VEGF for the treatment of castration resistant prostate cancer and osteoblastic bone metastases
INVENTOR(S): Smith, David; Hussain, Maha
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012044577	A1	20120405	WO 2011-US53245	20110926

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2812744	A1	20120405	CA 2011-2812744	20110926
AU 2011307309	A1	20130502	AU 2011-307309	20110926
EP 2621483	A1	20130807	EP 2011-764657	20110926

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2013537918	T	20131007	JP 2013-530392	20110926
CN 103391773	A	20131113	CN 2011-80056999	20110926
US 20140057908	A1	20140227	US 2013-13876306	20131108

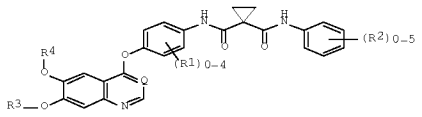
PRIORITY APPLN. INFO.: US 2010-61386971 P 20100927
US 2010-61386983 P 20100927
US 2010-61386993 P 20100927
WO 2011-US53245 W 20110926
OTHER SOURCE(S): CASREACT 156:469435; MARPAT 156:469435
AB This invention discloses compds. directed at the treatment of cancer, particularly castration- resistant prostate cancer and osteoblastic bone metastases, with a dual inhibitor of MET and VEGF.
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 299 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:425741 CAPLUS Full-text
DOCUMENT NUMBER: 156:412018
TITLE: Methods of using C-met modulators as Anticancer agents
INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-Ming; Forsyth, Timothy Patrick; Khoury, Richard George; Leahy, James

William; Mac, Morrison B.; Mann, Larry W.; Nuss, John M.; Parks, Jason Jevious; Wang, Yong; Xu, Wei; Simeone, Diane
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 25pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120070368	A1	20120322	US 2011-13087094	20110414
US 20150202196	A1	20150723	US 2014-14518733	20141020
PRIORITY APPLN. INFO.:			US 2010-61325095 P	20100416
			US 2011-13087094 B1	20110414

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:412018; MARPAT 156:412018
GI



I

AB Disclosed are methods of treating cancer by administering a compd. of Formula I (wherein R1, R2 = independently, halo; R3, R4 = independently, (C1-C6)-alkyl; Q = CH, N) in combination with gemcitabine (GEM).

L8 ANSWER 300 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:373163 CAPLUS Full-text
DOCUMENT NUMBER: 157:622817
TITLE: Multi-targeted tyrosine kinase inhibitors in clinical development: focus on XL-184 (cabozantinib)
AUTHOR(S): Bowles, D. W.; Kessler, E. R.; Jimeno, A.
CORPORATE SOURCE: Division of Medical Oncology, University of Colorado Denver, Aurora, CO, USA
SOURCE: Drugs of Today (2011), 47(11), 857-868
CODEN: MDACAP; ISSN: 1699-3993
DIGITAL OBJECT ID: 10.1358/dot.2011.47.11.1688487
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. XL-184 (cabozantinib) is a novel, small-mol., multi-targeted receptor tyrosine kinase inhibitor with particular activity against hepatocyte growth factor receptor (tyrosine-protein kinase Met), vascular endothelial growth factor receptor 2 (VEGFR-2) and proto-oncogene tyrosine-protein kinase receptor Ret. There is ample evidence of Met, VEGFR-2 and Ret signaling in several tumor types. Preclin. data suggest that XL-184 has activity in tumors derived from both epithelial and mesenchymal origins. Phase I and II clin. studies support significant antitumor activity, particularly in medullary thyroid cancer and cancers metastatic to the bone. This review will evaluate XL-184's preclin. pharmacol., pharmacokinetics, drug interactions and clin. activity in phase I through phase III studies.
OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 301 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:345887 CAPLUS Full-text
DOCUMENT NUMBER: 156:388076
TITLE: C-met biomarker in treatment efficacy and prognosis
INVENTOR(S): Patel, Premal; Peterson, Amy C.; Yauch, Robert L.; Zha, Jiping
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 134pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012031027	A1	20120308	WO 2011-US50069	20110831
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2808236	A1	20120308	CA 2011-2808236	20110831
US 20120089541	A1	20120412	US 2011-13223173	20110831
AU 2011295919	A1	20130307	AU 2011-295919	20110831
IL 224962	A	20130430	IL 2011-224962	20110831
EP 2612151	A1	20130710	EP 2011-754597	20110831
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 103221825	A	20130724	CN 2011-80051781	20110831
KR 2013103734	A	20130924	KR 2013-7008025	20110831
JP 2013537966	T	20131007	JP 2013-526209	20110831
ZA 2013001175	A	20140430	ZA 2013-1175	20110831
SG 10201408229	A1	20150227	SG 2014-10201408229	20110831
MX 2013002084	A	20130509	MX 2013-2084	20130221
IN 2013DN01711	A	20141024	IN 2013-DN1711	20130225
AU 2013202759	A1	20130502	AU 2013-202759	20130406
US 20140037625	A1	20140206	US 2013-14046867	20131004
PRIORITY APPLN. INFO.:			US 2010-61378911 P	20100831
			US 2010-61389922 P	20101005
			US 2010-61390995 P	20101007
			US 2010-61420703 P	20101207
			US 2011-61487527 P	20110518
			US 2011-61492338 P	20110601
			US 2011-61503489 P	20110630
			AU 2011-295919 A3	20110831
			US 2011-13223173 B1	20110831
			WO 2011-US50069 W	20110831

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose the use of c-met as a biomarker for patient selection and patient prognosis in cancer. In a clin. trial, combination treatment with MetMAb (onartuzumab) and erlotinib provided a clin. meaningful benefit to patients with non-small cell lung cancer (NSCLC) that expressed high levels of c-met biomarker. The results showed that the efficacy, as evaluated by progression free survival (PFS) and overall survival (OS), was pos. especially when compared to PFS and OS data for erlotinib treatment alone. The addition of MetMAb to erlotinib nearly doubled the progression free and overall survival in patients with NSCLC that expressed high levels of c-met biomarker. The clin. trial data also showed that treatment with MetMAb in combination with erlotinib increased the risk of progression and death in patients with NSCLC that expressed low levels of c-met biomarker.
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 302 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:340365 CAPLUS Full-text
DOCUMENT NUMBER: 156:380310
TITLE: Synergistic drug combination for the treatment of cancer
INVENTOR(S): Gusenbauer, Simone; Ullrich, Axel
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 111pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2425830	A1	20120307	EP 2010-75382	20100903
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BA, ME, RS				
PRIORITY APPLN. INFO.:			EP 2010-75382	20100903

AB The invention relates to synergistic drug combinations and the use of said drug combinations for the treatment of proliferative diseases such as cancer. Combination of drugs include e.g. chlorethamine, cyclophosphamide, trofosfamide, daunorubicin, doxorubicin, mitomycin C.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 303 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:265414 CAPLUS Full-text
DOCUMENT NUMBER: 156:357951
TITLE: Circulating biomarkers for disease
INVENTOR(S): Spetzler, David; Holterman, Daniel; Pawlowski, Traci; Kuslich, Christine
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, Luxembourg
SOURCE: PCT Int. Appl., 639pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012024543	A1	20120223	WO 2011-US48327	20110818
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2808417	A1	20120223	CA 2011-2808417	20110818
AU 2011291599	A1	20130307	AU 2011-291599	20110818
AU 2011291599	B2	20150910		
EP 2606353	A1	20130626	EP 2011-818814	20110818
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2013540995	T	20131107	JP 2013-526012	20110818
US 20140148350	A1	20140529	US 2013-13817383	20130520
US 20150301055	A1	20151022	US 2015-14789729	20150701
PRIORITY APPLN. INFO.:			US 2010-61374951 P	20100818
			US 2010-61379670 P	20100902
			US 2010-61381305 P	20100909
			US 2010-61383305 P	20100915
			US 2010-61391504 P	20101008
			US 2010-61393823 P	20101015
			US 2010-61411890 P	20101109
			US 2010-61413377 P	20101112
			US 2010-61414870 P	20101117
			US 2010-61416560 P	20101123
			US 2010-61421851 P	20101210
			US 2010-61423557 P	20101215
			US 2010-61428196 P	20101229
			US 2011-61471417 P	20110404
			US 2010-61321392 P	20100406
			US 2010-61321407 P	20100406
			US 2010-61322690 P	20100409
			US 2010-61332174 P	20100506

US 2010-61334547	P	20100513
US 2010-61348214	P	20100525
US 2010-61348685	P	20100526
US 2010-61354125	P	20100611
US 2010-61355387	P	20100616
US 2010-61356974	P	20100621
US 2010-61357517	P	20100622
US 2010-61362674	P	20100708
US 2010-61364785	P	20100715
US 2010-61370088	P	20100802
WO 2011-US31479	A	20110406
WO 2011-US48327	W	20110818
US 2013-13639756	A2	20130424
US 2013-13817383	A1	20130520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Biomarkers can be assessed for diagnostic, therapy-related or prognostic methods to identify phenotypes, such as a condition or disease, or the stage or progression of a disease. Circulating biomarkers from a bodily fluid can be used in profiling of physiol. states or determining phenotypes. These include nucleic acids, protein, and circulating structures such as vesicles. Biomarkers can be used for theranostic purposes to select candidate treatment regimens for diseases, conditions, disease stages, and stages of a condition, and can also be used to determine treatment efficacy. The biomarkers can be circulating biomarkers, including vesicles and microRNA. Various anti-DLL4 antibodies were tethered to beads and used to capture vesicles in blood samples from subjects with breast cancer, colorectal cancer or normal subjects. The bead captured vesicles were detected with fluorescently-labeled antibodies against the tetraspanins CD9, CD63, and CD81. The median fluorescence intensity of the captured and labeled vesicles was measured using laser detection. There were noticeable differences both among normals and breast cancer plasma as well as between the avs. of normals and cancer patients.

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 304 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:155432 CAPLUS Full-text

DOCUMENT NUMBER: 157:565304

TITLE: Drug development to overcome resistance to EGFR inhibitors in lung and colorectal cancer

AUTHOR(S): Dienstmann, Rodrigo; De Dosso, Sara; Felip, Enriqueta; Tabernero, Josep

CORPORATE SOURCE: Medical Oncology Department, Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, 08035, Spain

SOURCE: Molecular Oncology (2012), 6(1), 15-26
CODEN: MOONC3; ISSN: 1574-7891

DIGITAL OBJECT ID: 10.1016/j.molonc.2011.11.009

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. Epidermal growth factor receptor (EGFR) is a validated target in different human malignancies. EGFR tyrosine kinase inhibitors (TKIs) are known to contribute considerably to the extension of progression-free survival in EGFR-mutant non-small cell lung cancer and monoclonal antibodies (mAbs) targeting EGFR have also improved the efficacy outcomes in KRAS wild-type colorectal cancer. Nevertheless, a significant percentage of lung and colorectal cancer patients do not respond to anti-EGFR agents and secondary resistance after initial benefit is a challenging reality faced by clinicians. Extensive preclin. work on the potential mechanisms of resistance to EGFR inhibitors in different disease settings has guided the development of second-generation irreversible EGFR TKIs, more efficient anti-EGFR mAbs, and combination strategies with agents targeting other receptors and downstream effectors. In order to elucidate the role of the multiple therapeutic strategies under investigation to overcome EGFR inhibitors-resistance, rational drug development based on stringent preclin. data, biomarker validation and proper selection of patients in the ongoing clin. trials are of paramount importance. Preliminary results of clin. trials evaluating these approaches will be discussed in this manuscript, with emphasis on TKIs in lung cancer and mAbs in advanced colorectal cancer.

OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 305 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:99813 CAPLUS Full-text

DOCUMENT NUMBER: 157:249246

TITLE: HGF/c-MET targeted therapeutics: novel strategies for cancer medicine

AUTHOR(S): Yap, Timothy A.; Sandhu, Shahneen K.; Alam, Salma M.; de Bono, Johann S.

CORPORATE SOURCE: The Royal Marsden NHS Foundation Trust, Sutton, Surrey, SM2 5PT, UK

SOURCE: Current Drug Targets (2011), 12(14), 2045-2058
CODEN: CDTUAU; ISSN: 1389-4501

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The hepatocyte growth factor/mesenchymal-epithelial transition factor (HGF/c-MET) receptor tyrosine kinase (RTK) pathway plays a pleotropic role in cell proliferation, migration, invasion, angiogenesis and survival. Although it has critical physiol. functions in embryonic development and tissue repair, this signaling cascade is frequently deregulated in a wide range of tumors. Aberrant HGF/c-MET signaling, driven by various mechanisms, including constitutive activation and over-expression, has multifunctional effects in oncogenesis and is implicated in the acquisition of an aggressive phenotype with metastatic potential. The central role of c-MET activity in cancer progression, as well as disparities between quiescent HGF/c-MET signaling in normal tissue and overexpression in tumor may provide a degree of tumor selectivity for therapeutic intervention, making HGF or c-MET inhibition an attractive proposition in oncol. This review focuses on the underlying oncogenic role of aberrant HGF/c-MET signaling in malignant progression, as well as recent preclin. and clin. data on the different strategies employed in inhibiting HGF/c-MET function.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

REFERENCE COUNT: 134 THERE ARE 134 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 306 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:94602 CAPLUS Full-text

DOCUMENT NUMBER: 156:167648

TITLE: Administration of hypoxia activated prodrugs and antiangiogenic agents for the treatment of cancer

INVENTOR(S): Hart, Charles; Curd, John; Kroll, Stewart; Sun, Jessica

PATENT ASSIGNEE(S): Threshold Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012009288	A2	20120119	WO 2011-US43594	20110711
WO 2012009288	A9	20120419		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2803675	A1	20120119	CA 2011-2803675	20110711
KR 2013045341	A	20130503	KR 2013-7002206	20110711
EP 2593139	A2	20130522	EP 2011-807356	20110711
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2013531038	T	20130801	JP 2013-519747	20110711
MX 2012014428	A	20130305	MX 2012-14428	20121210
ZA 2013000692	A	20130925	ZA 2013-692	20130125
US 20140010805	A1	20140109	US 2013-13809135	20130724
PRIORITY APPLN. INFO.:			US 2010-61363610 P	20100712
			US 2011-61470412 P	20110331
			US 2011-61470812 P	20110401
			WO 2011-US43594 W	20110711

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Administration of a hypoxia activated prodrug in combination with an antiangiogenic agent is useful for treating cancer. Hypoxia activated prodrug is selected from the group consisting of TH-281, TH-302, and TH-308. The antiangiogenic agent is selected from the group consisting of an anti-VEGF antibody, a VEGF-trap, an anti-VEGFR antibody, a VEGFR inhibitor, thalidomide etc.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L8 ANSWER 307 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:90800 CAPLUS Full-text

DOCUMENT NUMBER: 156:186804

TITLE: C-met modulator pharmaceutical compositions comprising N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide

INVENTOR(S): Wilson, Jo Ann

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 40pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012009722	A1	20120119	WO 2011-US44378	20110718
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2805645	A1	20120119	CA 2011-2805645	20110718
AR 82252	A1	20121121	AR 2011-102584	20110718
AU 2011278950	A1	20130307	AU 2011-278950	20110718
IL 224189	A	20130324	IL 2011-224189	20110718
EP 2593090	A1	20130522	EP 2011-740764	20110718
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 103221035	A	20130724	CN 2011-80044602	20110718
JP 2013531045	T	20130801	JP 2013-519870	20110718
KR 2013137586	A	20131217	KR 2013-7003043	20110718
NZ 607118	A	20150529	NZ 2011-607118	20110718
IN 2013KN00112	A	20130705	IN 2013-KN112	20130114
MX 2013000567	A	20130501	MX 2013-567	20130115
ZA 2013000458	A	20130925	ZA 2013-458	20130117
US 20130337015	A1	20131219	US 2013-13810537	20130826
PRIORITY APPLN. INFO.:			US 2010-61365253 P	20100716
			US 2010-61370843 P	20100805
			WO 2011-US44378 W	20110718

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 156:186804

AB Pharmaceutical compns. and unit dosage forms comprising N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (I) are disclosed. Thus, 6,7-dimethoxyquinolin-4-ol was converted to 4-chloro-6.7-dimethoxyquinoline followed by reaction with 4-aminphenol to give 4-(6,7-dimethoxy-quinolin-4-yloxy)-phenylamine. This was further allowed to react with 1-(4-fluorophenylcarbamoyl)cyclopropanecarbonyl chloride to give I. A tablet composition comprised 31.68% along with excipients such as microcryst. cellulose 38.85, lactose, HPC, and Croscarmellose sodium.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 308 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:10093 CAPLUS Full-text
DOCUMENT NUMBER: 157:152076
TITLE: In the clinic: ongoing clinical trials evaluating c-MET-inhibiting drugs
AUTHOR(S): Sharma, Neelesh; Adjei, Alex A.
CORPORATE SOURCE: Department of Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA
SOURCE: Therapeutic Advances in Medical Oncology (2011), 3(Suppl. 1), S37-S50
CODEN: TAMOB8; ISSN: 1758-8340
DIGITAL OBJECT ID: 10.1177/1758834011423403
PUBLISHER: Sage Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The c-MET (mesenchymal-epithelial transition factor) pathway is dysregulated in many human cancers and promotes tumor growth, invasion and dissemination. The c-MET receptor tyrosine kinase can be activated via gene mutation, gene amplification, protein overexpression and/or a Ligand-dependent autocrine/paracrine loop. Abnormalities in c-MET signaling have been reported to correlate with poor clin. outcomes and drug resistance in patients with cancer. Significant progress has been made in advancement of c-MET pathway inhibitors through to clin. trials. A robust pipeline of high-quality inhibitors targeting different aspects of c-MET activation is currently being explored in phase I, II and III clin. trials across multiple tumor types. Preliminary data demonstrate promising clin. activity with these agents, along with an acceptable toxicity profile. In this manuscript, the pharmacol. profile of drugs targeting the c-MET pathway and available data from ongoing clin. trials of these drugs are discussed.
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 309 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:1586879 CAPLUS Full-text
DOCUMENT NUMBER: 156:655505
TITLE: Cabozantinib (XL184), a Novel MET and VEGFR2 Inhibitor, Simultaneously Suppresses Metastasis, Angiogenesis, and Tumor Growth
AUTHOR(S): Yakes, F. Michael; Chen, Jason; Tan, Jenny; Yamaguchi, Kyoko; Shi, Yongchang; Yu, Peiwen; Qian, Fawn; Chu, Felix; Bentzien, Frauke; Cancilla, Belinda; Orf, Jessica; You, Andrew; Laird, A. Douglas; Engst, Stefan; Lee, Lillian; Lesch, Justin; Chou, Yu-Chien; Joly, Alison H.
CORPORATE SOURCE: Exelixis, Inc., South San Francisco, CA, 94083, USA
SOURCE: Molecular Cancer Therapeutics (2011), 10(12), 2298-2308
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-11-0264
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The signaling pathway of the receptor tyrosine kinase MET and its ligand hepatocyte growth factor (HGF) is important for cell growth, survival, and motility and is functionally linked to the signaling pathway of VEGF, which is widely recognized as a key effector in angiogenesis and cancer progression. Dysregulation of the MET/VEGF axis is found in a number of human malignancies and has been associated with tumorigenesis. Cabozantinib (XL184) is a small-mol. kinase inhibitor with potent activity toward MET and VEGF receptor 2 (VEGFR2), as well as a number of other receptor tyrosine kinases that have also been implicated in tumor pathobiol., including RET, KIT, AXL, and FLT3. Treatment with cabozantinib inhibited MET and VEGFR2 phosphorylation in vitro and in tumor models in vivo and led to significant redns. in cell invasion in vitro. In mouse models, cabozantinib dramatically altered tumor pathol., resulting in decreased tumor and endothelial cell proliferation coupled with increased apoptosis and dose-dependent inhibition of tumor growth in breast, lung, and glioma tumor models. Importantly, treatment with cabozantinib did not increase lung tumor burden in an exptl. model of metastasis, which has been observed with inhibitors of VEGF signaling that do not target MET. Collectively, these data suggest that cabozantinib is a promising agent for inhibiting tumor angiogenesis and metastasis in cancers with dysregulated MET and VEGFR signaling. Mol Cancer Ther; 10(12); 2298-308.
OS.CITING REF COUNT: 201 THERE ARE 201 CAPLUS RECORDS THAT CITE THIS RECORD (202 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 310 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:1503311 CAPLUS Full-text
DOCUMENT NUMBER: 155:694113
TITLE: Replication-competent retroviral vectors carrying expression cassettes for cytosine deaminase variants
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Perez, Omar D.; Logg, Christopher R.
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 207pp., Cont.-in-part of Appl. No. PCT/US2009/058512.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20110287020	A1	20111124	US 2011-13072704	20110326
US 8829173	B2	20140909		
WO 2010036986	A2	20100401	WO 2009-US58512	20090926
WO 2010036986	A3	20100701		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
WO 2011126864	A2	20111013	WO 2011-US30402	20110329
WO 2011126864	A3	20120419		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2547353	A2	20130123	EP 2011-766479	20110329
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2013523754	T	20130617	JP 2013-502771	20110329
US 20130130986	A1	20130523	US 2013-13638490	20130116
AU 2013205006	A1	20130516	AU 2013-205006	20130413
JP 2015119712	A	20150702	JP 2015-4923	20150114
JP 2015186479	A	20151029	JP 2015-97980	20150513

PRIORITY APPLN. INFO.:
US 2008-61100666 P 20080926
US 2008-61120618 P 20081208
US 2009-61186823 P 20090613
WO 2009-US58512 A2 20090926
US 2010-61318728 P 20100329
AU 2009-303690 A3 20090926
JP 2011-529291 A3 20090926
JP 2011-529292 A3 20090926
WO 2011-US30402 W 20110329

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Methods of delivering cytosine deaminase variants for prodrug activation using retroviral expression vectors are described. The vector includes the viral gag, pol, and env genes with the cytosine deaminase gene being coexpressed using an internal ribosome entry site. Vectors were derived from the prior art pACE-GFPemd vector. The envelope protein of the virus is amphotropic and excess viral sequences outside the long terminal repeats were removed. The resulting vector was named pACE-emdGFP. The vector was stable in storage and replicated efficiently in mammalian cells and could be used to deliver a range of therapeutic genes. The Saccharomyces cerevisiae cytosine deaminase gene was modified to give a codon usage suitable for mammalian cells and to improve thermostability of the enzyme. Use of these vectors results in high intracellular copy nos. for the therapeutic gene and these cells can be superinfected by the vector.
OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

L8 ANSWER 311 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:1304241 CAPLUS Full-text
DOCUMENT NUMBER: 155:559702
TITLE: Detection of circulating mRNA, microRNA, protein and vesicle markers in disease diagnosis and selection of therapies
INVENTOR(S): Kuslich, Christine; Poste, George; Klass, Michael; Spetzler, David; Pawlowski, Traci
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, Luxembourg
SOURCE: PCT Int. Appl., 584pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011127219	A1	20111013	WO 2011-US31479	20110406
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2795776	A1	20111013	CA 2011-2795776	20110406
AU 2011237669	A1	20121101	AU 2011-237669	20110406
IL 222232	A	20121129	IL 2011-222232	20110406
EP 2556172	A1	20130213	EP 2011-766687	20110406
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
CN 103025890	A	20130403	CN 2011-80027541	20110406
KR 2013043104	A	20130429	KR 2012-7028831	20110406
JP 2013526852	T	20130627	JP 2013-503934	20110406
IN 2012DN09454	A	20160101	IN 2012-DN9454	20121101
US 20140162888	A1	20140612	US 2013-13639756	20130424
US 20150301055	A1	20151022	US 2015-14789729	20150701

PRIORITY APPLN. INFO.:
US 2010-61321392 P 20100406
US 2010-61321407 P 20100406
US 2010-61322690 P 20100409
US 2010-61332174 P 20100506
US 2010-61334547 P 20100513
US 2010-61348214 P 20100525
US 2010-61348685 P 20100526
US 2010-61354125 P 20100611
US 2010-61355387 P 20100616
US 2010-61356974 P 20100621
US 2010-61357517 P 20100622
US 2010-61362674 P 20100708
US 2010-61364785 P 20100715
US 2010-61370088 P 20100802
US 2010-61379670 P 20100902
US 2010-61381305 P 20100909
US 2010-61383305 P 20100915
US 2010-61391504 P 20101008

US 2010-61393823	P	20101015
US 2010-61411890	P	20101109
US 2010-61413377	P	20101112
US 2010-61416560	P	20101123
US 2010-61374951	P	20100818
US 2010-61414870	P	20101117
US 2010-61421851	P	20101210
US 2010-61423557	P	20101215
US 2010-61428196	P	20101229
US 2011-61471417	P	20110404
WO 2011-US31479	W	20110406
WO 2011-US48327	A	20110818
US 2013-13639756	A2	20130424
US 2013-13817383	A1	20130520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Biomarkers can be assessed for diagnostic, therapy-related or prognostic methods to identify phenotypes, such as a condition or disease, or the stage or progression of a disease. Circulating biomarkers from a bodily fluid can be used in profiling of physiol. states or determining phenotypes. These include nucleic acids, protein, and circulating structures such as vesicles. Biomarkers can be used for theranostic purposes to select candidate treatment regimens for diseases, conditions, disease stages, and stages of a condition, and can also be used to determine treatment efficacy. The biomarkers can be circulating biomarkers, including microvesicles and their protein content and microRNAs.

OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 312 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:1016190 CAPLUS Full-text

DOCUMENT NUMBER: 156:353197

TITLE: Biologically targeted therapies for thyroid cancers

AUTHOR(S): Sherman, Steven I.

CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders Division of Internal Medicine, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

SOURCE: Thyroid Cancer (2011), 329-349. Editor(s): Carpi, Angelo; Mechanick, Jeffrey I. CRC Press: Boca Raton, Fla.
CODEN: 69OKVM; ISBN: 978-1-4398-6221-6

DIGITAL OBJECT ID: 10.1201/b10945-21

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review. Systemic chemotherapies for advanced or metastatic thyroid carcinomas have been of only limited effectiveness. For patients with differentiated thyroid epithelial or medullary thyroid carcinomas unresponsive to conventional treatments, novel therapies are needed to improve disease outcomes. Multiple novel therapies primarily targeting angiogenesis have entered clin. trials for metastatic thyroid carcinoma. Partial response rates up to 30% have been reported in single agent studies, but prolonged disease stabilization is more commonly seen. The most successful agents target the vascular endothelial growth factor receptors, with potential targets including the mutant kinases associated with papillary and medullary oncogenesis. Two drugs approved for other malignancies, sorafenib and sunitinib, have had promising preliminary results reported, and are being used selectively for patients who do not qualify for clin. trials. Addnl. agents targeting tumor vasculature, nuclear receptors, epigenetic abnormalities, and the immune response to neoplasia have also been investigated. Randomized trials for several agents are under way that may lead to eventual drug approval for thyroid cancer. Treatment for patients with metastatic or advanced thyroid carcinoma now emphasizes clin. trial opportunities for novel agents with considerable promise. Alternative options now exist for use of these mol. targeted therapies, especially tyrosine kinase inhibitors, which are well tolerated and may prove worthy of regulatory approval for this disease.

REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 313 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:991678 CAPLUS Full-text

DOCUMENT NUMBER: 156:440657

TITLE: Activity of XL184 (cabozantinib), an oral tyrosine kinase inhibitor, in patients with medullary thyroid cancer

AUTHOR(S): Kurzrock, Razelle; Sherman, Steven I.; Ball, Douglas W.; Forastiere, Arlene A.; Cohen, Roger B.; Mehra, Ranee; Pfister, David G.; Cohen, Ezra E. W.; Janisch, Linda; Nauling, Forlisa; Hong, David S.; Ng, Chaan S.; Ye, Lei; Gagel, Robert F.; Frye, John; Muller, Thomas; Ratain, Mark J.; Salgia, Ravi

CORPORATE SOURCE: The University of Texas MD Anderson Cancer Center, Houston, USA

SOURCE: Journal of Clinical Oncology (2011), 29(19), 2660-2666
CODEN: JCONDN; ISSN: 0732-183X

DIGITAL OBJECT ID: 10.1200/JCO.2010.32.4145

PUBLISHER: American Society of Clinical Oncology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: XL184 (cabozantinib) is a potent inhibitor of MET, vascular endothelial growth factor receptor 2 (VEGFR2), and RET, with robust antiangiogenic, antitumor, and anti-invasive effects in preclin. models. Early observations of clin. benefit in a phase I study of cabozantinib, which included patients with medullary thyroid cancer (MTC), led to expansion of an MTC-enriched cohort, which is the focus of this article. Patients and Methods: A phase I dose-escalation study of oral cabozantinib was conducted in patients with advanced solid tumors. Primary end points included evaluation of safety, pharmacokinetics, and maximum-tolerated dose (MTD) determination Addnl. end points included RECIST (Response Evaluation Criteria in Solid Tumors) response, pharmacodynamics, RET mutational status, and biomarker analyses. Results: Eighty-five patients were enrolled, including 37 with MTC. The MTD was 175 mg daily. Dose-limiting toxicities were grade 3 palmar plantar erythrodysesthesia (PPE), mucositis, and AST, ALT, and lipase elevations and grade 2 mucositis that resulted in dose interruption and reduction Ten (29%) of 35 patients with MTC with measurable disease had a confirmed partial response. Overall, 18 patients experienced tumor shrinkage of 30% or more, including 17 (49%) of 35 patients with MTC with measurable disease. Addnl., 15 (41%) of 37 patients with MTC had stable disease (SD) for at least 6 mo, resulting in SD for 6 mo or longer or confirmed partial response in 68% of patients with MTC. Conclusion: Cabozantinib has an acceptable safety profile and is active in MTC. Cabozantinib may provide clin. benefit by simultaneously targeting multiple pathways of importance in MTC, including MET, VEGFR2, and RET. A global phase III pivotal study in MTC is ongoing (ClinicalTrials.gov number NCT00215605).

OS.CITING REF COUNT: 146 THERE ARE 146 CAPLUS RECORDS THAT CITE THIS RECORD (147 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 314 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:945715 CAPLUS Full-text

DOCUMENT NUMBER: 156:301829

TITLE: Current status of molecularly targeted drugs for the treatment of advanced thyroid cancer

AUTHOR(S): Takami, Hiroshi E.

CORPORATE SOURCE: Department of Surgery, Teikyo University School of Medicine, Tokyo, 173-8605, Japan

SOURCE: Endocrine Journal (Kyoto, Japan) (2011), 58(3), 151-153
CODEN: ENJOEO; ISSN: 0918-8959

DIGITAL OBJECT ID: 10.1507/endocrj.K11E-076

PUBLISHER: Japan Endocrine Society

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The prognosis of almost all thyroid cancers is good, but some patients have indications for these molecularly targeted drugs. Some of these drugs, i.e., vandetanib, XL-184, sorafenib, motesanib, axitinib, and pazopanib, are clearly useful clin.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 315 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:724271 CAPLUS Full-text

DOCUMENT NUMBER: 155:290943

TITLE: The effects of four different tyrosine kinase inhibitors on medullary and papillary thyroid cancer cells

AUTHOR(S): Verbeek, Hans H. G.; Alves, Maria M.; de Groot, Jan-Willem B.; Osinga, Jan; Plukker, John T. M.; Links, Thera P.; Hofstra, Robert M. W.

CORPORATE SOURCE: Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, 9700 RB, Neth.

SOURCE: Journal of Clinical Endocrinology and Metabolism (2011), 96(6), E991-E995
CODEN: JCEMAZ; ISSN: 0021-972X

DIGITAL OBJECT ID: 10.1210/jc.2010-2381

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Medullary and papillary thyroid carcinoma (MTC and PTC) are 2 types of thyroid cancer that can originate from activating mutations or rearrangements in the RET gene. Therapeutic options are limited in recurrent disease, but because RET is a tyrosine kinase (TK) receptor involved in cellular growth and proliferation, treatment with a TK inhibitor might be promising. Several TK inhibitors were tested in clin. trials, but it is unknown which inhibitor is most effective and whether there is any specificity for particular RET mutations. We aimed to compare the effect of 4 TK inhibitors (axitinib, sunitinib, vandetanib, and XL184) on cell proliferation, RET expression and autophosphorylation, and ERK activation in cell lines expressing a MEN2A (MTC-TT), a MEN2B (MZ-CRC-1) mutation, and a RET/PTC (TPC-1) rearrangement. The 3 cell lines were cultured and treated with the 4 TK inhibitors. Effects on cell proliferation and RET and ERK expression and activation were determined XL184 and vandetanib most effectively inhibited cell proliferation, RET autophosphorylation in combination with a reduction of RET expression, and ERK phosphorylation in MTC-TT and MZ-CRC-1, resp. TPC-1 cells showed a decrease in RET autophosphorylation after treatment with XL184, but no effect was observed on ERK activation. There is indeed specificity for different RET mutations, with XL184 being the most potent inhibitor in MEN2A and PTC and vandetanib the most effective in MEN2B in vitro. No TK inhibitor was superior for all the cell lines tested, indicating that mutation-specific therapies could be beneficial in treating MTC and PTC.

OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 316 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:461207 CAPLUS Full-text

DOCUMENT NUMBER: 156:46100

TITLE: Novel agents and new therapeutics in castration-resistant prostate cancer

AUTHOR(S): Wu, Yichao; Rosenberg, Jonathan E.; Taplin, Mary-Ellen

CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

SOURCE: Current Opinion in Oncology (2011), 23(3), 290-296
CODEN: CUOOE8; ISSN: 1040-8746

DIGITAL OBJECT ID: 10.1097/CCO.0b013e3283449400

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB Purpose of review: This review highlights recent therapeutic advances in systemic therapies for prostate cancer (PCa). Recent findings: Progress in PCa therapeutics has been made during the past year with the approval of a vaccine therapy, second-line chemotherapy, and reported survival advantage for a CYP (17,20) lyase inhibitor in castration-resistant prostate cancer (CRPC). This report will summarize the recently reported and expected data for PCa trials including an evaluation of intermittent vs. continuous androgen deprivation therapy. Denosumab is shown to support bone mineral d. in hormonal sensitive PCa patients. Targeting of androgen-dependent pathways in CRPC postchemotherapy has been shown to improve survival with the lyase inhibitor abiraterone, and lead to prostate-specific antigen and objective responses with an androgen receptor antagonist (MDV3100). However, the addition of bevacizumab to docetaxel/prednisone in treating metastatic CRPC failed to provide a survival benefit. Cabazitaxel in metastatic CRPC postdocetaxel did demonstrate a survival benefit. Provenge, an autologous dendritic cell-based vaccine, demonstrated a reduction in the risk of death in metastatic CRPC. Other immunotherapy agents, including Prostvac and ipilimumab are under investigation. We also discuss the receptor tyrosine kinase inhibitor XL184 and poly (ADP-ribose) polymerase inhibitors which are in early clin. trials. Summary: Recent advances in androgen targeting, chemotherapy, immunotherapy, and other

targeted therapies have led to significant improvements in the care of CRPC patients.

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 317 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:174316 CAPLUS Full-text

DOCUMENT NUMBER: 154:225400

TITLE: C-met modulators as antitumor agents

INVENTOR(S): Aftab, Dana T.; Mueller, Thomas; Weitzman, Aaron; Holland, Jaymes

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011017639	A1	20110210	WO 2010-US44749	20100806
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2770100	A1	20110210	CA 2010-2770100	20100806
AU 2010279234	A1	20120301	AU 2010-279234	20100806
KR 2012059540	A	20120608	KR 2012-7006111	20100806
EP 2461810	A1	20120613	EP 2010-742985	20100806
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR				
CN 102647985	A	20120822	CN 2010-80045677	20100806
JP 2013501731	T	20130117	JP 2012-523982	20100806
IL 217889	A	20130228	IL 2010-217889	20100806
NZ 598055	A	20140530	NZ 2010-598055	20100806
IL 238849	A	20150630	IL 2010-238849	20100806
IN 2012MN00278	A	20120824	IN 2012-MN278	20120203
ZA 2012000842	A	20121128	ZA 2012-842	20120203
MX 2012001654	A	20120314	MX 2012-1654	20120207
US 20120282179	A1	20121108	US 2012-13389266	20120712

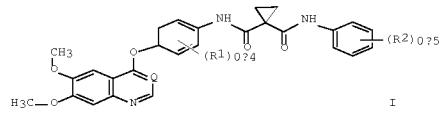
PRIORITY APPLN. INFO.:

US 2009-61232382	P	20090807
IL 2010-217889	A3	20100806
WO 2010-US44749	W	20100806

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 154:225400; MARPAT 154:225400

GI



I

AB Methods of treating cancer by administering a compd. of Formula I (wherein R1 = halo; R2 = halo; Q = CH, N; n = 0-4; m = 0-5) or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments are described.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 318 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:111410 CAPLUS Full-text

DOCUMENT NUMBER: 155:346258

TITLE: Antiangiogenic agents in the treatment of recurrent or newly diagnosed glioblastoma: analysis of single-agent and combined modality approaches

AUTHOR(S): Beal, Kathryn; Abrey, Lauren E.; Gutin, Philip H.

CORPORATE SOURCE: Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA

SOURCE: Radiation Oncology (2011), 6, 2
CODEN: ROANCM; ISSN: 1748-717X
URL: http://www.ro-journal.com/content/pdf/1748-717X-6-2.pdf

DIGITAL OBJECT ID: 10.1186/1748-717X-6-2

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. Surgical resection followed by radiotherapy and temozolomide in newly diagnosed glioblastoma can prolong survival, but it is not curative. For patients with disease progression after frontline therapy, there is no standard of care, although further surgery, chemotherapy, and radiotherapy may be used. Antiangiogenic therapies may be appropriate for treating glioblastomas because angiogenesis is critical to tumor growth. In a large, noncomparative phase II trial, bevacizumab was evaluated alone and with irinotecan in patients with recurrent glioblastoma; combination treatment was associated with an estimated 6-mo progression-free survival (PFS) rate of 50.3%, a median overall survival of 8.9 mo, and a response rate of 37.8%. Single-agent bevacizumab also exceeded the predetd. threshold of activity for salvage chemotherapy (6-mo PFS rate, 15%), achieving a 6-mo PFS rate of 42.6% (p<0.0001). On the basis of these results and those from another phase II trial, the US Food and Drug Administration granted accelerated approval of single-agent bevacizumab for the treatment of glioblastoma that has progressed following prior therapy. Potential antiangiogenic agents - such as cilengitide and XL184 - also show evidence of single-agent activity in recurrent glioblastoma. Moreover, the use of antiangiogenic agents with radiation at disease progression may improve the therapeutic ratio of single-modality approaches. Overall, these agents appear to be well tolerated, with adverse event profiles similar to those reported in studies of other solid tumors. Further research is needed to determine the role of antiangiogenic therapy in frontline treatment and to identify the optimal schedule and partnering agents for use in combination therapy.

OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)

REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 319 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:80577 CAPLUS Full-text

DOCUMENT NUMBER: 154:174225

TITLE: Drug selection for gastric cancer therapy using antibody-based arrays

INVENTOR(S): Singh, Sharat; Kim, Phillip; Liu, Xinjun; Ybarrondo, Belen

PATENT ASSIGNEE(S): Prometheus Laboratories Inc., USA

SOURCE: PCT Int. Appl., 189pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011008990	A1	20110120	WO 2010-US42182	20100715
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2768013	A1	20110120	CA 2010-2768013	20100715
AU 2010273319	A1	20120223	AU 2010-273319	20100715
AU 2010273319	B2	20150122		
EP 2454598	A1	20120523	EP 2010-800567	20100715
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BA, ME, RS				
JP 2012533738	T	20121227	JP 2012-520794	20100715
JP 5795311	B2	20151014		
US 20110281748	A1	20111117	US 2011-13014674	20110126
US 20130237436	A9	20130912		
US 20120270745	A1	20121025	US 2012-13354257	20120119
AU 2013202682	A1	20130502	AU 2013-202682	20130405
AU 2013202682	B2	20150716		

PRIORITY APPLN. INFO.:

US 2009-61225866	P	20090715
US 2009-61265218	P	20091130
US 2010-61325000	P	20100416
US 2006-61007527	P	20060921
US 2007-60913087	P	20070420
AU 2007-299774	A3	20070920
WO 2007-US79002	A1	20070920
US 2008-46381	A2	20080311
WO 2010-US42182	W	20100715
US 2011-13014674	A2	20110126
US 2011-61436945	P	20110127
US 2011-61467950	P	20110325

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods for selecting a suitable anticancer therapy, and for identifying and predicting response for the treatment of a gastric cancer. The present invention provides compns. and methods for detecting the status (e.g., expression and/or activation levels) of components of signal transduction pathways in tumor cells (e.g., gastric tumor cells). Information on the expression and/or activation states of components of signal transduction pathways (e.g., HER2 and/or c-Met signal transduction pathway components) derived from practice of the present invention can be used for gastric cancer diagnosis, prognosis, and in the design of gastric cancer treatments. The compns. and methods of the present invention advantageously provide accurate prediction, selection, and monitoring of cancer patients (e.g., gastric cancer patients) most likely to benefit from targeted therapy by performing pathway profiling on easily accessible tumor cells using multiplexed, antibody-based proximity assays.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 320 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2010:1570396 CAPLUS Full-text

DOCUMENT NUMBER: 155:177406

TITLE: Targeting RET Receptor Tyrosine Kinase Activation in Cancer

AUTHOR(S): Phay, John E.; Shah, Manisha H.

CORPORATE SOURCE: Department of Surgery, Division of Surgical Oncology, Department of Internal Medicine, and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA

SOURCE: Clinical Cancer Research (2010), 16(24), 5936-5941
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-09-0786

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. After ligand binding induces dimerization, the RET receptor tyrosine kinase activates multiple signal transduction pathways. Constitutively activating mutations and chromosomal rearrangements are the primary oncogenic event in a significant number of medullary thyroid cancers (MTC) and papillary thyroid cancers (PTC), resp. When specific germline mutations in RET are identified early, prophylactic thyroidectomy can be

timed to remove at-risk tissue in patients with multiple endocrine neoplasia 2 (MEN2) syndromes who would otherwise develop MTC. Conventional therapy for progressive metastatic MTC is limited. Small-mol. tyrosine kinase inhibitors can target multiple kinases at nanomolar concns., including RET, and have shown efficacy against a variety of malignancies. Initial clin. evidence suggests that several of these inhibitors, including sorafenib, vandetanib, motesanib, sunitinib, and XL-184, may have some benefit in treating progressive MTC. Although initial success seen in these trials seems to be modest, it represents a major breakthrough in the treatment of patients with widespread metastatic MTC. Clin Cancer Res; 16(24); 5936-41.

OS.CITING REF COUNT: 46 THERE ARE 46 CAPLUS RECORDS THAT CITE THIS RECORD (46 CITINGS)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 321 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2010:1240526 CAPLUS Full-text

DOCUMENT NUMBER: 153:595314

TITLE: Tyrosine kinase inhibitors in thyroid cancer

AUTHOR(S): Illouz, Frederic

CORPORATE SOURCE: Service EDN, Centre de reference des pathologies de la receptivite hormonale, CHU d'Angers, Fr.

SOURCE: Correspondances en Metabolismes, Hormones, Diabetes et Nutrition (2010), 14(7), 210-214
CODEN: CMHDBH; ISSN: 2100-9619

PUBLISHER: Edimark SAS

DOCUMENT TYPE: Journal; General Review

LANGUAGE: French

AB A review.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 322 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2010:1003327 CAPLUS Full-text

DOCUMENT NUMBER: 153:278035

TITLE: Treatment of lung cancer with a PARP inhibitor in combination with a growth factor inhibitor

INVENTOR(S): Sherman, Barry M.; Bradley, Charles; Ossovskaya, Valeria S.

PATENT ASSIGNEE(S): BiPar Sciences, Inc., USA

SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010091140	A1	20100812	WO 2010-US23137	20100204

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2751397	A1	20100812	CA 2010-2751397	20100204
AR 75239	A1	20110316	AR 2010-100305	20100204
AU 2010210636	A1	20110922	AU 2010-210636	20100204
KR 2011113648	A	20111017	KR 2011-7020246	20100204
EP 2393364	A1	20111214	EP 2010-739097	20100204

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS

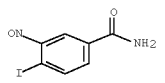
CN 102307475	A	20120104	CN 2010-80006536	20100204
JP 2012516895	T	20120726	JP 2011-549246	20100204
IL 214366	A	20130131	IL 2010-214366	20100204
MX 2011008221	A	20110817	MX 2011-8221	20110804
IN 2011CN06195	A	20121012	IN 2011-CN6195	20110829
US 20120130144	A1	20120524	US 2011-13146865	20111222

PRIORITY APPLN. INFO.: US 2009-61149977 P 20090204
WO 2010-US23137 W 20100204

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 153:278035

GI



AB In one aspect, the present invention provides a method of treating lung cancer, comprising administering to a subject at least one PARP inhibitor in combination with at least one growth factor inhibitor. In another aspect, the present invention provides a method of treating non-small cell lung cancer comprising administering to a subject at least one PARP inhibitor in combination with at least one growth factor inhibitor.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 323 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2010:944155 CAPLUS Full-text

DOCUMENT NUMBER: 155:230334

TITLE: Patients with advanced head and neck cancers have similar progression-free survival on phase I trials and their last food and drug administration-approved treatment

AUTHOR(S): Garrido-Laguna, Ignacio; Janku, Filip; Falchook, Gerald S.; Fu, Siqing; Hong, David S.; Naing, Aung; Aaron, Joanne; Wang, Xuemei; Kies, Merrill; Kurzrock, Razelle

CORPORATE SOURCE: Departments of Investigational Cancer Therapeutics (Phase I Clinical Trials Program), The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

SOURCE: Clinical Cancer Research (2010), 16(15), 4031-4037
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-10-0672

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: To compare clin. outcomes of metastatic head and neck cancer patients treated in phase I clin. trials with clin. outcomes of those patients who had their last Food and Drug Administration (FDA)-approved therapy in the setting of metastatic disease. Exptl. Design: We retrospectively reviewed the outcomes of 61 consecutive patients with head and neck tumors treated in 36 phase I trials at The University of Texas M.D. Anderson Cancer Center between July 2004 and Sept. 2009. Results: The most common histol. was head and neck squamous cell carcinoma (62%). Median age was 55 years (range, 26-80). Eastern Cooperative Oncol. Group performance status was 0 to 1 for 95% of patients. Fifty-nine patients had received FDA-approved drugs as the backbone of their last systemic therapy before inclusion in phase I trials (median, 2 systemic therapies). Progression-free survival (PFS) on phase I trials was not inferior to PFS on their last FDA-approved therapies (12 vs. 10.7 wk, log-rank P = 0.87). Fifty-three patients were evaluable for response by Response Evaluation Criteria in Solid Tumors criteria. Four (7%) had partial responses and 16 (26%) had stable disease for ≥4 mo. In univariate anal., number of metastatic sites, lactate dehydrogenase (LDH) levels at baseline, and Royal Marsden Hospital prognosis scores were significant predictors of survival. Only LDH was significant in multivariate anal. (hazard ratio, 6.35; P ≤ 0.0001). Conclusions: For patients with heavily pretreated advanced head and neck tumors, PFS on phase I trials is not inferior to PFS with their last FDA-approved therapy. The only significant predictor of survival in the multivariate anal. was baseline LDH.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 324 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2010:928655 CAPLUS Full-text

DOCUMENT NUMBER: 154:425137

TITLE: XL-184, a MET, VEGFR-2 and RET kinase inhibitor for the treatment of thyroid cancer, glioblastoma multiforme and NSCLC

AUTHOR(S): Zhang, Ying; Guessous, Fadila; Kofman, Alex; Schiff, David; Abounader, Roger

CORPORATE SOURCE: Department of Microbiology, University of Virginia, Charlottesville, VA, 22903, USA

SOURCE: IDrugs (2010), 13(2), 112-121
CODEN: IDRUFN; ISSN: 2040-3410
URL: http://www.biomedcentral.com/content/pdf/cd-1071541.pdf

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. XL-184 (BMS-907351), under development by Exelixis Inc and Bristol-Myers Squibb Co, is a pan-tyrosine kinase inhibitor for the potential oral treatment of medullary thyroid cancer, glioblastoma multiforme and NSCLC. The prinicipal targets of XL-184 are MET, VEGFR-2 and RET, but the drug is also reported to display inhibitory activity against KIT, FLT3 and TEK. Preclin. studies demonstrated that XL-184 potently inhibited multiple receptor tyrosine kinases in various cancer cell lines and animal xenograft models, and that the drug exhibited significant oral bioavailability and blood-brain barrier penetration. A phase I clin. trial in patients with advanced solid malignancies indicated that XL-184 accumulated dose-dependently in the plasma and had a long terminal half-life. A phase II trial in patients with progressive or recurrent glioblastoma revealed modest but promising median progression-free survival. Toxicity and side effects for the drug have generally been of low-to-moderate severity. At the time of publication, three addnl. trials of XL-184 were recruiting patients, including a phase I trial in combination with standard of care in patients with glioblastoma, a phase I/II trial in combination with erlotinib in patients with NSCLC, and a phase III trial in patients with medullary thyroid cancer.

OS.CITING REF COUNT: 46 THERE ARE 46 CAPLUS RECORDS THAT CITE THIS RECORD (46 CITINGS)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 325 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2010:912816 CAPLUS Full-text

DOCUMENT NUMBER: 153:204211

TITLE: Preparation of malate salts of N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide and crystalline forms thereof for the treatment of cancer.

INVENTOR(S): St Clair Brown, Adrian; Lamb, Peter; Gallagher, William P.

PATENT ASSIGNEE(S): Exelixis, Inc., USA; Bristol-Meyers Squibb Company

SOURCE: PCT Int. Appl., 72pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010083414	A1	20100722	WO 2010-US21194	20100115

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2758030	A1	20100722	CA 2010-2758030	20100115

AR 75025	A1	20110302	AR 2010-100098		20100115
AU 2010204619	A1	20110901	AU 2010-204619		20100115
EP 2387563	A1	20111123	EP 2010-701175		20100115
EP 2387563	B1	20130306			
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KR 2012013301	A	20120214	KR 2011-7018924		20100115
CN 102388024	A	20120321	CN 2010-80012656		20100115
JP 2012515220	T	20120705	JP 2011-546390		20100115
JP 5677318	B2	20150225			
IL 214086	A	20130131	IL 2010-214086		20100115
PT 2387563	E	20130325	PT 2010-701175		20100115
ES 2402524	T3	20130506	ES 2010-701175		20100115
NZ 594594	A	20131129	NZ 2010-594594		20100115
EA 19959	B1	20140730	EA 2011-70941		20100115
TW I447108	B	20140801	TW 2010-101140		20100115
IL 234097	A	20140930	IL 2010-234097		20100115
NZ 618004	A	20150626	NZ 2010-618004		20100115
ZA 2011005167	A	20120328	ZA 2011-5167		20110713
MX 2011007620	A	20111104	MX 2011-7620		20110715
IN 2011KN03402	A	20121102	IN 2011-KN3402		20110811
US 20120035212	A1	20120209	US 2011-13145054		20111020
US 8877776	B2	20141104			
HK 1164305	A1	20131108	HK 2012-104893		20120518
AU 2013203780	A1	20130502	AU 2013-203780		20130411
US 20150057310	A1	20150226	US 2014-14340871		20140725
JP 2015096543	A	20150521	JP 2014-264071		20141226
PRIORITY APPLN. INFO.:			US 2009-61145421	P	20090116
			AU 2010-204619	A3	20100115
			IL 2010-214086	A3	20100115
			JP 2011-546390	A3	20100115
			NZ 2010-594594	A3	20100115
			WO 2010-US21194	W	20100115
			US 2011-13145054	A3	20111020

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 153:204211

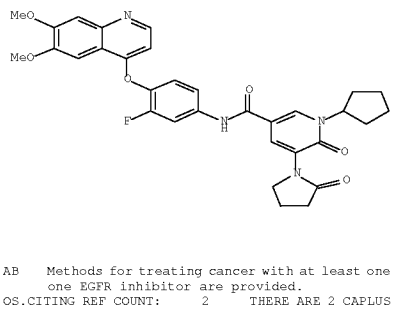
AB N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide malate salts were prepared Thus, 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid (preparation given) was stirred with (COCl)2 in THF/DMF at ≤30° and the mixture was added to 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine (preparation given) and K2CO3 in THF/H2O followed by addition of H2O and stirring for 10 h to give N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide. The latter in EtOH was treated with malic acid in H2O followed by addition of C, thiol silica, heating to 78°, and addition of H2O followed by filtration, addition of Me2CHOH, cooling, and filtration to give N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide malate.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 326 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

			SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
AU 2009300328	A1	20100408	AU 2009-300328		20090930
CA 2738583	A1	20100408	CA 2009-2738583		20090930
EP 2349328	A1	20110803	EP 2009-740207		20090930
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS					
JP 2012504606	T	20120223	JP 2011-530051		20090930
MX 2011003363	A	20110427	MX 2011-3363		20110329
US 20110229469	A1	20110922	US 2011-13122106		20110613
JP 2015107974	A	20150611	JP 2014-256872		20141219
AU 2015201812	A1	20150430	AU 2015-201812		20150410
PRIORITY APPLN. INFO.:			US 2008-61101971	P	20081001
			AU 2009-300328	A3	20090930
			JP 2011-530051	A3	20090930
			WO 2009-US5421	W	20090930

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 152:422278
GI



AB Methods for treating cancer with at least one HGF-Met inhibitor and at least one EGFR inhibitor are provided.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 328 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:402977 CAPLUS Full-text
DOCUMENT NUMBER: 152:423197
TITLE: Recombinant replication-competent retroviral vectors expressing therapeutic products for treatment of proliferative disorders
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas; Perez, Omar
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: PCT Int. Appl., 194 pp.

ACCESSION NUMBER: 2010:726266 CAPLUS Full-text
DOCUMENT NUMBER: 153:633557
TITLE: Targeted therapy for thyroid cancer: an updated review of investigational agents
AUTHOR(S): Deshpande, Hari A.; Gettinger, Scott N.; Sosa, Julie A.
CORPORATE SOURCE: Yale Cancer Center, New Haven, CT, 06520, USA
SOURCE: Current Opinion in Investigational Drugs (BioMed Central) (2010), 11(6), 661-668
CODEN: COIDAZ; ISSN: 2040-3429
URL: http://www.biomedcentral.com/content/pdf/cd-1102161.pdf

PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. The treatment of thyroid cancer is evolving. The mol. mechanisms of carcinogenesis for many thyroid cancers have been investigated, and have yielded targets for potential therapies. These targets include VEGFR in the treatment of all thyroid cancers, BRAF in the treatment of papillary thyroid cancer, and RET in the treatment of medullary thyroid cancer (MTC). Many promising drugs that target one or more of these proteins are currently being evaluated, including sorafenib and sunitinib, both of which are still under development for the treatment of thyroid cancer but which have been approved for use in other malignancies. In addition, compds. such as vandetanib (AstraZeneca plc) and XL-184 (Bristol-Myers Squibb Co/Exelixis Inc) have demonstrated activity in early-phase clin. trials of MTC and are being tested further in randomized trials.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 327 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:439254 CAPLUS Full-text
DOCUMENT NUMBER: 152:422278
TITLE: Methods for the treatment of cancer
INVENTOR(S): Johns, Terrance
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 139pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010039248	A1	20100408	WO 2009-US5421	20090930
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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			CODEN: PIXXD2		
DOCUMENT TYPE:			Patent		
LANGUAGE:			English		
FAMILY ACC. NUM. COUNT:			4		
PATENT INFORMATION:					
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2010036986	A2	20100401	WO 2009-US58512		20090926
WO 2010036986	A3	20100701			
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 2344648	A2	20110720	EP 2009-816967		20090926
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS					
CN 102227503	A	20111026	CN 2009-80147515		20090926
CN 102227503	B	20151021			
JP 2012503987	T	20120216	JP 2011-529292		20090926
JP 5684130	B2	20150311			
ZA 2011002115	A	20120725	ZA 2011-2115		20090926
US 20110287020	A1	20111124	US 2011-13072704		20110326
US 8829173	B2	20140909			
AU 2013205006	A1	20130516	AU 2013-205006		20130413
JP 2015119712	A	20150702	JP 2015-4923		20150114
JP 2015186479	A	20151029	JP 2015-97980		20150513
PRIORITY APPLN. INFO.:			US 2008-61100666	P	20080926
			US 2008-61120618	P	20081208
			US 2009-61186823	P	20090613
			AU 2009-303690	A3	20090926
			JP 2011-529291	A3	20090926
			JP 2011-529292	A3	20090926
			WO 2009-US58512	W	20090926
			US 2010-61318728	P	20100329

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Recombinant replication-competent retroviral (RCR) vectors are provided comprising: a retroviral gag protein; a retroviral pol protein; a retroviral envelop, a retroviral polynucleotide comprising long terminal repeat (LTR) sequence at the 3' end of the retroviral polynucleotide sequence; a mammalian-suitable promoter sequence at the 5' end of the retroviral polynucleotide, a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous polynucleotide; and cis-acting sequences necessary for reverse transcription, packaging and integration in a target cell. The RCR maintains higher replication competency after 6 passages compared to a pACE vector. The heterologous polynucleotide may encode modified cytosine deaminase (thermostabilized and codon optimized), single-chain antibody to CTLA-4, microRNAs miR-128-1 and miR-128-2, γ-interferon, interleukin 2, or other therapeutic proteins of interest. The

disclosure further relates to cells and vector expressing or comprising such modified CDs and methods of using such modified CDs in the treatment of disease and disorders, and in particular cell proliferative disorders such as cancer.

L8 ANSWER 329 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:55413 CAPLUS Full-text
DOCUMENT NUMBER: 152:163651
TITLE: Methods for diagnosis, prognosis and treatment
INVENTOR(S): Fantl, Wendy J.; Rosen, David B.; Cesano, Alessandra; Putta, Santosh K.; Nolan, Garry P.; Cohen, Aileen C.; Evenson, Erik
PATENT ASSIGNEE(S): Nodality, Inc., USA
SOURCE: PCT Int. Appl., 201pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010006291	A1	20100114	WO 2009-US50295	20090710
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2304436	A1	20110406	EP 2009-790295	20090710
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
US 20150017119	A1	20150115	US 2014-14279905	20140516

PRIORITY APPLN. INFO.:

US 2008-61079766	P	20080710
US 2008-61085789	P	20080801
US 2008-61104666	P	20081010
US 2008-61120320	P	20081205
US 2009-460029	A3	20090710
WO 2009-US50295	W	20090710
US 2012-13473829	A1	20120517

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention provides an approach for the detn. of the activation states of a plurality of proteins in single cells. This approach permits the rapid detection of heterogeneity in a complex cell population based on activation states, expression markers and other criteria, and the identification of cellular subsets that exhibit correlated changes in activation within the cell population. Moreover, this approach allows the correlation of cellular activities or properties. In addition, the use of modulators of cellular activation allows for characterization of pathways and cell populations. Several exemplary diseases that can be analyzed using the invention include AML, MDS, and MPN.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 330 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:1534585 CAPLUS Full-text
DOCUMENT NUMBER: 153:76060
TITLE: Antiangiogenic strategies for treatment of malignant gliomas
AUTHOR(S): Chi, Andrew S.; Norden, Andrew D.; Wen, Patrick Y.
CORPORATE SOURCE: Stephen E. and Catherine Pappas Center for Neuro-Oncology, Department of Neurology, Division of Hematology and Oncology, Dana-Farber/Harvard Cancer Center, Harvard Medical School, Massachusetts General Hospital Cancer Center, USA
SOURCE: Neurotherapeutics (2009), 6(3), 513-526
CODEN: NEURNV; ISSN: 1933-7213
DIGITAL OBJECT ID: 10.1016/j.nurt.2009.04.010
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Numerous antiangiogenic agents with diverse mechanisms of action are currently under investigation for the treatment of patients with glioblastoma (GBM), a diagnosis that continues to carry a poor prognosis despite maximal conventional therapy. Early clin. trials suggest that antiangiogenic drugs, which target the blood vessels of these highly angiogenic tumors, may have clin. benefit in GBM patients. Antiangiogenic agents have potent antiedema and steroid-sparing effects in patients, and emerging data suggest that these drugs may modestly improve progression-free survival. Although these early results are encouraging, several issues arise regarding the use and efficacy of these agents. Interpretation of the radiog. changes that occur after treatment with antiangiogenic agents presents a major challenge. Still lacking are reliable radiog. and biol. markers that can predict which patients will benefit from treatment and that accurately indicate response and progression during therapy. In addition, most patients treated with antiangiogenic drugs eventually progress, and the mechanisms by which tumors escape from therapy are only beginning to be understood. Larger prospective trials that incorporate correlative biomarker studies will be required to address these challenges. Here, we summarize the clin. experience with antiangiogenic therapy in patients with malignant gliomas (MG), review the major issues concerning the use and development of these agents, and discuss strategies that may build upon the initial gains observed with antiangiogenic agents.
OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 331 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:1435911 CAPLUS Full-text
DOCUMENT NUMBER: 151:565112
TITLE: Combinations VEGF(R) inhibitors and hepatocyte growth factor (c-met) inhibitors for the treatment of cancer

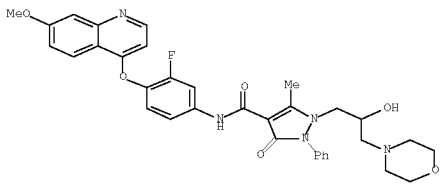
INVENTOR(S): Burgess, Theresa L.; Coxon, Angela; Dussault, Isabelle; Kaplan-Lefko, Paula; Polverino, Anthony J.; Beaupre, Darrin
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009140549	A1	20091119	WO 2009-US44034	20090514
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2009246263	A1	20091119	AU 2009-246263	20090514
AU 2009246263	B2	20140821		
CA 2723617	A1	20091119	CA 2009-2723617	20090514
EP 2288383	A1	20110302	EP 2009-747630	20090514
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, RS				
JP 2011520908	T	20110721	JP 2011-509721	20090514
JP 5699075	B2	20150408		
MX 2010012290	A	20110221	MX 2010-12290	20101110
US 20110104161	A1	20110505	US 2011-992359	20110111
US 20140243339	A1	20140828	US 2014-14194431	20140228

PRIORITY APPLN. INFO.:

US 2008-61127753	P	20080514
WO 2009-US44034	W	20090514
US 2011-992359	B3	20110111

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 151:565112
GI



AB This invention is in the field of pharmaceutical agents and specifically relates to compds., comps., uses and methods for treating cancer, by combining VEGF(R) inhibitors and inhibitors of HGF/SF:c-Met. E.g., enhanced activity was observed when AMG 706 (Motesanib) was combined with Amgen Compound 3 [N-[4-[4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)-2-fluorophenoxy]pyridin-2-yl]morpholine-4-carboxamide] compared to either single agent alone when tested on human gastric adenocarcinoma cancer cells.
OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 332 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:1001773 CAPLUS Full-text
DOCUMENT NUMBER: 152:349858
TITLE: Novel treatment of medullary thyroid cancer
AUTHOR(S): Sugawara, Masahiro; Geffner, David L.; Martinez, Dorothy; Hershman, Jerome M.
CORPORATE SOURCE: aEndocrinology and Diabetes Division, Veterans Affairs Greater Los Angeles Medical Center, Department of Medicine, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA
SOURCE: Current Opinion in Endocrinology, Diabetes and Obesity (2009), 16(5), 367-372
CODEN: COEDFK; ISSN: 1752-296X
DIGITAL OBJECT ID: 10.1097/MED.0b013e3283304f0c
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: Metastatic medullary thyroid cancer (MTC) is an incurable disease once metastasis becomes unresectable. Many therapeutic drugs and methods have been tried to circumvent this difficulty. We review currently published treatments and hope for future developments of more effective treatment methods. Recent findings: Motesanib, vandetanib, axitinib (tyrosine kinase inhibitors), and XL184 (multikinase inhibitor) have been shown to achieve partial response or stable disease state of metastatic MTC. Sunitinib and sorafenib, currently available tyrosine kinase inhibitors, can also be tried for patients with MTC. However, these medications are not curative and do not improve survival rate. Only carcinoembryonic

antigen-I-iodine-based radioimmunotherapy improved survival of a subset of patients with a very aggressive type of MTC. Drugs currently available for possible use of MTC treatment include bortezomib (proteasome inhibitor), valproic acid (histone deacetylase inhibitor), capecitabine (5-fluorouracil prodrug), and indomethacin (NSAID), although clin. studies have yet to be done. Cardiac natriuretic hormones and an extract of the plant Cautleya gracilis are new agents to be studied for MTC. Summary: Kinase inhibitors are the first drugs showing some efficacy in MTC. To improve survival, unconventional drugs or other therapies with or without kinase inhibitors need to be considered.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 333 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2009:378374 CAPLUS Full-text

DOCUMENT NUMBER: 153:495871

TITLE: EGFR agonist: irreversible EGFR-TKI and c-Met inhibitors combination

AUTHOR(S): Yadoya, Takehito; Takahashi, Toshiaki; Yamamoto, Nobuyuki

CORPORATE SOURCE: Dep. of Respiratory Diseases, Shizuoka Cancer Center, Shizuoka, Japan

SOURCE: Mebio Oncology (2009), 6(1), 23-31
CODEN: MOENAJ; ISSN: 1349-2179

PUBLISHER: Mejikarubyusha

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review discussing (1) resistant mechanism to reversible epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), (2) irreversible EGFR-TKIs HKI-272, BIBW-2992, PF-299804 and CI-1033 and (3) c-Met inhibitors AMG-102, XL-184, XL-880 and ARQ-197.

L8 ANSWER 334 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2009:239386 CAPLUS Full-text

DOCUMENT NUMBER: 150:275539

TITLE: Methods for diagnosis, prognosis and methods of treatment

INVENTOR(S): Fantl, Wendy J.; Putta, Santosh K.; Perez, Omar D.; Francis-Lang, Helen L.; Cohen, Aileen C.

PATENT ASSIGNEE(S): Nodality, Inc., USA

SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009025847	A2	20090226	WO 2008-US9975	20080821
WO 2009025847	A3	20090611		

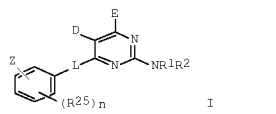
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

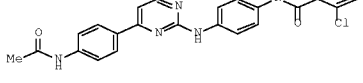
PRIORITY APPLN. INFO.: US 2007-60962776 P 20070801

OTHER SOURCE(S): CASREACT 150:214411; MARPAT 150:214411

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I



II

AB A method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a JAK-2 compound of formula I, or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of formula I and a pharmaceutically acceptable carrier, in combination with an active agent selected from of a Raf inhibitor, an EGFR inhibitor, a VEGFR inhibitor, a ErbB2 inhibitor, a BCR-Abl, inhibitor, a Flt3 inhibitor, a Src inhibitor, a c Kit inhibitor, an Akt inhibitor, a Ret inhibitor, an IFG1R inhibitor, an m-Tor inhibitor, a PI3K inhibitor, a PI3Kalpha inhibitor, wherein the mammal is in need of the treatment. Compds. of formula I wherein D and E are independently H, halo, CF3, heterocycloalkyl and alkyl; D and E taken together to form a 5- to 7-membered heteroaryl, and 5- to 7-membered heterocycloalkyl; L is a bond, O and NH; Z is alkoxy, cycloalkyl, and (un)substitued heteroaryl; Z and R25 taken together for form a 5- to 6-membered heterocycloalkyl, 5- to 6-membered heteroaryl, 5- to 6-membered cycloalkyl, etc.; each R25 is independently alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, etc.; R1 is H; R2 is (un)substituted aryl, (un)substituted heteroaryl, alkyl, etc.; n is 0 - 4; and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by acylation of 2-(4-aminophenylamino)-5-(4-acetylaminophenyl)pyrimidine with 2,6-dichlorobenzoyl chloride. All the invention compds. were evaluated for their JAK-2 inhibitory activity (some data given).

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L8 ANSWER 335 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2009:140345 CAPLUS Full-text

DOCUMENT NUMBER: 150:214411

TITLE: Pyrimidine derivatives as JAK-2 inhibitors in combination with other agents and their preparation and use in the treatment of diseases

INVENTOR(S): Lamb, Peter

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 854pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

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AU 2008289442	A1	20090226	AU 2008-289442	20080821
CA 2696402	A1	20090226	CA 2008-2696402	20080821
US 20090098594	A1	20090416	US 2008-229476	20080821
EP 2179037	A2	20100428	EP 2008-795509	20080821

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS

CN 101802182	A	20100811	CN 2008-80107737	20080821
JP 2010536371	T	20101202	JP 2010-521884	20080821
EP 2860247	A1	20150415	EP 2014-189449	20080821

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IN 2010DN01966	A	20100820	IN 2010-DN1966	20100319
US 20120309029	A1	20121206	US 2012-13493857	20120611
US 9182385	B2	20151110		

PRIORITY APPLN. INFO.:

US 2007-60957160	P	20070821
US 2008-61048920	P	20080429
EP 2008-795509	A3	20080821
US 2008-229476	A1	20080821
WO 2008-US9975	W	20080821

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB This invention is directed to methods and compns. for diagnosis, prognosis and for determining methods of treatment. The physiol. status of cells present in a sample (e.g. clin. sample) can be used in diagnosis or prognosis of a condition (e.g. chronic lymphocytic leukemia), in patient selection for therapy, to monitor treatment and to modify or optimize therapeutic regimens. The physiol. status of a cell can be determined by comparing the intracellular status of one or more activation elements (e.g. the phosphorylation status of a signaling mol.) in a cell (e.g. a cancer cell) to that of another cell (e.g. a normal cell). The physiol. status of a cell can be further classified by adding one or more modulators (e.g. an inhibitor or activator) to the cell in question. In some embodiments, the invention is directed to methods of determining a phenotypic profile of a population of cells.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

L8 ANSWER 336 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2008:1282443 CAPLUS Full-text

DOCUMENT NUMBER: 149:486836

TITLE: Methods for treating cancer resistant to ErbB therapeutics

INVENTOR(S): Janne, Pasi A.; Engelman, Jeffrey; Cantley, Lewis C.

PATENT ASSIGNEE(S): Dana Farber Cancer Institute, USA; Beth Israel Deaconess Medical Center; Massachusetts General Hospital

SOURCE: PCT Int. Appl., 96pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008127710	A2	20081023	WO 2008-US4804	20080411
WO 2008127710	A3	20081204		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

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AU 2008239594	A1	20081023	AU 2008-239594	20080411
AU 2008239594	B2	20131024		
CA 2683559	A1	20081023	CA 2008-2683559	20080411
EP 2076289	A2	20090708	EP 2008-742861	20080411
EP 2076289	B1	20141112		

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JP 2010523680	T	20100715	JP 2010-503084	20080411
ES 2529790	T3	20150225	ES 2008-742861	20080411
EP 2851091	A1	20150325	EP 2014-189064	20080411

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI,

SK, TR

US 20120225870	A1	20120906	US 2010-450826	20100318
US 8715665	B2	20140506		
AU 2013203111	A1	20130502	AU 2013-203111	20130409
AU 2013203111	B2	20151008		
US 20140296100	A1	20141002	US 2014-14256418	20140418
JP 2014141530	A	20140807	JP 2014-97474	20140509

PRIORITY APPLN. INFO.: US 2007-60923384 P 20070413
AU 2008-239594 A3 20080411
EP 2008-742861 A3 20080411
JP 2010-503084 A3 20080411
WO 2008-US4804 W 20080411
US 2010-450826 A1 20100318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided herein are methods for treating cancer that is resistant to treatment with an anti- ErbB therapeutic agent and which is associated with an activating MET gene mutation or a MET gene amplification. The methods involve administering to a subject a combination of an anti- ErbB therapeutic and an anti-MET therapeutic. Also provided are methods for reducing ErbB mediated signaling or PI3 kinase mediated signaling in a cancer cell.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 337 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2008:771167 CAPLUS Full-text
DOCUMENT NUMBER: 149:104583
TITLE: N-Acylazetidine derivatives as MEK inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer
INVENTOR(S): Lamb, Peter
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 534pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

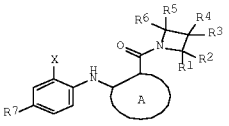
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008076415	A1	20080626	WO 2007-US25751	20071214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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AU 2007334402	A1	20080626	AU 2007-334402	20071214
AU 2007334402	B2	20140213		
CA 2671982	A1	20080626	CA 2007-2671982	20071214
US 20080166359	A1	20080710	US 2007-2340	20071214
US 7999006	B2	20110816		
EP 2101759	A1	20090923	EP 2007-853418	20071214
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
CN 101605540	A	20091216	CN 2007-80051355	20071214
JP 2010513288	T	20100430	JP 2009-541420	20071214
JP 5311673	B2	20131009		
CN 105106199	A	20151202	CN 2015-10422958	20071214
AU 2013204026	A1	20130516	AU 2013-204026	20130411
JP 2013151569	A	20130808	JP 2013-102016	20130514

PRIORITY APPLN. INFO.: US 2006-60875412 P 20061214
AU 2007-334402 A3 20071214
CN 2007-80051355 A3 20071214
JP 2009-541420 A3 20071214
WO 2007-US25751 W 20071214

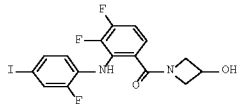
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 149:104583; MARPAT 149:104583

GI



I



II

AB The invention provides methods of treating cancer by administering a compound of formula I, or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments. Compds. of formula I wherein ring A is (un)substituted (hetero)arylene; X is (halo)alkyl, halo and haloalkoxy; R1, R2, R3, R4, R5 and R6 are independently H, halo, NO2, NH2 and derivs., OH and derivs., NHSO2H and derivs., CN, SH and derivs., etc.; R7 is H, halo and alkyl; and their pharmaceutically acceptable salts and solvates thereof are claimed. Example compound II was prepared by amidation of 3,4-difluoro-2-[(2-fluoro-4- iodophenyl)amino]benzoic acid with azetidin-3-ol hydrochloride. All the invention compds. were evaluated for their MEK inhibitory activity (some data given).

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 338 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2008:699999 CAPLUS Full-text
DOCUMENT NUMBER: 149:30417
TITLE: Antibodies and inhibitory nucleic acids for targeing HIF-1α and for diagnosing/treating tumor or metastasis
INVENTOR(S): Huang, L. Eric
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 157pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008070616	A2	20080612	WO 2007-US86264	20071203
WO 2008070616	A3	20090430		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20100074897	A1	20100325	US 2009-517132	20090710

PRIORITY APPLN. INFO.: US 2006-60868188 P 20061201
WO 2007-US86264 W 20071203

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed are compns. and methods related to HIF-1α (hypoxia-inducible factor 1α). The compns. and methods comprise use of HIF-1α inhibitors for reducing tumor growth or metastatic tumor growth. The HIF-1α inhibitor is an antibody (including monoclonal, human and humanized antibody), small mol., siRNA, shRNA, or antisense polynucleotide.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L8 ANSWER 339 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2007:671771 CAPLUS Full-text
DOCUMENT NUMBER: 147:93969
TITLE: Combination of anti-angiopoietin 2 human monoclonal antibody and of VEGF-A, KDR and/or FLT1 antagonist for treating cancer
INVENTOR(S): Brown, Jeffrey Lester; Emery, Stephen Charles; Blakey, David Charles
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007068895	A1	20070621	WO 2006-GB4611	20061212
WO 2007068895	A9	20080612		
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2006324477	A1	20070621	AU 2006-324477	20061212
CA 2633211	A1	20070621	CA 2006-2633211	20061212
KR 2008073766	A	20080811	KR 2008-7015745	20061212
KR 1371773	B1	20140307		
EP 1962903	A1	20080903	EP 2006-820476	20061212
EP 1962903	B1	20130313		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
CN 101370519	A	20090218	CN 2006-80052740	20061212
CN 101370519	B	20130724		
JP 2009521412	T	20090604	JP 2008-545075	20061212
JP 5179373	B2	20130410		
NZ 569787	A	20110729	NZ 2006-569787	20061212
EP 2518083	A2	20121031	EP 2011-167374	20061212
EP 2518083	A3	20121205		
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ES 2411505	T3	20130705	ES 2006-820476	20061212
CN 103341168	A	20131009	CN 2013-10251494	20061212
AR 58359	A1	20080130	AR 2006-105550	20061215
NO 2008002448	A	20080710	NO 2008-2448	20080528
IN 2008DN04540	A	20090320	IN 2008-DN4540	20080528
MX 2008007686	A	20080627	MX 2008-7686	20080613
US 20090123474	A1	20090514	US 2008-97384	20080613
HK 1121674	A1	20131011	HK 2008-112903	20081125
US 20110097321	A1	20110428	US 2010-890101	20100924
AU 2011201326	A1	20110414	AU 2011-201326	20110323
AU 2011201326	B2	20120112		
AU 2012202120	A1	20120503	AU 2012-202120	20120412
US 20120288497	A1	20121115	US 2012-13472862	20120516
JP 2012211155	A	20121101	JP 2012-131988	20120611
US 20140023654	A1	20140123	US 2013-13952997	20130729

PRIORITY APPLN. INFO.: US 2005-60750551 P 20051215
AU 2006-324477 A3 20061212
CN 2006-80052740 A3 20061212
EP 2006-820476 A3 20061212
JP 2008-545075 A3 20061212

		WO 2006-GB4611	W	20061212
		US 2008-97384	B1	20080613
		US 2010-890101	A1	20100924
		AU 2011-201326	A3	20110323
		US 2012-13472862	A1	20120516

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to agents which possess anti-angiogenic activity and are accordingly useful in methods of treatment of disease states associated with angiogenesis in the animal or human body. More specifically the invention concerns a combination of a monoclonal antibody against human angiopoietin 2 (anti-Ang-2) and an antagonist of the biol. activity of VEGF-A, and/or KDR receptor, and/or FLT1, and uses of such antagonists. The nucleotide sequences and the encoded amino acid sequences of anti-Ang-2 monoclonal antibodies are disclosed.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 340 OF 340 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2005:300201 CAPLUS Full-text

DOCUMENT NUMBER: 142:373856

TITLE: Preparation of quinolines and quinazolines as inhibitors of c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases

INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-ming; Chen, Jeff; Dalrymple, Lisa Esther; Forsyth, Timothy Patrick; Huynh, Tai Phat; Jammalamadaka, Vasu; Khoury, Richard George; Leahy, James William; Mac, Morrison B.; Mann, Grace; Mann, Larry W.; Nuss, John M.; Parks, Jason Jevious; Takeuchi, Craig Stacy; Wang, Yong; Xu, Wei

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 428 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030140	A2	20050407	WO 2004-US31523	20040924
WO 2005030140	A3	20050519		
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AU 2004275842	A1	20050407	AU 2004-275842	20040924
AU 2004275842	B2	20100902		
CA 2537812	A1	20050407	CA 2004-2537812	20040924
CA 2537812	C	20130122		
CA 2744997	A1	20050407	CA 2004-2744997	20040924
EP 1673085	A2	20060628	EP 2004-789057	20040924
EP 1673085	B1	20111109		
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JP 2007506777	T	20070322	JP 2006-528265	20040924
JP 4638436	B2	20110223		
EP 2210607	A1	20100728	EP 2010-160517	20040924
EP 2210607	B1	20110817		
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EP 2213661	A1	20100804	EP 2010-160518	20040924
EP 2213661	B1	20110720		
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AT 517091	T	20110815	AT 2010-160518	20040924
AT 520403	T	20110915	AT 2010-160517	20040924
AT 532782	T	20111115	AT 2004-789057	20040924
ES 2369652	T3	20111202	ES 2010-160518	20040924
EP 2392564	A1	20111207	EP 2011-179941	20040924
EP 2392564	B1	20131023		
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EP 2392565	A1	20111207	EP 2011-179942	20040924
EP 2392565	B1	20140319		
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PT 2213661	E	20111215	PT 2010-160518	20040924
ES 2371383	T3	20111230	ES 2010-160517	20040924
EP 2409704	A2	20120125	EP 2011-179944	20040924
EP 2409704	A3	20130213		
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PT 2210607	E	20120131	PT 2010-160517	20040924
EP 2609919	A2	20130703	EP 2013-151957	20040924
EP 2609919	A3	20140226		
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ES 2436888	T3	20140107	ES 2011-179941	20040924
ES 2466818	T3	20140611	ES 2011-179942	20040924
US 20070054928	A1	20070308	US 2006-586751	20061026
US 9174947	B2	20151103		
US 20070225307	A1	20070927	US 2007-753462	20070524
US 8178532	B2	20120515		
US 20070244116	A1	20071018	US 2007-753503	20070524
US 8476298	B2	20130702		
US 20090105299	A1	20090423	US 2007-753514	20070524
US 8067436	B2	20111129		
US 20090170896	A1	20090702	US 2009-393806	20090226
US 7579473	B2	20090825		
JP 2010235631	A	20101021	JP 2010-158335	20100712
JP 5185331	B2	20130417		
JP 2010235632	A	20101021	JP 2010-158336	20100712
JP 5185332	B2	20130417		
JP 2010265302	A	20101125	JP 2010-158334	20100712
JP 5325172	B2	20131023		
JP 2010280674	A	20101216	JP 2010-158337	20100712
JP 5325173	B2	20131023		
AU 2010204459	A1	20100819	AU 2010-204459	20100727
AU 2010204459	B2	20130620		
AU 2010204461	A1	20100819	AU 2010-204461	20100727
AU 2010204461	B2	20130620		
HK 1141799	A1	20120323	HK 2010-108175	20100827
HK 1143068	A1	20120518	HK 2010-109531	20101006
US 20110077233	A1	20110331	US 2010-911442	20101025
JP 2011042686	A	20110303	JP 2010-256317	20101116
US 20120022065	A1	20120126	US 2011-13249815	20110930
US 8497284	B2	20130730		
US 20120184523	A1	20120719	US 2012-13427093	20120322
HK 1164312	A1	20140704	HK 2012-105022	20120522
HK 1164313	A1	20141017	HK 2012-105023	20120522
AU 2013204031	A1	20130502	AU 2013-204031	20130411
US 20130252940	A1	20130926	US 2013-13888592	20130507
US 20140155378	A9	20140605		
US 20140155396	A1	20140605	US 2013-13928977	20130627
JP 2014055190	A	20140327	JP 2013-268454	20131226
JP 5694501	B2	20150401		
JP 2014055191	A	20140327	JP 2013-268455	20131226
JP 2014074059	A	20140424	JP 2013-268453	20131226
JP 2015131859	A	20150723	JP 2015-87327	20150422
US 20150376133	A1	20151231	US 2015-14847801	20150908

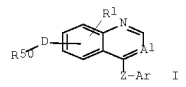
PRIORITY APPLN. INFO.:

US 2003-60506181	P	20030926
US 2004-60535377	P	20040109
US 2004-60577384	P	20040604
AU 2004-275842	A3	20040924
CA 2004-2537812	A3	20040924
EP 2004-789057	A3	20040924
EP 2011-179942	A3	20040924
EP 2011-179944	A3	20040924
JP 2006-528265	A3	20040924
WO 2004-US31523	W	20040924
US 2006-573336	B1	20060918
US 2006-586751	A1	20061026
US 2007-753462	A1	20070524
US 2007-753503	A1	20070524
US 2007-753514	A1	20070524
JP 2010-158337	A3	20100712
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JP 2013-268455	A3	20131226

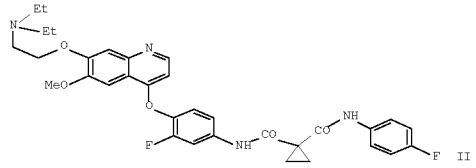
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 142:373856; MARPAT 142:373856

GI



I



II

AB The present invention provides compds. (shown as I; variables defined below; e.g. N-[4-[[7-[[2-(diethylamino)ethyl]oxy]-6-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide (shown as II)) for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. More specifically, the invention provides quinazolines and quinolines which inhibit, regulate and/or modulate kinase receptors, particularly c-Met, KDR, c-Kit, flt-3 and flt-4, signal transduction pathways related to the changes in cellular activities as mentioned above, compns. which contain these compds., and methods of using them to treat kinase-dependent diseases and conditions. The present invention also provides methods for making compds. as mentioned above, and compns. which contain these compds. For I: R1 = H, halogen, OR3, NO2, NH2, NR3R4, and (un)substituted lower alkyl; A1 = :N-, :C(H)-, and :C(CN)-; Z = -S(O)0-2-, -O-, and -NR5-; Ar is aryl or heteroaryl; D = -O-, -S(O)0-2-, and -NR15-; R50 = R3 or bicyclic radical; addnl. details are given in the claims. Methods of preparation are claimed and .apprx.80 example prepns. of I and intermediates are included. For example, II was prepared (34 %) from 2-(diethylamino)ethanol and cyclopropane-1,1-dicarboxylic acid N-[3-fluoro-4-[(7-hydroxy-6-methoxyquinolin-4-yl)oxy]phenyl]amide N-(4-fluorophenyl)amide, which was prepared (89 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-[4-[(7-benzyloxy-6-methoxyquinolin-4-yl)oxy]-3-fluorophenyl]amide N-(4-fluorophenyl)amide, which was prepared (48 %) from trifluoromethanesulfonic acid 7-benzyloxy-6-methoxyquinolin-4-yl ester and cyclopropane-1,1-dicarboxylic acid N-(3-fluoro-4-hydroxyphenyl)amide N-(4-fluorophenyl)amide, which was prepared (85 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-(4-benzyloxy-3-fluorophenyl)amide N-(4-fluorophenyl)amide, which was prepared (98 %) from (4-benzyloxy-3-fluorophenyl)amine and 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid; addnl. details are given in the examples.

OS.CITING REF COUNT: 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS RECORD (53 CITINGS)

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FULL ESTIMATED COST                              1317.66    1818.05

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CA INDEXING COPYRIGHT (C) 2016 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 7 Jan 2016 (20160107/PD)
FILE LAST UPDATED: 7 Jan 2016 (20160107/ED)
HIGHEST GRANTED PATENT NUMBER: US9232686
HIGHEST APPLICATION PUBLICATION NUMBER: US20160007519
CA INDEXING IS CURRENT THROUGH 3 Jan 2016 (20160103/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 7 Jan 2016 (20160107/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

USPATFULL includes complete International Patent Classification (IPC)
reclassification data for the first quarter of 2016.

USPATFULL now includes the comprehensive Cooperative Patent Classification
(CPC).  See HELP CPC for details.

To ensure comprehensive retrieval of US patent information, including
US patent application information, search USPATFULL in combination with
USPAT2.

SELECT PN, PNK, PATS, AP, APPS, PRN and PRAI now bears a charge in this
file.  Please see HELP COST for pricing.

=> s us2014-0200242/pn
L9            1 US2014-0200242/PN
                (US20140200242/PN)

=> d ind

L9   ANSWER 1 OF 1  USPATFULL on STN
INCL   INCLM: 514/312.000
       INCLS: 546/153.000
NCL    NCLM:  514/312.000
       NCLS:  546/153.000
CPC    CPCI   A61K0031-47 [I]; C07D0215-233 [I]
IPC    IPCI   A61K0031-47 [I]; C07D0215-233 [I]
       IPCR   A61K0031-47 [I]; C07D0215-233 [I]

CHEMICAL ABSTRACTS INDEXING    COPYRIGHT 2016 ACS on STN
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                          PATENT      KIND   DATE
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OS    CA 157:382704 * WO   2012109510  A1  20120816
* CA Indexing for this record included
CC    27-17 (Heterocyclic Compounds (One Hetero Atom))
ST    chloroquinoline aminophenol etherification; quinolinyloxyaniline prepn
      cyclopropanecarbonyl chloride acylation; quinolinyldicarboxamide prepn
      addn malic acid; quinoline maleate prepn
IT    Acylation
      Amidation
      Chlorination
      Drug delivery systems
      Etherification
      Pharmaceutical capsules
        (process for preparing quinoline derivs. and pharmaceutical compns.
        thereof)
IT    1219937-98-0P, 1-[(4-Fluorophenyl)carbamoyl]cyclopropanecarbonyl
chloride
        (process for preparing quinoline derivs. and pharmaceutical compns.
        thereof)
IT    35654-56-9P, 4-Chloro-6,7-dimethoxyquinoline   190728-25-7P,
      [4-[(6,7-Dimethoxyquinolin-4-yl)oxy]phenyl]amine   849217-48-7P,
      1-(4-Fluorophenyl)carbamoylcyclopropanecarboxylic acid
        (process for preparing quinoline derivs. and pharmaceutical compns.
        thereof)
IT    849217-68-1P
        (process for preparing quinoline derivs. and pharmaceutical compns.
        thereof)
IT    1140909-48-3P
        (process for preparing quinoline derivs. and pharmaceutical compns.
        thereof)
IT    97-67-6, L-Malic acid   123-30-8, 4-Aminophenol   371-40-4,
      4-Fluoroaniline   399-96-2   598-10-7, 1,1-Cyclopropanedicarboxylic acid
      13425-93-9, 6,7-Dimethoxyquinolin-4-ol
        (process for preparing quinoline derivs. and pharmaceutical compns.
        thereof)
IT    347161-74-4P, [4-[(6,7-Dimethoxyquinolin-4-yl)oxy]-3-fluorophenyl]amine
        (process for preparing quinoline derivs. and pharmaceutical compns.
        thereof)


=> log y

     (FILE 'HOME' ENTERED AT 13:27:04 ON 07 JAN 2016)

     FILE 'REGISTRY' ENTERED AT 13:27:19 ON 07 JAN 2016
L1              STRUCTURE UPLOADED
                D
L2            2 SEA FILE=REGISTRY SSS SAM L1
L3           47 SEA FILE=REGISTRY SSS FUL L1

     FILE 'CAPLUS' ENTERED AT 13:27:57 ON 07 JAN 2016
L4          341 SEA FILE=CAPLUS SPE=ON  ABB=ON  PLU=ON  L3

     FILE 'REGISTRY' ENTERED AT 13:28:09 ON 07 JAN 2016
L5              STRUCTURE UPLOADED
                D
L6            2 SEA FILE=REGISTRY SSS SAM L5
L7           31 SEA FILE=REGISTRY SSS FUL L5

     FILE 'CAPLUS' ENTERED AT 13:28:46 ON 07 JAN 2016
L8          340 SEA FILE=CAPLUS SPE=ON  ABB=ON  PLU=ON  L7
                D IBIB ABS -340

     FILE 'USPATFULL' ENTERED AT 13:30:18 ON 07 JAN 2016
L9            1 SEA FILE=USPATFULL SPE=ON  ABB=ON  PLU=ON  US2014-0200242/PN
                D IND

COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                15.86    1833.91

STN INTERNATIONAL LOGOFF AT 13:35:06 ON 07 JAN 2016
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Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13984559
Filing Date	2014-03-20
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	Timothy R. Rozof
Attorney Docket Number	224990/10-039C-US/343999

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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NON-PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	1	European Medicines Agency, "Specifications: Test procedures and acceptance criteria for new drug substances and new drug products: chemical substances", May 2000.	☐
	2	Sigma-Aldrich Corporation, "Cabozantinib Material Safety Data Sheet", Version 5.0, October 20, 2014, retrieved from the internet at http://www.sigmaaldrich.com/MSDS/MSDS/DisplayMSDSPage.do?country=US&language=en&productNumber=CDS009101&brand=ALDRICH&PageToGoToURL=http%3A%2F%2Fwww.sigmaaldrich.com%2Fcatalog%2Fproduct%2Faldrich%2Fcds009101%3Flang%3Den on October 1, 2015.	☐
	3	United States Department of Health and Human Services, "Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products", Revision 2, November 2003, retrieved from the internet at www.fda.gov/downloads/drugs/guidancecomplianceregulatory information/guidances/ucm073369.pdf on October 1, 2015.	☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature	/TIMOTHY R ROZOF/	Date Considered	01/07/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1]See Kind Codes of USPTO Patent Documents at www.USPTO.GOVor MPEP 901.04. [2]Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3]For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4]Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5]Applicant is to place a check mark here if English language translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature		Date (YYYY-MM-DD)	2015-10-01
Name/Print	Heidi M. Berven	Registration Number	48,951

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1924	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
L2	7064	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:23
L3	5473	L2 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
L4	494	L3 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
L5	96	L4 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
L6	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:23
L7	755	L3 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
L8	12	L5 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
L10	1924	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
L11	7064	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:23
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L14	96	L13 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
L15	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:23
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L17	12	L14 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	ON	2016/01/07 13:23

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L19	0	((A61K31/47.cpc.) or (C07D215/233.cpc.)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:33
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L22	546	L21 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:34
L23	81	L22 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:34
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S2	6107	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2014/10/04 13:12
S3	4920	S2 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 13:12
S4	476	S3 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 13:14
S5	88	S4 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 13:14
S6	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2014/10/04 13:14
S7	735	S3 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 15:14
S8	11	S5 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 15:15
S10	1907	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S11	6748	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2015/06/03 13:56
S12	5294	S11 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S13	492	S12 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S14	96	S13 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S15	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	OFF	2015/06/03 13:56

			DERWENT			
S16	748	S12 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S17	12	S14 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L9	0	((546/153) or (514/312)).CCLS.	* No UPAD	OR	OFF	2016/01/07 13:23
L18	0	((546/153) or (514/312)).CCLS.	* No UPAD	OR	OFF	2016/01/07 13:23
S9	1	((546/153) or (514/312)).CCLS.	* No UPAD	OR	OFF	2014/10/04 13:43
S18	1	((546/153) or (514/312)).CCLS.	* No UPAD	OR	OFF	2015/06/03 13:56

1/7/2016 1:34:44 PM
C:\Users\trozof\Documents\EAST\Workspaces\13984559.wsp

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON, JO ANN
	Examiner	Art Unit
	TIMOTHY R ROZOF	1625

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
Class, inventor, STN and EAST search	1/7/2016	TRR

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
A61K	31/47	1/7/2016	TRR
C07D	215/233	1/7/2016	TRR

	/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625

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BIB DATA SHEET

CONFIRMATION NO. 6725

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/984,559	03/20/2014	514	1625	224990/10-039C-US/343999

APPLICANTS

INVENTORS

Jo Ann Wilson, San Francisco, CA;
Khalid Shah, South San Francisco, CA;

**** CONTINUING DATA ***************************

This application is a 371 of PCT/US12/24591 02/10/2012
which claims benefit of 61/441,520 02/10/2011
and claims benefit of 61/441,527 02/10/2011

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED **** ** SMALL ENTITY **

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☐ No Verified and Acknowledged /TIMOTHY R ROZOF/ Examiner's Signature	☐ Met after Allowance TRR Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		CA	0	25	6

ADDRESS

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800
UNITED STATES

TITLE

Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

FILING FEE RECEIVED		
3890	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
13/984,559	03/20/2014	1625	3890	224990/10-039C-US/343999	25	6

CONFIRMATION NO. 6725

UPDATED FILING RECEIPT

91684
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800



Date Mailed: 01/08/2016

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Jo Ann Wilson, San Francisco, CA;
Khalid Shah, South San Francisco, CA;

Applicant(s)

Jo Ann Wilson, San Francisco, CA;
Khalid Shah, South San Francisco, CA;

Assignment For Published Patent Application

Exelixis, Inc., San Francisco, CA

Power of Attorney: The patent practitioners associated with Customer Number 91684

Domestic Priority data as claimed by applicant

This application is a 371 of PCT/US12/24591 02/10/2012
which claims benefit of 61/441,520 02/10/2011
and claims benefit of 61/441,527 02/10/2011

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: No

Permission to Access Search Results: No

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Projected Publication Date: Not Applicable
Non-Publication Request: No
Early Publication Request: No
**** SMALL ENTITY ****
Title

Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Preliminary Class

514

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

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The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop

technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999

CONFIRMATION NO. 6725

91684
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

37 CFR 1.48 ACKNOWLEDGEMENT LETTER



Date Mailed: 01/08/2016

NOTICE OF ACCEPTANCE OF REQUEST UNDER 37 CFR 1.48(a)

This is in response to the applicant's request under 37 CFR 1.48(a) submitted on 01/05/2016.

The request under 37 CFR 1.48(a) to correct the inventorship, to correct or update the name of an inventor, or to correct the order of names of joint inventors is accepted.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/hsarwari/

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST TO CORRECT INVENTORSHIP UNDER 37 C.F.R. § 1.48

Dear Sir or Madam:

The present communication is filed to request correction of the inventorship for U.S. patent application Serial No. 13/984,559 by adding the name of omitted inventor Khalid Shah of South San Francisco, CA. The Applicant requested this correction previously on October 1, 2015; however, the Supplemental Application Data Sheet (PTO/SB/14) provided was not marked up. The Applicant submits herewith a marked-up Supplemental Application Data Sheet indicating the correct inventorship for U.S. patent application Serial No. 13/984,559.

Currently, the U.S. Patent and Trademark Office lists the following as inventors for U.S. patent application Serial No. 13/984,559: Jo Ann Wilson. The correct inventors for U.S. patent application Serial No. 13/984,559 are: Khalid Shah and Jo Ann Wilson. The name of inventor Khalid Shah was omitted in U.S. patent application Serial No. 13/984,559 through error without any deceptive intention on the part of the omitted inventor. The Applicant respectfully requests issuance of a revised filing receipt reflecting the correct inventorship for this application.

In support of this request, the Applicant submits the following documents:

(1) An Application Data Sheet (PTO/SB/14) in accordance with 37 C.F.R. § 1.76 that identifies each inventor by his or her legal name, as required by § 1.48(a)(1), is submitted herewith;

(2) The processing fee set forth in § 1.17(i), as required by § 1.48(a)(2), was previously submitted on October 1, 2015;

(3) The fee set forth in § 1.17(d), as required by § 1.48(c), was previously submitted on October 1, 2015;

(4) A statement from Khalid Shah that the error in inventorship occurred without deceptive intention on his part, as required by § 1.497(d), is submitted herewith;

(5) Written consent of the Assignee to add this inventor to U.S. patent application Serial No. 13/984,559, as required by § 1.497(d), is submitted herewith; and

(6) A declaration under § 1.63 executed by Khalid Shah for U.S. patent application Serial No. 13/984,559 is submitted herewith.

The requisite $70.00 processing fee set forth in 37 C.F.R. § 1.17(i) and $300.00 fee set forth in § 1.17(d) for correction of inventorship after a first action on the merits were submitted in this application previously on October 1, 2015. The Applicant believes that no additional fees are required for this Request to Correct Inventorship. However, if there are any further charges, or any credits, in relation to this submission, please apply them to Deposit Account Number 503145, referencing Attorney Docket No. 224990/10-039C-US/343999.

Respectfully submitted,
By: Honigman Miller Schwartz and Cohn LLP

Date: January 5, 2016

Heidi M. Berven, Ph.D.
Reg. No. 48,951
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Suite 300
Kalamazoo, Michigan 49007
Telephone: (269) 337-7710
Facsimile: (269) 337-7711

SUPPLEMENTAL APPLICATION DATA SHEET

PTO/SB/14 (11-08)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	224990/10-039C-US/343999
	Application Number	13/984,559
Title of Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Applicant Information:

Applicant 1

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Jo Ann		Wilson	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	San Francisco	State/Province	CA	Country of Residence	US

Citizenship under 37 CFR 1.41(b) US

Mailing Address of Applicant:

Address 1	74 Seward Street		
Address 2			
City	San Francisco	State/Province	CA
Postal Code	94114	Country	US

Applicant 2

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Khalid		Shah	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	South San Francisco	State/Province	CA	Country of Residence	US

Citizenship under 37 CFR 1.41(b) US

Mailing Address of Applicant:

Address 1	12 Amberwood Circle		
Address 2			
City	South San Francisco	State/Province	CA
Postal Code	94080	Country	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

SUPPLEMENTAL APPLICATION DATA SHEET

PTO/SB/14 (11-08)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	224990/10-039C-US/343999
	Application Number	13/984,559
Title of Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds	

Customer Number	91684		
Email Address	patent@honigman.com	Add Email	Remove Email

Application Information:

Title of the Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds		
Attorney Docket Number	224990/10-039C-US/343999	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Suggested Class (if any)		**Sub Class (if any)**	
Suggested Technology Center (if any)			
Total Number of Drawing Sheets (if any)		**Suggested Figure for Publication (if any)**	

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Enter either Customer Number or complete the Representative Name section below. If both sections are completed the Customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	91684		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification.

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
13984559	a 371 of international	PCT/US2012/024591	2012-02-10
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
PCT/US2012/024591	non provisional of	61441520	2011-02-10

SUPPLEMENTAL APPLICATION DATA SHEET

PTO/SB/14 (11-08)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office. U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	224990/10-039C-US/343999
	Application Number	13/984,559
Title of Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
PCT/US2012/024591	non provisional of	61441527	2011-02-10

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button.

Foreign Priority Information:

This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(a).

Remove

Application Number	Country	Parent Filing Date (YYYY-MM-DD)	Priority Claimed
			(•) Yes ( ) No

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.

Assignee Information:

Providing this information in the application data sheet does not substitute for compliance with any requirement of part 3 of Title 37 of the CFR to have an assignment recorded in the Office.

Assignee 1

If the Assignee is an Organization check here. [x]

Organization Name	Exelixis, Inc.		
Mailing Address Information:			
Address 1	210 East Grand Ave.		
Address 2			
City	South San Francisco	**State/Province**	CA
Country	US	Postal Code	94080
Phone Number		Fax Number	
Email Address			

Additional Assignee Data may be generated within this form by selecting the **Add** button.

Signature:

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.

Signature				Date (YYYY-MM-DD)	2016-01-05
First Name	Heidi M	Last Name	Berven	Registration Number	48951

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	224990/10-039C-US/343999
	Application Number	13/984,559
Title of Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds	

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT OF INVENTOR KHALID SHAH

Dear Sir or Madam:

I, Khalid Shah, state that the error in inventorship in the above-identified application occurred without deceptive intention on my part.

Khalid Shah

15 SEP 2015

Date

12 Amberwood Circle, South San Francisco, CA 94080

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CONSENT OF ASSIGNEE TO CORRECTION OF INVENTORSHIP

Exelixis, Inc. is a corporation organized and existing under the laws of the State of Delaware and having a place of business at 210 East Grand Ave., South San Francisco, CA, and is the Assignee of record of the entire right, title, and interest in U.S. patent application Serial No. 13/984,559. Evidence of ownership has been established by recordation of an Assignment of Rights at the United States Patent and Trademark Office on May 26, 2015, under Reel/Frame No. 035737/0207.

I, Jeffrey Hessekiel, have authority to act for and on behalf of the Assignee, Exelixis, Inc.

Exelixis, Inc., being the Assignee of the entire right, title and interest of U.S. patent application Serial No. 13/984,559, hereby consents to correction of inventorship of this application, whereby Khalid Shah will be added as an inventor. Following the correction of inventorship, the inventors for U.S. patent application Serial No. 13/984,559 will be Khalid Shah and Jo Ann Wilson.

Date: 9/15/15

Jeffrey Hessekiel
Executive Vice President & General Counsel
Exelixis, Inc.

DECLARATION AND POWER OF ATTORNEY

We, the below named inventors, hereby declare that our citizenship, residency, and mailing address is as identified below next to our respective names; we have reviewed and understand the content of the specification, including the claims, of the attached specification; We believe that we are the original, first, and sole/joint inventors of the subject matter which is claimed therein and for which a patent is sought on the invention or discovery entitled:

Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

This application, United States Serial No. 13/984,559 is a United States National Phase filing of PCT/US2012/024591, filed February 10, 2012, which claims priority to U.S. Provisional Application No. 61/441,520, filed February 10, 2011, and 61/441,527, filed February 10, 2011, which are incorporated herein by reference.

We acknowledge our duty to disclose information of which we are aware that is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

We hereby appoint the practitioners associated with Customer No. 91684, as our attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark office connected therewith.

Please recognize the address associated with Customer Number 91684 as the correspondence address for the above-identified application.

We further declare that all statements made herein of our own knowledge are true and that all statements made herein on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, Section 1001, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Khalid Shah — 15 Sep 2015

Name: Khalid Shah Date:
Address: 12 Amberwood Circle, South San Francisco, CA 94080
Citizenship: US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

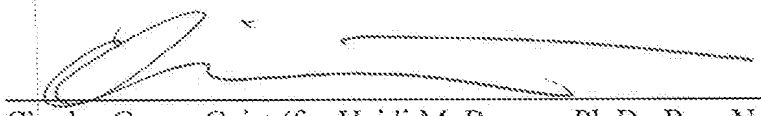
Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8(a)

The undersigned hereby certifies that the following documents are being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4) on this 5th day of January, 2016:

1. Cover Letter to the Commissioner for Patents;
2. Request to Correct Inventorship under 37 C.F.R. § 1.48;
3. Supplemental Application Data Sheet (PTO/SB/14);
4. Statement of Inventor Khalid Shah;
5. Written Consent of Assignee to Correction of Inventorship;
6. Combined Power of Attorney and Declaration under 37 C.F.R. § 1.63 for inventor Khalid Shah; and
7. This Certificate of Transmission under 37 C.F.R. § 1.8(a).



Charles Gregg-Geist (for Heidi M. Berven, Ph.D., Reg. No.: 48,951)

Electronic Acknowledgement Receipt

EFS ID:	24534339
Application Number:	13984559
International Application Number:	
Confirmation Number:	6725
Title of Invention:	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
First Named Inventor/Applicant Name:	Jo Ann Wilson
Customer Number:	91684
Filer:	Heid Marie Berven/Charles Gregg-Geist
Filer Authorized By:	Heid Marie Berven
Attorney Docket Number:	224990/10-039C-US/343999
Receipt Date:	05-JAN-2016
Filing Date:	20-MAR-2014
Time Stamp:	18:13:33
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		10-039c-us.pdf	2384901 d647e7e22f7ef56c20cf9e8758ecc84505e25898	yes	12

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Transmittal Letter	1	2
	Request under Rule 48 correcting inventorship	3	4
	Application Data Sheet	5	8
	Miscellaneous Incoming Letter	9	9
	Miscellaneous Incoming Letter	10	10
	Oath or Declaration filed	11	11
	Transmittal Letter	12	12

Warnings:	
Information:	
Total Files Size (in bytes):	2384901

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

HONIGMAN

Honigman Miller Schwartz and Cohn LLP
Attorneys and Counselors

Heidi M. Berven, Ph.D.

(269) 337-7710
Fax: (269) 337-7711
hberven@honigman.com

Via EFS

January 5, 2016

Commissioner for Patents
United States Patent and Trademark Office
P. O. Box 1450
Alexandria, VA 22313

Re: ***Application No.: 13/984,559***
Inventor: Jo Ann Wilson
Filing Date: March 20, 2014
Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
Confirmation No.: 6725
Attorney Docket No.: 224990/10-039C-US/343999

Dear Sir or Madam:

Enclosed for filing please find the following documents:

1. This Cover Letter to the Commissioner for Patents;
2. Request to Correct Inventorship under 37 C.F.R. § 1.48;
3. Supplemental Application Data Sheet (PTO/SB/14);
4. Statement of Inventor Khalid Shah;
5. Written Consent of Assignee to Correction of Inventorship;
6. Combined Power of Attorney and Declaration under 37 C.F.R. § 1.63 for inventor Khalid Shah; and
7. Certificate of Transmission under 37 C.F.R. § 1.8(a).

It is believed that no fees are due for this submission. The requisite $70.00 processing fee set forth in 37 C.F.R. § 1.17(i) and $300.00 fee set forth in § 1.17(d) for correction of inventorship after a first action on the merits were submitted in this application previously on October 1, 2015. However, if there are any fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Very truly yours,

HONIGMAN MILLER SCHWARTZ AND COHN LLP

Heidi M. Berven, Ph.D.
Reg. No. 48,951

HMB/cwg

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999

CONFIRMATION NO. 6725

IMPROPER CFR REQUEST

91684
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

OC000000077868961

Date Mailed: 10/06/2015

RESPONSE TO REQUEST FOR CORRECTED FILING RECEIPT

Power of Attorney, Claims, Fees, System Limitations, and Miscellaneous

In response to your request for a corrected Filing Receipt, the Office is unable to comply with your request because:

- The ADS submitted on 10/01/2015 was not properly marked up to show the desired changes. For information being changed relative to the informatio already n of record, additions must be shown with underlining, and deletions must be shown with strike-through or brackets. See 37 CFR 1.76(c)(2)

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/hsarwari/

Doc code: RCEX
Doc description: Request for Continued Examination (RCE)

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	13/984,559	Filing Date	2014-03-20	Docket Number (if applicable)	224990/10-039C-US/343999	Art Unit	1625
First Named Inventor	Jo Ann Wilson			Examiner Name	Timothy R. Rozof		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☒ Enclosed

- ☒ Amendment/Reply
- ☒ Information Disclosure Statement (IDS)
- ☒ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

☒ **The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.**
The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to
Deposit Account No 503145

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Signature of Registered U.S. Patent Practitioner			
Signature		Date (YYYY-MM-DD)	2015-10-01
Name	Heidi M. Berven	Registration Number	48951

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/SB/08a (03-15)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13984559
Filing Date	2014-03-20
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	Timothy R. Rozof
Attorney Docket Number	224990/10-039C-US/343999

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	1	European Medicines Agency, "Specifications: Test procedures and acceptance criteria for new drug substances and new drug products: chemical substances", May 2000.	☐
	2	Sigma-Aldrich Corporation, "Cabozantinib Material Safety Data Sheet", Version 5.0, October 20, 2014, retrieved from the internet at http://www.sigmaaldrich.com/MSDS/MSDS/DisplayMSDSPage.do?country=US&language=en&productNumber=CDS009101&brand=ALDRICH&PageToGoToURL=http%3A%2F%2Fwww.sigmaaldrich.com%2Fcatalog%2Fproduct%2Faldrich%2Fcds009101%3Flang%3Den on October 1, 2015.	☐
	3	United States Department of Health and Human Services, "Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products", Revision 2, November 2003, retrieved from the internet at www.fda.gov/downloads/drugs/guidancecomplianceregulatory information/guidances/ucm073369.pdf on October 1, 2015.	☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1]See Kind Codes of USPTO Patent Documents at www.USPTO.GOVor MPEP 901.04. [2]Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3]For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4]Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5]Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature		Date (YYYY-MM-DD)	2015-10-01
Name/Print	Heidi M. Berven	Registration Number	48,951

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST TO CORRECT INVENTORSHIP UNDER 37 C.F.R. § 1.48

Dear Sir or Madam:

The present communication is filed to request correction of the inventorship for U.S. patent application Serial No. 13/984,559 by adding the name of omitted inventor Khalid Shah of South San Francisco, CA. The Applicant hereby submits a marked-up Supplemental Application Data Sheet (PTO/SB/14) indicating the correct inventorship for U.S. patent application Serial No. 13/984,559.

Currently, the U.S. Patent and Trademark Office lists the following as inventors for U.S. patent application Serial No. 13/984,559: Jo Ann Wilson. The correct inventors for U.S. patent application Serial No. 13/984,559 are: Khalid Shah and Jo Ann Wilson. The name of inventor Khalid Shah was omitted in U.S. patent application Serial No. 13/984,559 through error without any deceptive intention on the part of the omitted inventor. The Applicant respectfully requests issuance of a revised filing receipt reflecting the correct inventorship for this application.

In support of this request, the Applicant submits herewith the following documents:

(1) An Application Data Sheet (PTO/SB/14) in accordance with 37 C.F.R. § 1.76 that identifies each inventor by his or her legal name, as required by § 1.48(a)(1);

(2) The processing fee set forth in § 1.17(i), as required by § 1.48(a)(2);

(3) The fee set forth in § 1.17(d), as required by § 1.48(c);

(4) A statement from Khalid Shah that the error in inventorship occurred without deceptive intention on his part, as required by § 1.497(d);

(5) Written consent of the Assignee to add this inventor to U.S. patent application Serial No. 13/984,559, as required by § 1.497(d); and

(6) A declaration under § 1.63 executed by Khalid Shah for U.S. patent application Serial No. 13/984,559.

It is believed that due for this submission are the $70.00 processing fee set forth in 37 C.F.R. § 1.17(i) and the $300.00 fee set forth in § 1.17(d) for correction of inventorship after a first action on the merits. The Applicant authorizes the Office to charge this $370.00 to Deposit Account No. 503145, referencing Attorney Docket No. 224990/10-039C-US/343999. The Applicant believes that no additional fees are required for this Request to Correct Inventorship; however, if there are any additional charges or any credits in relation to this submission, please apply them to Deposit Account Number 503145, referencing Attorney Docket No. 224990/10-039C-US/343999.

Respectfully submitted,

By: Honigman Miller Schwartz and Cohn LLP

Date: October 1, 2015

Heidi M. Berven, Ph.D.
Reg. No. 48,915
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Suite 300
Kalamazoo, Michigan 49007
Telephone: (269) 337-7710
Facsimile: (269) 337-7711

SUPPLEMENTAL APPLICATION DATA SHEET

PTO/SB/14 (11-08)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	224990/10-039C-US/343999
	Application Number	13/984,559
Title of Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Applicant Information:

Applicant 1

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Jo Ann		Wilson	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	San Francisco	State/Province	CA	Country of Residence	US

Citizenship under 37 CFR 1.41(b) US

Mailing Address of Applicant:

Address 1	74 Seward Street		
Address 2			
City	San Francisco	State/Province	CA
Postal Code	94114	Country	US

Applicant 2

Applicant Authority ◉ Inventor ○ Legal Representative under 35 U.S.C. 117 ○ Party of Interest under 35 U.S.C. 118

Prefix	Given Name	Middle Name	Family Name	Suffix
	Khalid		Shah	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	South San Francisco	State/Province	CA	Country of Residence	US

Citizenship under 37 CFR 1.41(b) US

Mailing Address of Applicant:

Address 1	12 Amberwood Circle		
Address 2			
City	South San Francisco	State/Province	CA
Postal Code	94080	Country	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

SUPPLEMENTAL APPLICATION DATA SHEET

PTO/SB/14 (11-08)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	224990/10-039C-US/343999
	Application Number	13/984,559
Title of Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds	

Customer Number	91684		
Email Address	patent@honigman.com	Add Email	Remove Email

Application Information:

Title of the Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds		
Attorney Docket Number	224990/10-039C-US/343999	**Small Entity Status Claimed**	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Suggested Class (if any)		**Sub Class (if any)**	
Suggested Technology Center (if any)			
Total Number of Drawing Sheets (if any)		**Suggested Figure for Publication (if any)**	

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Enter either Customer Number or complete the Representative Name section below. If both sections are completed the Customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	91684		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification.

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
13984559	a 371 of international	PCT/US2012/024591	2012-02-10
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
PCT/US2012/024591	non provisional of	61441520	2011-02-10

SUPPLEMENTAL APPLICATION DATA SHEET

PTO/SB/14 (11-08)
Approved for use through 04/30/2017. OMB 0651-0032
U.S. Patent and Trademark Office. U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	224990/10-039C-US/343999
	Application Number	13/984,559
Title of Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds	

Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
PCT/US2012/024591	non provisional of	61441527	2011-02-10

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button.

Foreign Priority Information:

This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(a).

Remove

Application Number	Country[i]	Parent Filing Date (YYYY-MM-DD)	Priority Claimed
			◉ Yes ○ No

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.

Assignee Information:

Providing this information in the application data sheet does not substitute for compliance with any requirement of part 3 of Title 37 of the CFR to have an assignment recorded in the Office.

Assignee 1

If the Assignee is an Organization check here. ☒

Organization Name	Exelixis, Inc.		
Mailing Address Information:			
Address 1	210 East Grand Ave.		
Address 2			
City	South San Francisco	**State/Province**	CA
Country[i]	US	Postal Code	94080
Phone Number		Fax Number	
Email Address			

Additional Assignee Data may be generated within this form by selecting the **Add** button.

Signature:

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.

Signature				Date (YYYY-MM-DD)	2015-10-01
First Name	Heidi M.	Last Name	Berven	Registration Number	48951

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	224990/10-039C-US/343999
	Application Number	13/984,559
Title of Invention	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds	

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT OF INVENTOR KHALID SHAH

Dear Sir or Madam:

I, Khalid Shah, state that the error in inventorship in the above-identified application occurred without deceptive intention on my part.

15 SEP 2015

Khalid Shah

Date

12 Amberwood Circle, South San Francisco, CA 94080

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CONSENT OF ASSIGNEE TO CORRECTION OF INVENTORSHIP

Exelixis, Inc. is a corporation organized and existing under the laws of the State of Delaware and having a place of business at 210 East Grand Ave., South San Francisco, CA, and is the Assignee of record of the entire right, title, and interest in U.S. patent application Serial No. 13/984,559. Evidence of ownership has been established by recordation of an Assignment of Rights at the United States Patent and Trademark Office on May 26, 2015, under Reel/Frame No. 035737/0207.

I, Jeffrey Hessekiel, have authority to act for and on behalf of the Assignee, Exelixis, Inc.

Exelixis, Inc., being the Assignee of the entire right, title and interest of U.S. patent application Serial No. 13/984,559, hereby consents to correction of inventorship of this application, whereby Khalid Shah will be added as an inventor. Following the correction of inventorship, the inventors for U.S. patent application Serial No. 13/984,559 will be Khalid Shah and Jo Ann Wilson.

Date: 9/15/15

Jeffrey Hessekiel
Executive Vice President & General Counsel
Exelixis, Inc.

DECLARATION AND POWER OF ATTORNEY

We, the below named inventors, hereby declare that our citizenship, residency, and mailing address is as identified below next to our respective names; we have reviewed and understand the content of the specification, including the claims, of the attached specification; We believe that we are the original, first, and sole/joint inventors of the subject matter which is claimed therein and for which a patent is sought on the invention or discovery entitled:

Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

This application, United States Serial No. 13/984,559 is a United States National Phase filing of PCT/US2012/024591, filed February 10, 2012, which claims priority to U.S. Provisional Application No. 61/441,520, filed February 10, 2011, and 61/441,527, filed February 10, 2011, which are incorporated herein by reference.

We acknowledge our duty to disclose information of which we are aware that is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

We hereby appoint the practitioners associated with Customer No. 91684, as our attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark office connected therewith.

Please recognize the address associated with Customer Number 91684 as the correspondence address for the above-identified application.

We further declare that all statements made herein of our own knowledge are true and that all statements made herein on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, Section 1001, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Khalid Shah — 15 Sep 2015

Name: Khalid Shah — Date:
Address: 12 Amberwood Circle, South San Francisco, CA 94080
Citizenship: US

PTO/SB/22 (03-13)
Approved for use through 3/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional): 224990/10-039C-US/343999

Application Number: 13/984,559

Filed: March 20, 2014

For: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Art Unit: 1625

Examiner: Timothy R. Rozof

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	Micro Entity Fee	
☑ One month (37 CFR 1.17(a)(1))	$200	$100	$50	$ 100.00
☐ Two months (37 CFR 1.17(a)(2))	$600	$300	$150	$
☐ Three months (37 CFR 1.17(a)(3))	$1,400	$700	$350	$
☐ Four months (37 CFR 1.17(a)(4))	$2,200	$1,100	$550	$
☐ Five months (37 CFR 1.17(a)(5))	$3,000	$1,500	$750	$

☑ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 503145.

☑ Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71. 37 CFR 3.73(b) statement is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration number 48,951.

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____.

Signature	2015-10-01 (Date)
Heidi M. Berven (Typed or printed name)	269-337-7710 (Telephone Number)

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ * Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

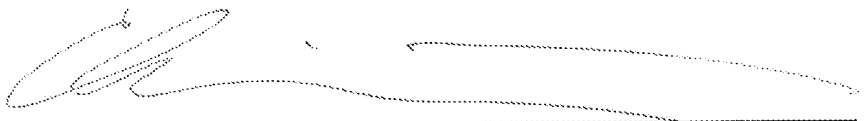
Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8(a)

The undersigned hereby certifies that the following documents are being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4) on this 1st day of October, 2015:

1. Cover Letter to the Commissioner for Patents;
2. Request for Continued Examination under 37 C.F.R. § 1.114;
3. Declaration of Khalid Shah under 37 C.F.R. § 1.131;
4. Request for Continued Examination Transmittal (PTO/SB/30);
5. Information Disclosure Statement (PTO/SB/08A);
6. Non-Patent Literature (1 document);
7. Request to Correct Inventorship under 37 C.F.R. § 1.48;
8. Supplemental Application Data Sheet (PTO/SB/14);
9. Statement of Inventor Khalid Shah;
10. Written Consent of Assignee to Correction of Inventorship;
11. Combined Power of Attorney and Declaration under 37 C.F.R. § 1.63 for inventor Khalid Shah;
12. Petition for Extension of Time (PTO/SB/22); and
13. This Certificate of Transmission under 37 C.F.R. § 1.8(a).



Charles Gregg-Geist (for Heidi M. Berven, Ph.D., Reg. No.: 48,951)

Electronic Patent Application Fee Transmittal

Application Number:	13984559
Filing Date:	20-Mar-2014
Title of Invention:	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
First Named Inventor/Applicant Name:	Jo Ann Wilson
Filer:	Heid Marie Berven/Charles Gregg-Geist
Attorney Docket Number:	224990/10-039C-US/343999

Filed as Small Entity

Filing Fees for U.S. National Stage under 35 USC 371

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
PROCESSING FEE, EXCEPT PROV. APPLS.	2830	1	70	70
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Extension - 1 month with $0 paid	2251	1	100	100
Miscellaneous:				
Request for Continued Examination	2801	1	600	600
Correction of Inventorship on Merits	2819	1	300	300
		Total in USD ($)		**1070**

Electronic Acknowledgement Receipt

EFS ID:	23670134
Application Number:	13984559
International Application Number:	
Confirmation Number:	6725
Title of Invention:	Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
First Named Inventor/Applicant Name:	Jo Ann Wilson
Customer Number:	91684
Filer:	Heid Marie Berven/Charles Gregg-Geist
Filer Authorized By:	Heid Marie Berven
Attorney Docket Number:	224990/10-039C-US/343999
Receipt Date:	01-OCT-2015
Filing Date:	20-MAR-2014
Time Stamp:	18:35:20
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1070
RAM confirmation Number	5178
Deposit Account	503145
Authorized User	BERVEN, HEIDI M.

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		10-039.pdf	7023371 126702caa6c53fe8dbbcbc18e518967cbb5861d4	yes	38

Multipart Description/PDF files in .zip description

Document Description	Start	End
Transmittal Letter	1	2
Miscellaneous Incoming Letter	3	3
Claims	4	6
Applicant Arguments/Remarks Made in an Amendment	7	16
Affidavit-traversing rejectns or objectns rule 132	17	22
Request for Continued Examination (RCE)	23	24
Information Disclosure Statement (IDS) Form (SB08)	25	27
Request under Rule 48 correcting inventorship	28	29
Application Data Sheet	30	33
Miscellaneous Incoming Letter	34	34
Miscellaneous Incoming Letter	35	35
Oath or Declaration filed	36	36
Extension of Time	37	37
Transmittal Letter	38	38

Warnings:

Information:

2	Non Patent Literature	CabozantinibMSDS_Sigma-Aldrich.pdf	120183 34242c08349b5873c43a6f4cd007a5a7a37f2f52	no	7
Warnings:					
Information:					
3	Non Patent Literature	EMA-EMEA-EuropeanMedicinesAgency-MalateSaltDocument-2008.pdf	183250 47a92c8ce2183914acff0e37bc91e9eaa5e6cc7b	no	10
Warnings:					
Information:					
4	Non Patent Literature	US_DHHS_GuidanceForIndustry-StabilityTesting_Nov2003.pdf	280128 b0891b05f0d5103a7b8e1ebee3e57f6157cb1790	no	25
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	36024 82bc98229854532bda39bd8553fc39aaaed57f91	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	7642956		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

HONIGMAN

Heidi M. Berven, Ph.D.

Honigman Miller Schwartz and Cohn LLP
Attorneys and Counselors

(269) 337-7710
Fax: (269) 337-7711
hberven@honigman.com

Via EFS

October 1, 2015

Commissioner for Patents
United States Patent and Trademark Office
P. O. Box 1450
Alexandria, VA 22313

Re: ***Application No.: 13/984,559***
Inventor: Jo Ann Wilson
Filing Date: March 20, 2014
Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
Confirmation No.: 6725
Attorney Docket No.: 224990/10-039C-US/343999

Dear Sir or Madam:

Enclosed for filing please find the following documents:

1. This Cover Letter to the Commissioner for Patents;
2. Request for Continued Examination under 37 C.F.R. § 1.114;
3. Declaration of Khalid Shah under 37 C.F.R. § 1.131;
4. Request for Continued Examination Transmittal (PTO/SB/30);
5. Information Disclosure Statement (PTO/SB/08A);
6. Non-Patent Literature (3 documents);
7. Request to Correct Inventorship under 37 C.F.R. § 1.48;
8. Supplemental Application Data Sheet (PTO/SB/14);
9. Statement of Inventor Khalid Shah;
10. Written Consent of Assignee to Correction of Inventorship;
11. Combined Power of Attorney and Declaration under 37 C.F.R. § 1.63 for inventor Khalid Shah;
12. Petition for Extension of Time (PTO/SB/22); and
13. Certificate of Transmission under 37 C.F.R. § 1.8(a).

It is believed that due for this submission are the $100.00 fee set forth in 37 C.F.R. § 1.17(a)(1) for a one-month extension of time, the $600.00 fee set forth in § 1.17(e)(1) for the first Request for Continued Examination in this application, and the $70.00 processing fee set forth in § 1.17(i) and $300.00 fee set forth in § 1.17(d) for the accompanying Request to Correct

Inventorship. The Applicant authorizes the Office to charge this total of $1,070.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Very truly yours,

HONIGMAN MILLER SCHWARTZ AND COHN LLP

Heidi M. Berven, Ph.D.
Reg. No. 48,951

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO THE FINAL REJECTION DATED JUNE 9, 2015, AND REQUEST FOR CONTINUED EXAMINATION UNDER 37 C.F.R. § 1.114

This Request for Continued Examination under 37 C.F.R. § 1.114 is submitted in response to the Final Rejection dated June 9, 2015. A submission and fee in support of the Applicant's Request is enclosed.

Amendments to the claims are reflected in the listing of claims that begins on page 2.

Remarks begin on page 5.

CLAIM AMENDMENTS

1-22. Cancelled.

23. (Currently amended) A capsule pharmaceutical composition selected from the group consisting of Table [[2A,]] 3, 4, 5, and 6.

~~**Table 2A**~~

~~**Ingredient**~~	~~**% w/w**~~
~~Compound IB (10 % drug load as Compound IA)~~	~~12.67~~
~~MCC~~	~~51.52~~
~~Lactose~~	~~25.76~~
~~Hydroxypropyl cellulose~~	~~3.0~~
~~Croscarmellose Sodium~~	~~6.0~~
~~Colloidal Silicon Dioxide~~	~~0.3~~
~~Magnesium Stearate~~	~~0.75~~
~~**Total**~~	~~**100**~~

Table 3

Ingredient	**mg/unit dose**
Compound IB with 5 ppm or less of 6,7-dimethoxy-quinoline-4-ol (10 % drug load as Compound IA)	25
Silicified Microcrystalline Cellulose	196.75
Croscarmellose sodium	12.5
Sodium starch glycolate	12.5
Fumed Silica	0.75
Stearic acid	2.5
Total Fill Weight	250

Table 4

Ingredient	**mg/unit dose**
Compound IB with 5 ppm or less of 6,7-dimethoxy-quinoline-4-ol (50 % drug load as Compound IA)	100
Silicified Microcrystalline Cellulose	75.40
Croscarmellose sodium	10.00

Sodium Starch Glycolate	10.00
Fumed silica	0.6
Stearic Acid	4.0
Total Fill Weight	200

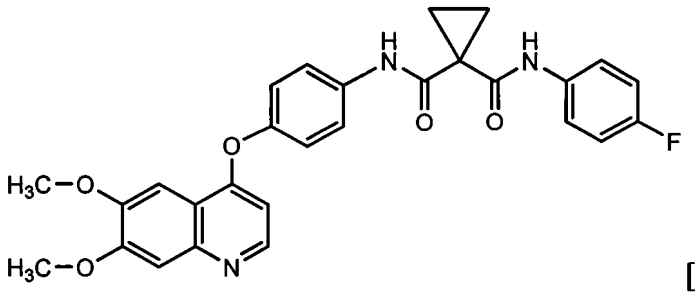
Table 5

	mg/unit dose
Ingredient	**50mg**
Compound IB with 5 ppm or less of 6,7-dimethoxy-quinoline-4-ol (10 % drug load as Compound IA)	63.35
Microcrystalline Cellulose	95.39
Croscarmellose sodium	9.05
Sodium starch glycolate	9.05
Fumed Silica	0.54
Stearic acid	3.62
Total Fill Weight	181.00

Table 6

	mg/unit dose
Ingredient	**60mg**
Compound IB with 5 ppm or less of 6,7-dimethoxy-quinoline-4-ol	73.95
Microcrystalline Cellulose	114.36
Croscarmellose sodium	10.85
Sodium starch glycolate	10.85
Fumed Silica	0.65
Stearic acid	4.34
Total Fill Weight	217.00

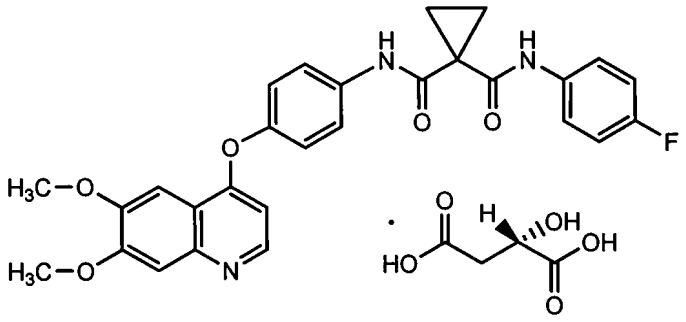
wherein Compound 1A has the structure:



[[;]]

IA;

compound IB has the structure:



IB;

and wherein at from 0 to 6 months at 25 °C and 60 percent relative humidity, the formation of 6,7-dimethoxy-quinoline-4-ol in the capsule pharmaceutical composition ~~formulation~~ is minimized to 50 ppm or less ~~over time~~.

24-29. Cancelled.

30. (Currently amended) The capsule pharmaceutical composition of claim 23, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 25 ppm or less ~~over time~~ from 0 to 6 months at 25 °C and 60 percent relative humidity.

31. (Currently amended) The capsule pharmaceutical composition of claim 23, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 15 ppm or less ~~over time~~ from 0 to 6 months at 25 °C and 60 percent relative humidity.

32. (Currently amended) The capsule pharmaceutical composition of claim 23, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 10 ppm or less ~~over time~~ from 0 to 6 months at 25 °C and 60 percent relative humidity.

33-39. Cancelled.

REMARKS

Claim Status

Claims 1-22, 24-29, and 33-39 are cancelled.

Claim 23 and 30-32 are currently amended for clarity. The amendments are supported by the specification as filed as summarized in the following table.

Claim	Language	Support in Specification
23 30-32	"...Compound IB with 10 ppm or less of 6,7-dimethoxy-quinoline-4-ol..."	Pages 21-22, paragraphs 90-95; page 32, paragraph 150-152
23	"...wherein at from 0 to 6 months at 25 °C and 60 percent relative humidity, the formation of 6,7-dimethoxy-quinoline-4-ol in the capsule pharmaceutical composition is minimized to 50 ppm or less... ."	Pages 34-36, paragraphs 161-163 and Tables 7A, 7B, 8A, and 8B

No new matter has been added to the amended claims.

Thus, claims 23 and 30-32 are currently pending.

The claim amendments are made in the interest of expediting prosecution. The Applicant does not intend to surrender any range of equivalents to which the Applicant would otherwise be entitled in view of the prior art, nor does the Applicant agree with the Examiner's comments or arguments about the art cited in the Office Action. Further, by the present amendment, it does not follow that the amended claims have become so perfect in their description that no one could devise an equivalent. After amendment, as before, limitations in the ability to describe the present invention in language in the patent claims naturally prevent the Applicant from capturing every nuance of the invention or describing with complete precision the range of its novelty or every possible equivalent. *See* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 62 USPQ2d 1705 (2002). By amending the claims, the Applicant does not concede that patent coverage available to them would not extend as far as the original claim. The Applicant reserves the right to file divisional and/or continuation applications to pursue the breadth of the claims as filed. The Applicant respectfully requests the timely allowance of the amended claims.

Claim Rejections under 35 U.S.C. § 103(a)

In the Office Action, the Examiner maintained the rejection of claims 23 and 30-39 under pre-AIA 35 U.S.C. § 103(a) as obvious over US2007/0054928 A1 to Bannen et al. (hereinafter, "Bannen"). The Examiner noted that Bannen teaches that compounds of the prior art are in pure

form and in an appropriate pharmaceutical composition that is of pharmaceutical grade. Citing MPEP 2112.1, the Examiner then concluded that the claimed invention is obvious, because a discovery of a previously unappreciated property of a prior art composition does not render the old composition patently new to the discoverer.

The Applicant respectfully disagrees. To establish a *prima facie* case of obviousness, the Examiner must show that the cited reference teaches or suggest all the features recited in the claim. Assuming *arguendo,* that even if the reference teaches each feature, the Examiner must provide some articulated reasoning with some rational underpinning regarding why a person having ordinary skill in the art would obtain the subject matter claimed by the Applicant from the reference. The Examiner must also show that in view of the cited art at the time of the Applicant's invention, a person having ordinary skill in the art would have had a reasonable expectation of successfully arriving at the claimed subject matter. *See id.* at 1740; *see also* M.P.E.P. § 2143.02 (*citing In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986)).

The Applicant's claims are directed to capsule pharmaceutical compositions of Cometriq™ (cabozantinib). Cometriq™ (Compound IB) is the L-malate salt of cyclopropane-1,1-dicarboxylic acid [4-(6,7-dimethoxy-quinoline-4-yloxy)-phenyl]-amide (4-fluoro-phenyl)-amide (Compound IA). Cometriq™ is approved in the United States for the treatment of medullary thyroid cancer.

Bannen fails to obviate the Applicant's claimed invention because Bannen does not teach or suggest a capsule pharmaceutical composition as claimed by the Applicant that (i) contains Compound IB with 10 ppm or less of 6,7-dimethoxy-quinoline-4-ol and (ii) that minimizes formation of 6,7-dimethoxy-quinoline-4-ol to 50 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity. One of ordinary skill in the art reading Bannen would not envision a pharmaceutical composition characterized by these two elements as claimed by the Applicant. Moreover, there is nothing in Bannen, which teaches pure compounds for use in pharmaceutical compositions, that would lead one of ordinary skill in the art to a capsule pharmaceutical composition as claimed by the Applicant.

Banned is silent as to the preparation of Cometriq™ (Compound IB) from Compound IA. The process is described at page 20, paragraph 87 and page 32, paragraph 150-152 of the above-captioned application, and requires reacting compound IA with L-malic acid. The Applicant discovered that this process can give rise to 6,7-dimethoxy-quinoline-4-ol as a decomposition

product. Any 6,7-dimethoxy-quinoline-4-ol that is formed is carried through to Compound IB. The Material Safety Data Sheet (MSDS) of 6,7-dimethoxy-quinoline-4-ol (attached herewith and cited in the Supplemental Information Disclosure Statement filed with this response) indicates that 6,7-dimethoxy-quinoline-4-ol has acute oral toxicity and is harmful if swallowed. Because 6,7-dimethoxy-quinoline-4-ol is toxic, it is necessary to minimize the amount of 6,7-dimethoxy-quinoline-4-ol in pharmaceutical compositions of Compound IB.

Bannen is also silent as to the development of the capsule pharmaceutical compositions as disclosed and claimed by the Applicant. The Applicant sought to develop a storage-stable capsule pharmaceutical composition of Cometriq™ that minimized formation of the toxic degradant 6,7-dimethoxy-quinoline-4-ol. As provided by the Declaration under 37 C.F.R. § 1.131 of Khalid Shah, Ph.D., which accompanies this response, development of the capsule pharmaceutical composition was made difficult because exposure to water, atmospheric moisture, or even residual moisture in gelatin capsules (which have a moisture content of 12 percent) can cause degradation of Compound IB to form 6,7-dimethoxy-quinoline-4-ol.

Thus, to minimize degradation, no water was used in preparing the capsule pharmaceutical compositions. According to the specification as filed, the pharmaceutical compositions were prepared by combining and blending the components and then placing the blend in a gelatin capsule (Specification as filed, paragraphs 115-116, pages 23-24). The capsule pharmaceutical compositions of Tables 3 and 4 (see claim 1 and pages 7 and 34-36) were prepared according to this method. The capsules were then stored in sealed containers.

The stability of the capsule pharmaceutical compositions of Tables 3 and 4 were evaluated as described at pages 34-36 of the specification as filed, in accordance with FDA recommendations as provided in *Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances* (posted at www.fda.gov/downloads/drugs/guidancecomplianceregulatory information/guidances/ucm073369.pdf *last visited* September 9, 2015) (attached herewith and cited in the Supplemental Information Disclosure Statement filed with this response). The *Guidance* provides recommended stability testing conditions (long-term, intermediate, and accelerated storage conditions) in the Table at page 10, which is reproduced here.

Study	Storage condition	Minimum time period covered by data at submission
Long-term*	25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH	12 months
Intermediate**	30°C ± 2°C/65% RH ± 5% RH	6 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

* It is up to the applicant to decide whether long-term stability sturdies are performed at 25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH.
** If 30°C ± 2°C/65% RH ± 5% RH is the long-term condition, there is no intermediate condition.

In the Applicant's stability studies as described at pages 34-36 of the application, capsules were placed in bottles or blister packs. The capsules were then stored under long-term 25 °C/60 percent relative humidity (RH), intermediate (30 °C/75 percent RH), or accelerated storage conditions (40 °C/75 percent RH). The bottles were monitored for 6,7-dimethoxy-quinoline-4-ol formation from Initial T=0 to 1 month, 3 months, 6, months, and 9 months. The results of the stability studies are given in Tables 7A-B and 8A-B of the '559 application, which are reproduced on the following pages for the Examiner's convenience.

Table 7A: Stability of 25 Mg Capsules (Table 3)

	Conditions	Bottle A1	Bottle A2	Bottle A3	Bottle A4
		PPM of 6,7-dimethoxy-quinoline-4-ol			
Initial T=0	25 °C/60% RH	2	2	3	3
1 Month	25 °C/60% RH	3	4	5	NA
	30 °C/75% RH	4	4	NA	NA
	40 °C/75% RH	9	9	10	NA
3 Months	25 °C/60% RH	5	5	7	NA
	30 °C/75% RH	7	6	NA	NA
	40 °C/75% RH	22	23	24	NA
6 Months	25 °C/60% RH	6	6	7	7 (3M in blister)
	30 °C/75% RH	9	9	NA	NA
	40 °C/75% RH	40	44	43	27 (3M in blister)
9 Months	25 °C/60% RH	7	7	9	8 (6M in blister)
	30 °C/75% RH	13	12	NA	NA
	40 °C/75% RH	NA	NA	68	60 (6M in blister)

M=Months; NA=Not Applicable; RH= Relative Humidity; PPM= Parts per Million. A portion of Bottle A4 was repackaged in a blister pack after being stored in bottles for 3 months.

Table 7B: Stability of 25 Mg Capsules (Table 3)

	Conditions	Bottle B1	Bottle B	Bottle B3	Bottle B4
		PPM of 6,7-dimethoxy-quinoline-4-ol			
Initial T=0	25 °C/60% RH	3	1	2	2
1 Month	25 °C/60% RH	<2	<2	<2	NA
	30 °C/75% RH	<2	<2	NA	NA
	40 °C/75% RH	2	<2	<2	NA
3 Months	25 °C/60% RH	2	<2	<2	NA
	30 °C/75% RH	2	<2	NA	NA
	40 °C/75% RH	3	<2	<2	NA
6 Months	25 °C/60% RH	<2	<2	<2	<2 (3M in blister)
	30 °C/75% RH	2	<2	NA	NA
	40 °C/75% RH	4	<2	3	3 (3M in blister)
9 Months	25 °C/60% RH	<2	<2	<2	<2 (6M in blister)
	30 °C/75% RH	3	<2	NA	NA
	40 °C/75% RH	NA	NA	5	4 (6M in blister)

A portion of Bottle B4 was repackaged in a blister pack after being stored in bottles for 3 months.

Table 8A: Stability of 100 Mg Capsules (Table 4)

	Conditions	Bottle A1	Blister A2	Bottle A3
		PPM of 6,7-dimethoxy-quinoline-4-ol		
Initial T=0	25 °C/60% RH	4	4	6
1 Month	25 °C/60% RH	4	4	6
	30 °C/75% RH	4	NA	6
	40 °C/75% RH	6	6	9
3 Months	25 °C/60% RH	5	5	7
	30 °C/75% RH	6	NA	7
	40 °C/75% RH	10	10	12
6 Months	25 °C/60% RH	5	5	
	30 °C/75% RH	6	NA	
	40 °C/75% RH	11	17	

Table 8B: Stability of 100 Mg Capsules (Table 4)

	Conditions	Bottle B1	Blister B2	Bottle B3
		PPM of 6,7-dimethoxy-quinoline-4-ol		
Initial T=0	25 °C/60% RH	1	1	2
1 Month	25 °C/60% RH	<2	<2	<2
	30 °C/75% RH	<2	<2	2
	40 °C/75% RH	<2	<2	2
3 Months	25 °C/60% RH	<2	<2	<2
	30 °C/75% RH	<2	NA	<2
	40 °C/75% RH	<2	<2	2

	Conditions	Bottle B1	Blister B2	Bottle B3
		PPM of 6,7-dimethoxy-quinoline-4-ol		
6 Months	25 °C/60% RH	<2	<2	
	30 °C/75% RH	<2	NA	
	40 °C/75% RH	2	2	

As provided by Tables 7A-B and 8A-B, the Applicant observed up to 44 ppm of 6,7-dimethoxy-quinoline-4-ol in capsules after six months of storage under accelerated conditions. Based on the accelerated conditions results, one of ordinary skill in the formulation art would have expected equally significant degradation of the long-term conditions samples over time. Surprisingly, according to Tables 7A-B and 8A-B, capsules stored under long-term conditions exhibited very little change from T=0 to T=6 Months or even T=9 Months.

Moreover, the Applicant found that capsules stored under long-term conditions for as long as 4 years gave less degradation than the capsules stored for six months under accelerated conditions, as evidenced from the results of additional stability studies.

Stability of 25mg Capsules

	Conditions	**Bottle A1**	**Bottle A2**	**Bottle A3**	**Blister A4**
		PPM of 6,7-dimethoxy-quinoline-4-ol			
Initial T=0	25°C/60%RH	2	<2	3	3
1 month	25°C/60%RH	3	4	5	N/A
	30°C/75%RH	4	4	N/A	N/A
3 month	25°C/60%RH	5	5	7	N/A
	30°C/75%RH	7	6	N/A	N/A
6 month	25°C/60%RH	6	6	7	7 (3M in blister)
	30°C/75%RH	9	9	N/A	N/A
9 month	25°C/60%RH	7	7	9	8 (6M in blister)
	30°C/75%RH	13	12	N/A	N/A
12 month	25°C/60%RH	9	9	10	10 (9M in blister)
	30°C/75%RH	17	17	N/A	N/A
18 month	25°C/60%RH	11	11	13	12 (15M in blister)
	30°C/75%RH	24	22	N/A	N/A
24 month	25°C/60%RH	14	13	15	16 (21M in blister)
36 month	25°C/60%RH	19	18	20	22 (33M in blister)
48 month	25°C/60%RH	24	25	26	N/A

Stability of 100mg Capsules

	Conditions	Bottle B1	Blister B2	Bottle B3
		PPM of 6,7-dimethoxy-quinoline-4-ol		
Initial T=0	25°C/60%RH	4	4	6
1 month	25°C/60%RH	4	4	6
	30°C/75%RH	4	N/A	6
3 month	25°C/60%RH	5	5	7
	30°C/75%RH	6	N/A	7
6 month	25°C/60%RH	5	5	8
	30°C/75%RH	6	N/A	10
9 month	25°C/60%RH	5	6	8
	30°C/75%RH	7	N/A	10
12 month	25°C/60%RH	6	7	9
	30°C/75%RH	9	N/A	12
18 month	25°C/60%RH	7	8	10
	30°C/75%RH	11	N/A	14
24 month	25°C/60%RH	8	8	11
	30°C/75%RH	12	N/A	16
36 month	25°C/60%RH	10	8	13
	30°C/75%RH	17	N/A	23
48 month	25°C/60%RH	11	10	16

These surprising and unexpected results are not are not disclosed or suggested by Bannen. As a result, the Applicant respectfully requests removal of the rejection and allowance of the claims.

REQUEST FOR CONTINUED EXAMINATION

The Applicant's amendments to the claims, arguments, Declaration under 37 C.F.R. § 1.131, Information Disclosure Statement submitted herewith satisfy the requirement under § 1.114 for a submission accompanying a Request for Continued Examination. The fee set forth in 37 C.F.R. § 1.17(e)(1) is also submitted herewith.

INFORMATION DISCLOSURE STATEMENT

The Applicant notes that the filing of the enclosed Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement qualifies as prior art under 35 U.S.C. §§ 102 or 103, or is considered to be material to patentability as defined in

37 C.F.R § 1.56(b). The Applicant believes that the fee set forth in 37 C.F.R. § 1.17(p) is not required at this time pursuant to § 1.97(b)(4).

EXTENSION OF TIME

The Applicant hereby petitions for a one-month extension of time under 37 C.F.R. § 1.136(a) for responding to the Final Office Action mailed in this application on June 9, 2015. The fee set forth in 37 C.F.R. § 1.17(a)(1) is submitted herewith.

OTHER C-MET INHIBITOR CASES

The Applicant wishes to make the Examiner aware of the Applicant's other applications related to c-Met inhibitors and their use in the treatment of cancer. For the Examiner's convenience, the Applicant is providing a list of the Applicant's applications directed to the treatment of cancer using c-Met inhibitors. The Applicant understands the Examiner has electronic access to these applications and to the Office Actions that have issued in these applications, and has therefore not included copies with this Response. The Applicant will gladly provide the applications and Office Actions to the Examiner, however, upon request.

Application No.	Filing or 371 Date	Patent No.	Examiner	Status
10/573,336	09/18/2006		Koontz, Tammy J	Abandoned
11/571,140	12/21/2006	7,977,345	Moore, Susanna	Issued
11/586,751	10/26/2006		Ward, Paul V.	Pending
11/753,462	05/24/2007	8,178,532	Ward, Paul V.	Issued
11/753,503	05/24/2007	8,476,298	Ward, Paul V.	Issued
11/753,514	05/24/2007	8,067,436	Bernhardt, Emily A.	Issued
12/393,806	02/26/2009	7,579,473	Seaman, D. Margaret M.	Issued
12/911,442	10/25/2010		Ward, Paul, V.	Abandoned
13/087,094	04/14/2011		Chickos, Sarah, J.	Abandoned
13/129,183	05/13/2011		Seaman, D. Margaret M.	Abandoned
13/132,650	06/03/2011		Seaman, D. Margaret M.	Abandoned
13/145,054	10/20/2011	8,877,776	Carter, Kendra D	Issued
13/249,815	09/30/2011	8,497,284	Bernhardt, Emily A.	Issued
13/384,451	07/12/2012	8,673,912	Anderson, Rebecca L.	Issued
13/389,266	07/12/2012		Perreira, Melissa Jean	Abandoned
13/427,093	03/22/2012		Ward, Paul V.	Abandoned
13/438,964	04/04/2012		Brown-Pettigrew, Angela C.	Abandoned
13/634,275	09/12/2012		Anderson, Rebecca L.	Abandoned
13/753,031	01/29/2013		Pagonakis, Anna	Abandoned
13/753,146	01/29/2013		Pagonakis, Anna	Abandoned

Application No.	Filing or 371 Date	Patent No.	Examiner	Status
13/810,537	08/26/2013		Pallay, Michael B.	Pending
13/810,546	08/27/2013		Branson, Daniel L.	Pending
13/876,290	11/05/2013		Stone, Christopher R.	Abandoned
13/876,306	11/08/2013		Lee, Andrew P.	Abandoned
13/876,318	10/25/2013		Karol, Jody Lynn	Pending
13/888,592	05/07/2013		Ward, Paul V.	Abandoned
13/928,977	06/27/2013		Bernhardt, Emily A.	Pending
14/021,614	09/09/2013		Matos Negron, Taina Del Mar	Pending
14/115,236	02/28/2014		Anderson, James D.	Pending
14/166,545	01/28/2014		Not Yet Assigned	Abandoned
14/173,973	02/06/2014		Johannsen, Diana B.	Pending
14/340,871	07/25/2014		Carter, Kendra D.	Pending
14/346,570	03/21/2014		Calvillo, Y. Jeanmarie Z.	Pending
14/353,251	04/21/2014		Murray, Jeffrey H.	Pending
14/356,927	05/08/2014		Baek, Bong-sook	Pending
14/356,938	05/08/2014		Cerioni, Daniel Lee	Pending
14/398,188	10/31/2014		Henley III, Raymond J.	Pending
14/426,580	03/06/2015		Not Yet Assigned	Pending
14/518,733	10/20/2014		Chickos, Sarah J.	Pending
14/668,312	03/25/2015		Not Yet Assigned	Pending
14/699,683	04/29/2015		Not Yet Assigned	Pending
14/776,337	09/14/2015		Not Yet Assigned	Pending
14/843,480	09/02/2015		Not Yet Assigned	Pending
14/847,801	09/08/2015		Not Yet Assigned	Pending

CONCLUSION

It is believed that due for this submission are the $100.00 fee set forth in 37 C.F.R. § 1.17(a)(1) for a one-month extension of time, the $600.00 fee set forth in § 1.17(e)(1) for the first Request for Continued Examination in this application, and the $70.00 processing fee set forth in § 1.17(i) and $300.00 fee set forth in § 1.17(d) for the accompanying Request to Correct Inventorship. The Applicant authorizes the Office to charge this total of $1,070.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Respectfully submitted,

Date: October 1, 2015

Heidi M. Berven, Ph.D.
Reg. No. 48,951
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Ste. 300
Kalamazoo, MI 49007-3800
Direct (269) 337-7710
Fax (269) 337-7711

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF KHALID SHAH UNDER 37 C.F.R. § 1.131

I, Khalid Shah, hereby state the following:

1. I am currently the Vice President, CMC, Pharmaceutical Operations and Supply Chain at Exelixis, Inc. ("Exelixis"). Prior to serving as Vice President, I served in a number of capacities of increasing responsibility within Exelixis starting in July 2009, including:

- Executive Director;
- Senior Director, Formulations Development, Manufacturing, and Clinical Supplies
- Director, Formulations Development

2. Prior to joining Exelixis (January 2002-July 2009), I held positions at Array BioPharma, Abbott Laboatories (Kos Pharma), and Abbott. From April 2006, to September, 2007, I was also an Adjunct Professor at Nova Eastern University College of Pharmacy.

3. I have authored articles in the field of formulation development.

4. I have held a post-doctoral research fellowship at Aston University (United Kingdom) working in the field of drug formulation design and drug delivery.

5. I have a Ph.D. degree in Oral Drug Delivery Systems from Aston University (United Kingdom).

6. I have a B.Sc. degree in Pharmaceutical Chemistry from Coventry University (United Kingdom).

7. I am an inventor of United States Application Serial Number 13/984,559 (the '559 application).

8. The '559 application is directed to capsule pharmaceutical compositions of Cometriq™ (cabozantinib). Cometriq (Compound IB) is the L-malate salt of cyclopropane-1,1-dicarboxylic acid [4-(6,7-dimethoxy-quinoline-4-yloxy)-phenyl]-amide (4-fluoro-phenyl)-amide (Compound IA). Cometriq™ is approved in the United States for the treatment of medullary thyroid cancer.

9. Cometriq™ (Compound IB) from Compound IA. The process is described at page 20, paragraph 87 and page 32, paragraph 150-152 of the '559 application. The process requires reacting compound IA with L-malic acid.

10. The process for making Cometriq™ can give rise to 6,7-dimethoxy-quinoline-4-ol as a decomposition product. Any 6,7-dimethoxy-quinoline-4-ol that is formed during the proves of making Cometriq™ from Compound IA is carried through to Compound IB.

11. I have reviewed the Material Safety Data Sheet (MSDS) of 6,7-dimethoxy-quinoline-4-ol. 6,7-Dimethoxy-quinoline-4-ol has acute oral toxicity and is harmful if swallowed. Because 6,7-dimethoxy-quinoline-4-ol is toxic, it was necessary to minimize the amount of 6,7-dimethoxy-quinoline-4-ol in pharmaceutical compositions of Compound IB.

12. Because of the toxicity of 6,7-dimethoxy-quinoline-4-ol, a storage-stable capsule pharmaceutical composition of Cometriq™ that minimized formation of the toxic degradant 6,7-dimethoxy-quinoline-4-ol was required.

13. The development of a storage-stable capsule pharmaceutical composition of Cometriq™ was made difficult because exposure to water, atmospheric moisture, or even residual moisture in gelatin capsules (which have a moisture content of 12 percent) can cause degradation of Cometriq™ to form 6,7-dimethoxy-quinoline-4-ol.

14. To minimize degradation, no water was used in preparing the capsule pharmaceutical compositions. According to paragraphs 115-116, pages 23-24 of the '559 application, the pharmaceutical compositions were prepared by combining and blending the components and then placing the blend in a gelatin capsule. The capsule pharmaceutical compositions of Tables 3 and 4 (see claim 1 and pages 7 and 34-36) were prepared according to this method. The capsules were then stored in sealed containers.

15. The stability of the capsule pharmaceutical compositions of Tables 3 and 4 were evaluated as described at pages 34-36 of the '559 application, in accordance with FDA recommendations as provided in *Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances* (posted at www.fda.gov/downloads/drugs/guidancecomplianceregulatory

information/guidances/ucm073369.pdf *last visited* September 9, 2015). The *Guidance* provides recommended stability testing conditions (long-term, intermediate, and accelerated storage conditions) in the Table at page 10, which is reproduced here.

Study	Storage condition	Minimum time period covered by data at submission
Long-term*	25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH	12 months
Intermediate**	30°C ± 2°C/65% RH ± 5% RH	6 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

* It is up to the applicant to decide whether long-term stability sturdies are performed at 25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH.
** If 30°C ± 2°C/65% RH ± 5% RH is the long-term condition, there is no intermediate condition.

16. In the stability studies described at pages 34-36 of the '559 application, capsules were placed in bottles or blister packs. The capsules were then stored under long-term 25 °C/60 percent relative humidity (RH), intermediate (30 °C/75 percent RH), or accelerated storage conditions (40 °C/75 percent RH). The bottles were monitored for 6,7-dimethoxy-quinoline-4-ol formation from Initial T=0 to 1 month, 3 months, 6, months, and 9 months. The results of the stability studies are given in Tables 7A-B and 8A-B of the '559 application, which are reproduced below.

Table 7A: Stability of 25 Mg Capsules (Table 3)

	Conditions	Bottle A1	Bottle A2	Bottle A3	Bottle A4
		PPM of 6,7-dimethoxy-quinoline-4-ol			
Initial T=0	25 °C/60% RH	2	2	3	3
1 Month	25 °C/60% RH	3	4	5	NA
	30 °C/75% RH	4	4	NA	NA
	40 °C/75% RH	9	9	10	NA
3 Months	25 °C/60% RH	5	5	7	NA
	30 °C/75% RH	7	6	NA	NA
	40 °C/75% RH	22	23	24	NA
6 Months	25 °C/60% RH	6	6	7	7 (3M in blister)
	30 °C/75% RH	9	9	NA	NA
	40 °C/75% RH	40	44	43	27 (3M in blister)
9 Months	25 °C/60% RH	7	7	9	8 (6M in blister)
	30 °C/75% RH	13	12	NA	NA
	40 °C/75% RH	NA	NA	68	60 (6M in blister)

M=Months; NA=Not Applicable; RH= Relative Humidity; PPM= Parts per Million. A portion of Bottle A4 was repackaged in a blister pack after being stored in bottles for 3 months.

Table 7B: Stability of 25 Mg Capsules (Table 3)

	Conditions	Bottle B1	Bottle B	Bottle B3	Bottle B4
		PPM of 6,7-dimethoxy-quinoline-4-ol			
Initial T=0	25 °C/60% RH	3	1	2	2
1 Month	25 °C/60% RH	<2	<2	<2	NA
	30 °C/75% RH	<2	<2	NA	NA
	40 °C/75% RH	2	<2	<2	NA
3 Months	25 °C/60% RH	2	<2	<2	NA
	30 °C/75% RH	2	<2	NA	NA
	40 °C/75% RH	3	<2	<2	NA
6 Months	25 °C/60% RH	<2	<2	<2	<2 (3M in blister)
	30 °C/75% RH	2	<2	NA	NA
	40 °C/75% RH	4	<2	3	3 (3M in blister)
9 Months	25 °C/60% RH	<2	<2	<2	<2 (6M in blister)
	30 °C/75% RH	3	<2	NA	NA
	40 °C/75% RH	NA	NA	5	4 (6M in blister)

A portion of Bottle B4 was repackaged in a blister pack after being stored in bottles for 3 months.

Table 8A: Stability of 100 Mg Capsules (Table 4)

	Conditions	Bottle A1	Blister A2	Bottle A3
		PPM of 6,7-dimethoxy-quinoline-4-ol		
Initial T=0	25 °C/60% RH	4	4	6
1 Month	25 °C/60% RH	4	4	6
	30 °C/75% RH	4	NA	6
	40 °C/75% RH	6	6	9
3 Months	25 °C/60% RH	5	5	7
	30 °C/75% RH	6	NA	7
	40 °C/75% RH	10	10	12
6 Months	25 °C/60% RH	5	5	
	30 °C/75% RH	6	NA	
	40 °C/75% RH	11	17	

Table 8B: Stability of 100 Mg Capsules (Table 4)

	Conditions	Bottle B1	Blister B2	Bottle B3
		PPM of 6,7-dimethoxy-quinoline-4-ol		
Initial T=0	25 °C/60% RH	1	1	2
1 Month	25 °C/60% RH	<2	<2	<2
	30 °C/75% RH	<2	<2	2
	40 °C/75% RH	<2	<2	2
3 Months	25 °C/60% RH	<2	<2	<2
	30 °C/75% RH	<2	NA	<2
	40 °C/75% RH	<2	<2	2

	Conditions	Bottle B1	Blister B2	Bottle B3
		PPM of 6,7-dimethoxy-quinoline-4-ol		
6 Months	25 °C/60% RH	<2	<2	
	30 °C/75% RH	<2	NA	
	40 °C/75% RH	2	2	

17. Tables 7A-B and 8A-B, show that up to 44 ppm of 6,7-dimethoxy-quinoline-4-ol in capsules after six months of storage under accelerated conditions.

18. Based on the accelerated conditions results, a trained formulation scientist would have expected significant degradation of the long-term conditions samples over time.

19. Surprisingly, according to Tables 7A-B and 8A-B,capsules stored under long-term conditions exhibited very little change from T=0 to T= 6 Months or even T= 9 Months.

20. Capsules stored under long-term conditions for as long as 4 years gave less degradation than the capsules stored for six months under accelerated conditions, as evidenced by the additional stability studies summarized in the following tables.

Stability of 25mg Capsules

	Conditions	**Bottle A1**	**Bottle A2**	**Bottle A3**	**Blister A4**
		PPM of 6,7-dimethoxy-quinoline-4-ol			
Initial T=0	25°C/60%RH	2	<2	3	3
1 month	25°C/60%RH	3	4	5	N/A
	30°C/75%RH	4	4	N/A	N/A
3 month	25°C/60%RH	5	5	7	N/A
	30°C/75%RH	7	6	N/A	N/A
6 month	25°C/60%RH	6	6	7	7 (3M in blister)
	30°C/75%RH	9	9	N/A	N/A
9 month	25°C/60%RH	7	7	9	8 (6M in blister)
	30°C/75%RH	13	12	N/A	N/A
12 month	25°C/60%RH	9	9	10	10 (9M in blister)
	30°C/75%RH	17	17	N/A	N/A
18 month	25°C/60%RH	11	11	13	12 (15M in blister)
	30°C/75%RH	24	22	N/A	N/A
24 month	25°C/60%RH	14	13	15	16 (21M in blister)
36 month	25°C/60%RH	19	18	20	22 (33M in blister)
48 month	25°C/60%RH	24	25	26	N/A

Stability of 100mg Capsules

	Conditions	Bottle B1	Blister B2	Bottle B3
		PPM of 6,7-dimethoxy-quinoline-4-ol		
Initial T=0	25°C/60%RH	4	4	6
1 month	25°C/60%RH	4	4	6
	30°C/75%RH	4	N/A	6
3 month	25°C/60%RH	5	5	7
	30°C/75%RH	6	N/A	7
6 month	25°C/60%RH	5	5	8
	30°C/75%RH	6	N/A	10
9 month	25°C/60%RH	5	6	8
	30°C/75%RH	7	N/A	10
12 month	25°C/60%RH	6	7	9
	30°C/75%RH	9	N/A	12
18 month	25°C/60%RH	7	8	10
	30°C/75%RH	11	N/A	14
24 month	25°C/60%RH	8	8	11
	30°C/75%RH	12	N/A	16
36 month	25°C/60%RH	10	8	13
	30°C/75%RH	17	N/A	23
48 month	25°C/60%RH	11	10	16

21. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Khalid Shah

11 SEP 2015

Date

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

CPC							
Symbol						**Type**	**Version**
C07D		215	/	233		F	2013-01-01
A61K		31	/	47		I	2013-01-01
			/				
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CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	12	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	05/23/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION												
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED							
		A	6	1	K	31 / 47 (2006.01.01)								
CROSS REFERENCE(S)		C	0	7	D	215 / 233 (2006.01.01)								
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)													

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	12	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	05/23/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	40														
2	41														
3	42														
4	43														
5	44														
6	45														
7	46														
8	47														
9	48														
10	49														
11	50														
12	51														

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	12	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	05/23/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Doc code: RCEX
Doc description: Request for Continued Examination (RCE)

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	13/984,559	Filing Date	2014-03-20	Docket Number (if applicable)	224990/10-039C-US/343999	Art Unit	1625
First Named Inventor	Jo Ann Wilson			Examiner Name	Timothy R. Rozof		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☒ Enclosed

- ☒ Amendment/Reply
- ☐ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____ (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 503145

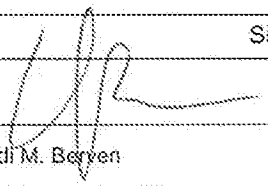
SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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Signature of Registered U.S. Patent Practitioner			
Signature		Date (YYYY-MM-DD)	2017-05-18
Name	Heidi M. Berven	Registration Number	48951

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

HONIGMAN

Honigman Miller Schwartz and Cohn LLP
Attorneys and Counselors

Heidi M. Berven

(269) 337-7710
Fax: (269) 337-7711
hberven@honigman.com

Via EFS

May 18, 2017

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313

Re: ***Application No.: 13/984,559***
Inventors: Jo Ann Wilson, et al.
Filing Date: March 20, 2014
Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
Confirmation No.: 6725
Attorney Docket No.: 224990/10-039C-US/343999

Dear Sir or Madam:

Enclosed for filing please find the following documents:

1. This Cover Letter to the Commissioner for Patents;
2. Petition under 37 C.F.R. § 1.313(c) to Withdraw Application from Issue after Payment of the Issue Fee;
3. Request for Continued Examination under 37 C.F.R. § 1.114;
4. Processing Fee Transmittal Form (PTO/SB/17p);
5. Request for Continued Examination Transmittal (PTO/SB/30); and
6. Certificate of Transmission under 37 C.F.R. § 1.8(a).

It is believed that required for this submission are the $70.00 petition fee set forth in 37 C.F.R. § 1.17(h) for a petition to withdraw from issue under § 1.313, and the $850.00 fee set forth in § 1.17(e)(2) for a small entity filing a second or subsequent Request for Continued Examination under § 1.114. The Applicant authorizes the Office to charge this total of $920.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Very truly yours,

HONIGMAN MILLER SCHWARTZ AND COHN LLP

Heidi M. Berven
Reg. No. 48,951

HMB/ayp
Enclosures

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors:	Jo Ann Wilson, et al.	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. § 1.313(C) TO WITHDRAW APPLICATION FROM ISSUE AFTER PAYMENT OF THE ISSUE FEE

Dear Sir or Madam:

The Applicant hereby petitions under 37 C.F.R. § 1.313(c) to withdraw this application from issue after payment of the issue fee on April 25, 2017.

In accordance with 37 C.F.R. § 1.313(c)(2), a Request for Continued Examination under § 1.114 is submitted herewith. The petition fee set forth in 37 C.F.R. § 1.17(h) is also submitted herewith, in accordance with § 1.313(a).

It is believed that required for this submission are the $70.00 petition fee set forth in 37 C.F.R. § 1.17(h) for a petition to withdraw from issue under § 1.313, and the $850.00 fee set forth in § 1.17(e)(2) for a small entity filing a second or subsequent Request for Continued Examination under § 1.114. The Applicant authorizes the Office to charge this total of $920.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Respectfully submitted,

/Heidi M. Berven/

Date: May 18, 2017

Heidi M. Berven
Reg. No. 48,951
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Ste. 300
Kalamazoo, MI 49007-3800
Direct (269) 337-7710
Fax (269) 337-7711

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors:	Jo Ann Wilson, et al.	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CONTINUED EXAMINATION UNDER 37 C.F.R. § 1.114 ACCOMPANYING PETITION TO WITHDRAW FROM ISSUE UNDER § 1.313(C)

This Request for Continued Examination under 37 C.F.R. § 1.114 is submitted in support of the petition to withdraw from issue under § 1.313(c)(2) filed concurrently. A submission and fee in support of the Request are submitted herewith.

Amendments to the claims are reflected in the listing of claims that begins on page 2.

Remarks begin on page 5.

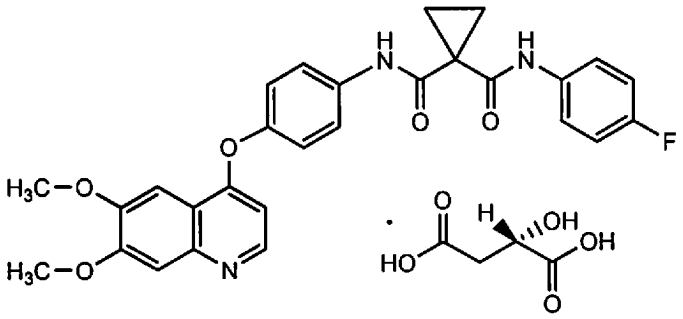
CLAIM AMENDMENTS

1-39. Cancelled.

40. (Currently amended) A capsule pharmaceutical composition:

Ingredient	**mg/unit dose / total fill weight X 100**	~~**mg/unit dose**~~
Compound IB with 50 ppm or less of 6,7-dimethoxy-quinoline-4-ol (10 percent drug load formulation)	10	~~25~~
Silicified Microcrystalline Cellulose	78.7	~~196.75~~
Croscarmellose sodium	5	~~12.5~~
Sodium starch glycolate	5	~~12.5~~
Fumed Silica	0.3	~~0.75~~
Stearic acid	1	~~2.5~~
Total ~~fill weight~~	100	~~250~~

wherein compound IB has the structure:



IB

41. (Currently amended) The capsule pharmaceutical composition of claim 40, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical ~~formulation~~ composition is minimized to 25 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

42. (Currently amended) The capsule pharmaceutical composition of claim 40, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical ~~formulation~~ composition is minimized to 15 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

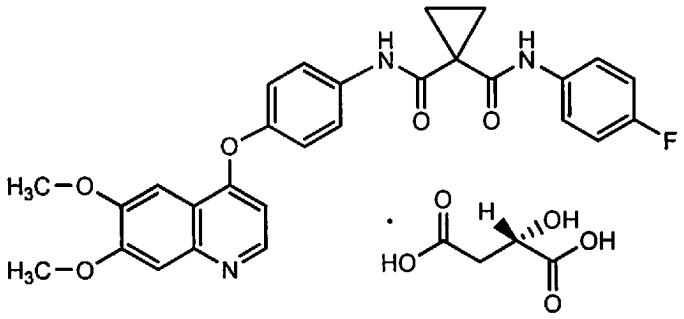
43. (Currently amended) The capsule pharmaceutical composition of claim 40, wherein the

formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical ~~formulation~~ composition is minimized to 10 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

44. (Currently amended) A capsule pharmaceutical composition:

Ingredient	$\frac{\textbf{mg/unit dose}}{\textbf{total fill weight}}$ **X 100**	~~**mg/unit dose**~~
Compound IB with 50 ppm or less of 6,7-dimethoxy-quinoline-4-ol (50 percent drug load formulation)	50	~~100~~
Silicified Microcrystalline Cellulose	37.7	~~75.40~~
Croscarmellose sodium	5	~~10.00~~
Sodium starch glycolate	5	~~10.00~~
Fumed Silica	0.3	~~0.6~~
Stearic acid	2	~~4.0~~
Total ~~fill weight~~	100	~~200~~

wherein compound IB has the structure:



IB ~~; and wherein the amount of carriers and excipients used in the capsule pharmaceutical composition can be varied proportionally according to the amount of Compound IB used~~.

45. (Currently amended) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical ~~formulation~~ composition is minimized to 25 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

46. (Currently amended) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical ~~formulation~~ composition is

minimized to 15 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

47. (Currently amended) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical ~~formulation~~ composition is minimized to 10 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

48. (New) The capsule pharmaceutical composition of claim 40 containing 25 mg of Compound IB.

49. (New) The capsule pharmaceutical composition of claim 48 containing:

Ingredient	mg/unit dose
Silicified Microcrystalline Cellulose	196.75
Croscarmellose sodium	12.5
Sodium starch glycolate	12.5
Fumed Silica	0.75
Stearic acid	2.5

.

50. (New) The capsule pharmaceutical composition of claim 44 containing 100 mg of Compound IB.

51. (New) The capsule pharmaceutical composition of claim 50 containing:

Ingredient	mg/unit dose
Silicified Microcrystalline Cellulose	75.40
Croscarmellose sodium	10.00
Sodium starch glycolate	10.00
Fumed Silica	0.6
Stearic acid	4.0

.

REMARKS

Claim Status

Claims 1-39 are cancelled.

Claims 40-47 are currently amended. The amendments are supported by the application as originally filed. No new matter is added through the entry of the amendments.

Claims 48-51 are new. The new claims are supported by the application as originally filed. No new matter is added through the entry of the new claims.

Thus, claims 40-51 are currently pending.

REQUEST FOR CONTINUED EXAMINATION

It is believed that the claim amendments submitted herewith satisfy the requirement under 37 C.F.R. § 1.114 for a submission accompanying a Request for Continued Examination. The fee set forth in 37 C.F.R. § 1.17(e)(2) is also submitted herewith.

OTHER C-MET INHIBITOR CASES

The Applicant wishes to make the Examiner aware of the Applicant's other applications related to c-Met inhibitors and their use in the treatment of cancer. For the Examiner's convenience, the Applicant is providing a list of the Applicant's applications directed to the treatment of cancer using c-Met inhibitors. The Applicant understands the Examiner has electronic access to these applications and to the Office Actions that have issued in these applications, and has therefore not included copies with this Response. The Applicant will gladly provide the applications and Office Actions to the Examiner, however, upon request.

Application Number	Filing or 371 Date	Patent Number	Examiner	Status
10/573,336	09/18/2006		Koontz, Tammy J.	Abandoned
11/571,140	12/21/2006	7977345	Moore, Susanna	Issued
11/586,751	10/26/2006	9174947	Ward, Paul V.	Issued
11/753,462	05/24/2007	8178532	Ward, Paul V.	Issued
11/753,503	05/24/2007	8476298	Ward, Paul V.	Issued
11/753,514	05/24/2007	8067436	Bernhardt, Emily A.	Issued
12/393,806	02/26/2009	7579473	Seaman, D. Margaret M.	Issued
12/911,442	10/25/2010		Ward, Paul, V.	Abandoned
13/087,094	04/14/2011		Chickos, Sarah, J.	Abandoned
13/129,183	05/13/2011		Seaman, D. Margaret M.	Abandoned
13/132,650	06/03/2011		Seaman, D. Margaret M.	Abandoned
13/145,054	10/20/2011	8877776	Carter, Kendra D	Issued

Application Number	Filing or 371 Date	Patent Number	Examiner	Status
13/249,815	09/30/2011	8497284	Bernhardt, Emily A.	Issued
13/384,451	07/12/2012	8673912	Anderson, Rebecca L.	Issued
13/389,266	07/12/2012		Perreira, Melissa Jean	Abandoned
13/427,093	03/22/2012		Ward, Paul V.	Abandoned
13/438,964	04/04/2012		Brown-Pettigrew, Angela C.	Abandoned
13/634,275	09/12/2012		Anderson, Rebecca L.	Abandoned
13/753,031	01/29/2013		Pagonakis, Anna	Abandoned
13/753,146	01/29/2013		Pagonakis, Anna	Abandoned
13/810,537	08/26/2013		Pallay, Michael B.	Pending
13/810,546	08/27/2013		Branson, Daniel L.	Abandoned
13/876,290	11/05/2013		Stone, Christopher R.	Abandoned
13/876,306	11/08/2013		Lee, Andrew P.	Abandoned
13/876,318	10/25/2013		Karol, Jody Lynn	Abandoned
13/888,592	05/07/2013		Ward, Paul V.	Abandoned
13/928,977	06/27/2013		Bernhardt, Emily A.	Abandoned
14/021,614	09/09/2013		Matos Negron, Taina Del Mar	Pending
14/115,236	02/28/2014		Anderson, James D.	Pending
14/166,545	01/28/2014		Not Yet Assigned	Abandoned
14/173,973	02/06/2014		Johannsen, Diana B.	Abandoned
14/340,871	07/25/2014		Carter, Kendra D.	Pending
14/346,570	03/21/2014		Calvillo, Y. Jeanmarie Z.	Pending
14/353,251	04/21/2014	9365516	Murray, Jeffrey H.	Issued
14/356,927	05/08/2014		Baek, Bong-sook	Pending
14/356,938	05/08/2014		Cerioni, Daniel Lee	Abandoned
14/398,188	10/31/2014		Henley III, Raymond J.	Pending
14/426,580	03/06/2015		Jean-Louis, Samira J.M.	Pending
14/518,733	10/20/2014		Chickos, Sarah J.	Pending
14/668,312	03/25/2015		Brown-Pettigrew, Angela C.	Abandoned
14/699,683	04/29/2015		Perreira, Melissa Jean	Pending
14/776,337	09/14/2015		Reese, Heidi L.	Pending
14/782,493	10/05/2015		Grazier, Nyeemah A.	Pending
14/782,537	10/05/2015		Alley, Genevieve S.	Pending
14/843,480	09/02/2015		Stone, Christopher R.	Pending
14/847,801	09/08/2015		Ward, Paul V.	Pending
14/933,801	11/05/2015		Brown-Pettigrew, Angela C.	Pending
15/066,872	03/10/2016		Bernhardt, Emily A.	Pending
15/118,738	08/12/2016		Not Yet Assigned	Pending
15/126,767	09/16/2016		Not Yet Assigned	Pending
15/133,708	04/20/2016		Murray, Jeffrey H.	Pending
15/305,854	10/21/2016		Not Yet Assigned	Pending
15/348,716	11/10/2016		Not Yet Assigned	Pending
15/500,312	01/30/2017		Not Yet Assigned	Pending

Application Number	Filing or 371 Date	Patent Number	Examiner	Status
15/501,582	02/03/2017		Not Yet Assigned	Pending
15/426,804	02/07/2017		Not Yet Assigned	Pending

CONCLUSION

It is believed that due for this submission are the $850.00 fee set forth in 37 C.F.R. § 1.17(e)(2) for a small entity filing a second or subsequent Request for Continued Examination under § 1.114, and the $70.00 petition fee set forth in § 1.17(h) for a petition to withdraw from issue under § 1.313. The Applicant authorizes the Office to charge this total of $920.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Respectfully submitted,

Date: May 18, 2017

Heidi M. Berven
Reg. No. 48,951
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Ste. 300
Kalamazoo, MI 49007-3800
Direct (269) 337-7710
Fax (269) 337-7711

PTO/SB/17p (03-13)
Approved for use through 07/31/2014. OMB 0651-0059
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PROCESSING FEE Under 37 CFR 1.17(f), (g) & (h) TRANSMITTAL

(Fees are subject to annual revision)

[Page 1 of 2]

Send completed form to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Application Number	13/984,559
Filing Date	2014-03-20
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	Timothy R. Rozof
Practitioner Docket No.	224990/10-039C-US/343999

Enclosed is a petition filed under 37 CFR 1.313 **that requires a processing fee (37 CFR 1.17(f), (g), or (h)).**

Payment of $ 70.00 **is enclosed.**

This form should be included with the above-mentioned petition and faxed or mailed to the Office using the appropriate Mail Stop (*e.g.*, Mail Stop Petition), if applicable. *For transmittal of processing fees under 37 CFR 1.17(i), see form PTO/SB/17i.*

☑ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

Payment of Fees

☑ The Commissioner is hereby authorized to charge the following fees to Deposit Account No. 503145 :

☑ petition fee under 37 CFR 1.17(f), (g) or (h) ☑ any deficiency of fees and credit of any overpayments

☐ Check in the amount of $ _____ is enclosed. ☑ Payment via EFS-Web.

☐ Payment by credit card (Form PTO-2038 or equivalent is enclosed). Do not provide credit card information on this form.

Processing Fees Under 37 CFR 1.17(f):

Undiscounted Fee $400 (Fee Code 1462) **Small Entity Fee $200 (Fee Code 2462)** **Micro Entity Fee $100 (Fee Code 3462)**

For papers filed under:
§ 1.36(a) - for revocation of a power of attorney by fewer than all of the applicants.
§ 1.53(e) - to accord a filing date.
§ 1.57(a) - to accord a filing date.
§ 1.182 - for decision on a question not specifically provided for.
§ 1.183 - to suspend the rules.
§ 1.378(e) - for reconsideration of decision on petition refusing to accept delayed payment of maintenance fee in an expired patent.
§ 1.741(b) - to accord a filing date to an application under § 1.740 for extension of a patent term.

Processing Fees Under 37 CFR 1.17(g):

Undiscounted Fee $200 (Fee Code 1463) **Small Entity Fee $100 (Fee Code 2463)** **Micro Entity Fee $50 (Fee Code 3463)**

For papers filed under:
§ 1.12 - for access to an assignment record.
§ 1.14 - for access to an application.
§ 1.47 - for filing by other than all the inventors or a person not the inventor.
§ 1.59 - for expungement of information.
§ 1.103(a) - to suspend action in an application.
§ 1.136(b) - for review of a request for extension of time when the provisions of § 1.136(a) are not available.
§ 1.295 - for review of refusal to publish a statutory invention registration.
§ 1.296 - to withdraw a request for publication of a statutory invention registration filed on or after the date the notice of intent to publish issued.
§ 1.377 - for review of decision refusing to accept and record payment of a maintenance fee filed prior to expiration of a patent.
§ 1.550(c) - for patent owner requests for extension of time in *ex parte* reexamination proceedings.
§ 1.956 - for patent owner requests for extension of time in *inter partes* reexamination proceedings.
§ 5.12 - for expedited handling of a foreign filing license.
§ 5.15 - for changing the scope of a license.
§ 5.25 - for retroactive license.

This collection of information is required by 37 CFR 1.17. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 5 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/SB/17p (03-13)
Approved for use through 07/31/2014. OMB 0651-0059
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PROCESSING FEE
Under 37 CFR 1.17(f), (g) & (h)
TRANSMITTAL

Processing Fees Under 37 CFR 1.17(h):

Undiscounted Fee $140 (Fee Code 1464) **Small Entity Fee $70 (Fee Code 2464)** **Micro Entity Fee $35 (Fee Code 3464)**

For papers filed under:

§ 1.19(g) - to request documents in a form other than provided in this part.
§ 1.84 – for accepting color drawings or photographs.
§ 1.91 – for entry of a model or exhibit.
§ 1.102(d) – to make an application special.
§ 1.138(c) - to expressly abandon an application to avoid publication.
§ 1.313 – to withdraw an application from issue.
§ 1.314 - to defer issuance of a patent.

SUBMITTED BY			
Signature		Registration No. (Attorney/Agent) 48,951	Telephone 269-337-7710
Name (Print/Type)	Heidi M. Berven, Ph.D.		Date 2017-05-18

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors:	Jo Ann Wilson, et al.	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8(a)

The undersigned hereby certifies that the following documents are being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4) on this 18th day of May, 2017:

1. Cover Letter to the Commissioner for Patents;
2. Petition under 37 C.F.R. § 1.313(c) to Withdraw Application from Issue after Payment of the Issue Fee;
3. Request for Continued Examination under 37 C.F.R. § 1.114;
4. Processing Fee Transmittal Form (PTO/SB/17p);
5. Request for Continued Examination Transmittal (PTO/SB/30); and
6. This Certificate of Transmission under 37 C.F.R. § 1.8(a).

Amy L. Peters (for Heidi M. Berven, Reg. No.: 48,951)

Electronic Patent Application Fee Transmittal

Application Number:	13984559
Filing Date:	20-Mar-2014
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Filer:	Heid Marie Berven/Amy Peters
Attorney Docket Number:	224990/10-039C-US/343999

Filed as Small Entity

Filing Fees for U.S. National Stage under 35 USC 371

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
PETITION FEE-37CFR 1.17(H) (GROUP II)	2464	1	70	70
RCE- 2ND AND SUBSEQUENT REQUEST	2820	1	850	850
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**920**

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Decision Date : May 18, 2017

In re Application of :

Jo Ann Wilson

DECISION ON PETITION
UNDER CFR 1.313(c)(2)

Application No : 13984559

Filed : 20-Mar-2014

Attorney Docket No : 224990/10-039C-US/343999

This is an electronic decision on the petition under 37 CFR 1.313(c)(2), filed May 18, 2017 , to withdraw the above-identified application from issue after payment of the issue fee.

The petition is **GRANTED.**

The above-identified application is withdrawn from issue for consideration of a submission under 37 CFR 1.114 (request for continued examination). See 37 CFR 1.313(c)(2).

Petitioner is advised that the issue fee paid in this application cannot be refunded. If, however, this application is again allowed, petitioner may request that it be applied towards the issue fee required by the new Notice of Allowance.

Telephone inquiries concerning this decision should be directed to the Patent Electronic Business Center (EBC) at 866-217-9197.

This application file is being referred to Technology Center AU 1625 for processing of the request for continuing examination under 37 CFR 1.114 .

Office of Petitions

Electronic Acknowledgement Receipt

EFS ID:	29251963
Application Number:	13984559
International Application Number:	
Confirmation Number:	6725
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Customer Number:	91684
Filer:	Heid Marie Berven/Amy Peters
Filer Authorized By:	Heid Marie Berven
Attorney Docket Number:	224990/10-039C-US/343999
Receipt Date:	18-MAY-2017
Filing Date:	20-MAR-2014
Time Stamp:	17:27:23
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$920
RAM confirmation Number	051917INTEFSW00003893503145
Deposit Account	
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Petition automatically granted by EFS	petition-request.pdf	31701 c2d21b00f8c8ba0aba4db4aac3a16b75999be42c	no	2
Warnings:					
Information:					
2	Request for Continued Examination (RCE)	RCE.pdf	241462 2fba665ca791dbfad1cb72e4ab8e8585e24bb4b0	no	2
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
3		2017_05_18_16_41_51.pdf	1092777 9340ec5e927ea3c4a8b39672edcb3d122632a82c	yes	14

Multipart Description/PDF files in .zip description

Document Description	Start	End
Transmittal Letter	1	2
Transmittal Letter	3	4
Amendment Submitted/Entered with Filing of CPA/RCE	5	5
Claims	6	8
Applicant Arguments/Remarks Made in an Amendment	9	11
Transmittal Letter	12	13
Transmittal Letter	14	14

Warnings:

Information:

4	Fee Worksheet (SB06)	fee-info.pdf	32226 9e4dfe6b82092d21d3344d03bfa04ea77b9d1a7e	no	2

Warnings:	
Information:	
Total Files Size (in bytes):	1398166

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: PET.AUTO Document Description: Petition automatically granted by EFS-Web	PTO/SB/140 U.S. Patent and Trademark Office Department of Commerce

Electronic Petition Request	**PETITION TO WITHDRAW AN APPLICATION FROM ISSUE AFTER PAYMENT OF THE ISSUE FEE UNDER 37 CFR 1.313(c)**
Application Number	13984559
Filing Date	20-Mar-2014
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	TIMOTHY ROZOF
Attorney Docket Number	224990/10-039C-US/343999
Title	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

An application may be withdrawn from issue for further action upon petition by the applicant. To request that the Office withdraw an application from issue, applicant must file a petition under this section including the fee set forth in § 1.17(h) and a showing of good and sufficient reasons why withdrawal of the application from issue is necessary.

APPLICANT HEREBY PETITIONS TO WITHDRAW THIS APPLICATION FROM ISSUE UNDER 37 CFR 1.313(c).

A grantable petition requires the following items:
(1) Petition fee; and
(2) One of the following reasons:
(a) Unpatentability of one or more claims, which must be accompanied by an unequivocal statement that one or more claims are unpatentable, an amendment to such claim or claims, and an explanation as to how the amendment causes such claim or claims to be patentable;
(b) Consideration of a request for continued examination in compliance with § 1.114 (for a utility or plant application only); or
(c) Express abandonment of the application. Such express abandonment may be in favor of a continuing application, but not a CPA under 37 CFR 1.53(d).

Petition Fee

◉	Small Entity
○	Micro Entity
○	Regular Undiscounted

Reason for withdrawal from issue

◯ One or more claims are unpatentable ◉ Consideration of a request for continued examination (RCE) (List of Required Documents and Fees) ◯ Applicant hereby expressly abandons the instant application (any attorney/agent signing for this reason must have power of attorney pursuant to 37 CFR 1.32(b)).
RCE request,submission, and fee. ☐ I certify, in accordance with 37 CFR 1.4(d)(4) that : The RCE request ,submission, and fee have already been filed in the above-identified application on ☒ Are attached.
THIS PORTION MUST BE COMPLETED BY THE SIGNATORY OR SIGNATORIES I certify, in accordance with 37 CFR 1.4(d)(4) that I am: ◉ An attorney or agent registered to practice before the Patent and Trademark Office who has been given power of attorney in this application. ◯ An attorney or agent registered to practice before the Patent and Trademark Office, acting in a representative capacity. ◯ A sole inventor ◯ A joint inventor; I certify that I am authorized to sign this submission on behalf of all of the inventors as evidenced by the power of attorney in the application ◯ A joint inventor; all of whom are signing this e-petition

Signature	/Heidi M. Berven/
Name	Heidi M. Berven
Registration Number	48951

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/984,559	Filing Date 03/20/2014	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	05/18/2017	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 12	Minus	** 34	= 0	X $40 =	0
	Independent (37 CFR 1.16(h))	* 2	Minus	***15	= 0	X $210 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

SLIE
APRIL WALKER

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	06/06/2017	9669017	224990/10-039C-US/343999	6725

91684 7590 05/17/2017

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Jo Ann Wilson, San Francisco, CA;
Khalid Shah, South San Francisco, CA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 01/25/2017
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$480	$480	04/25/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Honigman Miller Schwartz & Cohn LLP
2 Heidi M. Berven, Ph.D.
3 Jonathan P. O'Brien, Ph.D.

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Exelixis, Inc.

(B) RESIDENCE: (CITY and STATE OR COUNTRY): South San Francisco, CA

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
☒ Issue Fee (Please apply issue fee paid in this application 11/10/2016)
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☒ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 503145 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
☐ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
☒ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
☐ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Meghan M. Klaric/ Date April 25, 2017
Typed or printed name Meghan M. Klaric Registration No. 71,226

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson, et al.	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8(a)

The undersigned hereby certifies that the following documents are being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4) on this 25th day of April, 2017:

1. Cover Letter to the Commissioner for Patents;
2. Part B Fee(s) Transmittal (PTOL-85); and
3. This Certificate of Transmission under 37 C.F.R. § 1.8(a).

/Amy L. Peters/

Amy L. Peters (for Meghan M. Klaric, Reg. No.: 71,226)

Electronic Acknowledgement Receipt

EFS ID:	29024070
Application Number:	13984559
International Application Number:	
Confirmation Number:	6725
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Customer Number:	91684
Filer:	Meghan Mary Klaric/Amy Peters
Filer Authorized By:	Meghan Mary Klaric
Attorney Docket Number:	224990/10-039C-US/343999
Receipt Date:	25-APR-2017
Filing Date:	20-MAR-2014
Time Stamp:	16:10:57
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		2017_04_25_15_57_24.pdf	202604 5b801d7cb157d4c0b6765601988039f872e2ff64	yes	4

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Miscellaneous Incoming Letter	1	2
	Issue Fee Payment (PTO-85B)	3	3
	Transmittal Letter	4	4
Warnings:			
Information:			
	Total Files Size (in bytes):	202604	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

HONIGMAN

Honigman Miller Schwartz and Cohn LLP
Attorneys and Counselors

Meghan M. Klaric

(734) 418-4294
Fax: (734) 418-4295
mklaric@honigman.com

Via EFS

April 25, 2017

Commissioner for Patents
United States Patent and Trademark Office
P. O. Box 1450
Alexandria, VA 22313

Re: ***Application No.: 13/984,559***
Inventors: Jo Ann Wilson, et al.
Filing Date: March 20, 2014
Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
Confirmation No.: 6725
Attorney Docket No.: 224990/10-039C-US/343999

Dear Sir or Madam:

Enclosed for filing please find the following documents:

1. This Cover Letter to the Commissioner for Patents;
2. Part B Fee(s) Transmittal (PTOL-85); and
3. Certificate of Transmission under 37 C.F.R. § 1.8(a).

On November 10, 2016, the Applicant paid the Issue Fee for a small entity in the amount of $480.00 under Fee Code 2501 and charged to Deposit Account No. 503145, referencing Attorney Docket No. 224990/10-039C-US/343999. On November 29, 2016, the Applicant filed a second Request for Continued Examination under 37 C.F.R. § 1.114 and a Petition to Withdraw an Application from Issue after Payment of the Issue Fee under 37 C.F.R. § 1.313(c). A further Notice of Allowance and Fee(s) Due issued January 25, 2017, to which this submission is in response.

The Applicant requests that the Office reapply the $480.00 Issue Fee previously paid in this application to the Notice of Allowance and Fee(s) Due mailed January 25, 2017. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Very truly yours,

HONIGMAN MILLER SCHWARTZ AND COHN LLP

/Meghan M. Klaric/

Meghan M. Klaric
Reg. No. 71,226

MMK/ayp
Enclosures

OPAP AKIMA-5
APR 25 2017
PATENT & TRADEMARK OFFICE

IEJ

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

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CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 01/25/2017
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$480	$480	04/25/2017

04/26/2017 CCHAU2 00000004 503145 13984559
01 FC:2501 480.00 DA

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Honigman Miller Schwartz & Cohn LLP
2 Heidi M. Berven, Ph.D.
3 Jonathan P. O'Brien, Ph.D.

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Exelixis, Inc.

(B) RESIDENCE: (CITY and STATE OR COUNTRY): South San Francisco, CA

04/26/2017 CCHAU2 00003573 503145 13984559
11/14/2016 INTEFSW
01 FC:2501 480.00 CR

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
☒ Issue Fee (Please apply issue fee paid in this application 11/10/2016)
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)
☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☒ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 503145 (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)
☐ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
☒ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
☐ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Meghan M. Klaric/ Date April 25, 2017
Typed or printed name Meghan M. Klaric Registration No. 71,226

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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NOTICE OF ALLOWANCE AND FEE(S) DUE

91684 7590 01/25/2017

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 01/25/2017

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$480	$480	04/25/2017

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 01/25/2017
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

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APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$480	$480	04/25/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29
  NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27
  NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status.
  NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

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EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	**PAPER NUMBER**
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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 13/984,559	Applicant(s) WILSON ET AL.	
	Examiner TIMOTHY R. ROZOF	Art Unit 1625	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *November 29, 2016, RCE*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *40-47*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/TIMOTHY R ROZOF/
Primary Examiner, Art Unit 1625

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON, JO ANN
	Examiner	Art Unit
	TIMOTHY R ROZOF	1625

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
Class, inventor, and EAST search	1/17/2017	TRR

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
A61K	31/47	1/17/2017	TRR
C07D	215/233	1/17/2017	TRR

	/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625

UNITED STATES PATENT AND TRADEMARK OFFICE

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BIB DATA SHEET

CONFIRMATION NO. 6725

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/984,559	03/20/2014	514	1625	224990/10-039C-US/343999
	RULE			

APPLICANTS

INVENTORS

Jo Ann Wilson, San Francisco, CA;
Khalid Shah, South San Francisco, CA;

**** CONTINUING DATA ***************************

This application is a 371 of PCT/US12/24591 02/10/2012
which claims benefit of 61/441,520 02/10/2011
and claims benefit of 61/441,527 02/10/2011

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED **** ** SMALL ENTITY **

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☐ No Verified and Acknowledged /TIMOTHY R ROZOF/ Examiner's Signature ☐ Met after Allowance TRR Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
	CA	0	25	6

ADDRESS

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800
UNITED STATES

TITLE

PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

FILING FEE RECEIVED		
3890	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	6433	A61K31/47.cpc. C07D215/233.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2017/01/17 13:35
L2	4302	L1 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2017/01/17 13:35
L3	573	L2 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2017/01/17 13:35
L4	83	L3 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2017/01/17 13:35

EAST Search History (Interference)

<This search history is empty>

1/17/2017 1:36:50 PM
C:\Users\trozof\Documents\EAST\Workspaces\13984559.wsp

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

CPC						
Symbol					**Type**	**Version**
A61K		31	/	47	F	2013-01-01
C07D		215	/	233	I	2013-01-01
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CPC Combination Sets								
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	01/17/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

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	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
		A	6	1	K	31 / 47 (2006.01.01)						
CROSS REFERENCE(S)		C	0	7	D	215 / 233 (2006.01.01)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)											

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	01/17/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

☒ **Claims renumbered in the same order as presented by applicant** ☐ **CPA** ☐ **T.D.** ☐ **R.1.47**

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	40														
2	41														
3	42														
4	43														
5	44														
6	45														
7	46														
8	47														

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	01/17/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

Change(s) applied to document, /J.H./ 12/2/2016	28	20150202196		07/2015 ~~2015-02-20~~	Bannen et al. ~~EXELIXIS, INC.~~	
	29	20150376133		12/2015 ~~2015-07-16~~	Bannen et al. ~~EXELIXIS, INC.~~	
	30	20160000772		01/2016 ~~2015-07-23~~	Aftab et al. ~~EXELIXIS, INC.~~	
	31	20160051532		02/2016 ~~2015-12-31~~	Aftab et al. ~~EXELIXIS, INC.~~	
	32	20160185725		06/2016 ~~2016-01-07~~	Bannen et al. ~~EXELIXIS, INC.~~	
	33	20050209247		2005-09-22	Cai et al. ~~CHIRON CORPORATION~~	
	34	20070078159		2007-04-05	MATSUSHIMA, et al.	
	35	20110059081		2011-03-10	Bacus ~~QUINTILES TRANSNATIONAL CORP.~~	

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

EFS Web 2.1.17

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

Change(s) applied to document, /J.H./ 12/2/2016	17	20140057943		02/2014 ~~2013-12-12~~	Smith et al. ~~EXELIXIS, INC.~~	
	18	20140057908		02/2014 ~~2013-12-19~~	Smith et al. ~~EXELIXIS, INC.~~	
	19	20140066444		03/2014 ~~2014-02-27~~	Smith et al. ~~EXELIXIS, INC.~~	
	20	20140155396		06/2014 ~~2014-02-27~~	Bannen et al. ~~EXELIXIS, INC.~~	
	21	20140179736		06/2014 ~~2014-03-06~~	Schwab et al. ~~EXELIXIS, INC.~~	
	22	20140200242		07/2014 ~~2014-06-05~~	Wilson ~~EXELIXIS, INC.~~	
	23	20140228401		08/2014 ~~2014-06-26~~	Aftab et al. ~~EXELIXIS, INC.~~	
	24	20140302012		10/2014 ~~2014-07-17~~	DeCillis et al. ~~EXELIXIS, INC.~~	
	25	20140323522		10/2014 ~~2014-08-14~~	Aftab et al. ~~EXELIXIS, INC.~~	
	26	20150057310		02/2015 ~~2014-10-09~~	Brown et al. ~~EXELIXIS, INC.~~	
	27	20150196545		07/2015 ~~2014-10-30~~	Aftab et al. ~~EXELIXIS, INC.~~	

EFS Web 2.1.17

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

Change(s) applied to document, /J.H./ 12/2/2016	6	20120252840		2012-10-04	Aftab et al. ~~EXELIXIS, INC.~~	
	7	20120282179		2012-11-08	Aftab et al. ~~EXELIXIS, INC.~~	
	8	20130030172		2013-01-31	Wilson et al. ~~EXELIXIS, INC.~~	
	9	20130142790		06/2013 ~~2013-01-31~~	Gilmer et al. ~~EXELIXIS, INC.~~	
	10	20130143881		06/2013 ~~2013-01-31~~	Cannon et al. ~~EXELIXIS, INC.~~	
	11	20130150363		2013-06-~~06~~	Gilmer et al. EXELIXIS, INC.	
	12	20130197230		08/2013 ~~2013-06-06~~	Wilson et al. ~~EXELIXIS, INC.~~	
	13	20130252940		09/2013 ~~2013-06-13~~	Bannen et al. ~~EXELIXIS, INC.~~	
	14	20130252956		09/2013 ~~2013-08-01~~	Kallender et al. ~~EXELIXIS, INC.~~	
	15	20130330377		12/2013 ~~2013-09-26~~	Wilson ~~EXELIXIS, INC.~~	
	16	20130337015		12/2013 ~~2013-09-26~~	Wilson ~~EXELIXIS, INC.~~	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
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	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

Change(s) applied to document, /J.H./ 12/2/2016

	9	8673912		2014-03-18	Cannon et al. ~~EXELIXIS, INC~~.	
	10	8877776		2014-11-04	Brown et al. ~~EXELIXIS, INC~~.	
	11	9174947		2015-11-03	Bannen et al. ~~EXELIXIS, INC~~.	
	12	9365516		2016-06-14	Wilson et al. ~~EXELIXIS, INC~~.	

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20080161305		2008-07-03	Forsyth et al. ~~EXELIXIS, INC~~.	
	2	20090274693		2009-11-05	Gilmer et al. ~~EXELIXIS, INC~~.	
	3	20110077233		2011-03-31	Bannen et al. ~~EXELIXIS, INC~~.	
	4	20120070368		2012-03-22	Bannen et al. ~~EXELIXIS, INC~~.	
	5	20120184523		2012-07-19	Bannen et al. ~~EXELIXIS, INC~~.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	13984559
Filing Date	2014-03-20
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	Timothy R. Rozof
Attorney Docket Number	224990/10-039C-US/343999

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
Change(s) applied to document, /JH/ 12/2/2016	1	7579473		2009-08-25	Bannen et al. ~~EXELIXIS, INC~~.	
	2	7977345		2011-07-12	Bannen et al. ~~EXELIXIS, INC~~.	
	3	7999006		2011-08-16	Lamb ~~EXELIXIS, INC~~.	
	4	8067436		2011-11-29	Bannen et al. ~~EXELIXIS, INC~~.	
	5	8178532		2012-05-15	Bannen et al. ~~EXELIXIS, INC~~.	
	6	8314232		2012-11-20	Deschamps et al. ~~EXELIXIS, INC~~.	
	7	8476298		2013-07-02	Bannen et al. ~~EXELIXIS, INC~~.	
	8	8497284		2013-07-30	Bannen et al. ~~EXELIXIS, INC~~.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	13/984,559	Filing Date	2014-03-20	Docket Number (if applicable)	224990/10-039C-US/343999	Art Unit	1625
First Named Inventor	Jo Ann Wilson			Examiner Name	Timothy R. Rozof		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☒ Enclosed

- ☒ Amendment/Reply
- ☐ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____ (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

☒ **The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.**
The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 503145

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Signature of Registered U.S. Patent Practitioner			
Signature	/Meghan M. Klaric/	Date (YYYY-MM-DD)	2016-11-29
Name	Meghan M. Klaric	Registration Number	71226

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Doc Code: PET.AUTO Document Description: Petition automatically granted by EFS-Web	PTO/SB/140 U.S. Patent and Trademark Office Department of Commerce

Electronic Petition Request	**PETITION TO WITHDRAW AN APPLICATION FROM ISSUE AFTER PAYMENT OF THE ISSUE FEE UNDER 37 CFR 1.313(c)**
Application Number	13984559
Filing Date	20-Mar-2014
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	TIMOTHY ROZOF
Attorney Docket Number	224990/10-039C-US/343999
Title	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

An application may be withdrawn from issue for further action upon petition by the applicant. To request that the Office withdraw an application from issue, applicant must file a petition under this section including the fee set forth in § 1.17(h) and a showing of good and sufficient reasons why withdrawal of the application from issue is necessary.

APPLICANT HEREBY PETITIONS TO WITHDRAW THIS APPLICATION FROM ISSUE UNDER 37 CFR 1.313(c).

A grantable petition requires the following items:
(1) Petition fee; and
(2) One of the following reasons:
(a) Unpatentability of one or more claims, which must be accompanied by an unequivocal statement that one or more claims are unpatentable, an amendment to such claim or claims, and an explanation as to how the amendment causes such claim or claims to be patentable;
(b) Consideration of a request for continued examination in compliance with § 1.114 (for a utility or plant application only); or
(c) Express abandonment of the application. Such express abandonment may be in favor of a continuing application, but not a CPA under 37 CFR 1.53(d).

Petition Fee

- (◉) Small Entity
- (○) Micro Entity
- (○) Regular Undiscounted

Reason for withdrawal from issue

◯ One or more claims are unpatentable ◉ Consideration of a request for continued examination (RCE) (List of Required Documents and Fees) ◯ Applicant hereby expressly abandons the instant application (any attorney/agent signing for this reason must have power of attorney pursuant to 37 CFR 1.32(b)).
RCE request,submission, and fee. ☐ I certify, in accordance with 37 CFR 1.4(d)(4) that : The RCE request ,submission, and fee have already been filed in the above-identified application on ☒ Are attached.
THIS PORTION MUST BE COMPLETED BY THE SIGNATORY OR SIGNATORIES I certify, in accordance with 37 CFR 1.4(d)(4) that I am: ◉ An attorney or agent registered to practice before the Patent and Trademark Office who has been given power of attorney in this application. ◯ An attorney or agent registered to practice before the Patent and Trademark Office, acting in a representative capacity. ◯ A sole inventor ◯ A joint inventor; I certify that I am authorized to sign this submission on behalf of all of the inventors as evidenced by the power of attorney in the application ◯ A joint inventor; all of whom are signing this e-petition

Signature	/Meghan M. Klaric/
Name	Meghan M. Klaric
Registration Number	71226

HONIGMAN

Honigman Miller Schwartz and Cohn LLP
Attorneys and Counselors

Meghan M. Klaric

(269) 337-7840
Fax: (269) 337-7841
mklaric@honigman.com

Via EFS

November 29, 2016

Commissioner for Patents
United States Patent and Trademark Office
P. O. Box 1450
Alexandria, VA 22313

Re: ***Application No.: 13/984,559***
Inventors: Jo Ann Wilson, et al.
Filing Date: March 20, 2014
Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
Confirmation No.: 6725
Attorney Docket No.: 224990/10-039C-US/343999

Dear Sir or Madam:

Enclosed for filing please find the following documents:

1. This Cover Letter to the Commissioner for Patents;
2. Petition under 37 C.F.R. § 1.313(c) to Withdraw Application from Issue after Payment of the Issue Fee;
3. Request for Continued Examination under 37 C.F.R. § 1.114;
4. Request for Continued Examination Transmittal (PTO/SB/30); and
5. Certificate of Transmission under 37 C.F.R. § 1.8(a).

It is believed that required for this submission are the $70.00 petition fee set forth in 37 C.F.R. § 1.17(h) for a petition to withdraw from issue under § 1.313, and the $850.00 fee set forth in § 1.17(e)(2) for a small entity filing a second Request for Continued Examination under § 1.114. The Applicant authorizes the Office to charge this total of $920.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Very truly yours,

HONIGMAN MILLER SCHWARTZ AND COHN LLP

/Meghan M. Klaric/

Meghan M. Klaric
Reg. No. 71,226

MMK/cwg
Enclosures

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors:	Jo Ann Wilson, et al.	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. § 1.313(C) TO WITHDRAW APPLICATION FROM ISSUE AFTER PAYMENT OF THE ISSUE FEE

Dear Sir or Madam:

The Applicant hereby petitions under 37 C.F.R. § 1.313(c) to withdraw this application from issue after payment of the issue fee on November 10, 2016.

In accordance with 37 C.F.R. § 1.313(c)(2), a Request for Continued Examination under § 1.114 is submitted herewith. The petition fee set forth in 37 C.F.R. § 1.17(h) is also submitted herewith, in accordance with § 1.313(a).

It is believed that required for this submission are the $70.00 petition fee set forth in 37 C.F.R. § 1.17(h) for a petition to withdraw from issue under § 1.313, and the $850.00 fee set forth in § 1.17(e)(2) for a small entity filing a second Request for Continued Examination under § 1.114. The Applicant authorizes the Office to charge this total of $920.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Respectfully submitted,

Date: November 29, 2016

/Meghan M. Klaric/

Meghan M. Klaric
Reg. No. 71,226
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Ste. 300
Kalamazoo, MI 49007-3800
Direct (269) 337-7840
Fax (269) 337-7841

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors:	Jo Ann Wilson, et al.	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CONTINUED EXAMINATION UNDER 37 C.F.R. § 1.114 ACCOMPANYING PETITION TO WITHDRAW FROM ISSUE UNDER § 1.313(C)

This Request for Continued Examination under 37 C.F.R. § 1.114 is submitted in support of the petition to withdraw from issue under § 1.313(c)(2) filed concurrently. A submission and fee in support of the Request are submitted herewith.

Amendments to the claims are reflected in the listing of claims that begins on page 2.

Remarks begin on page 5.

CLAIM AMENDMENTS

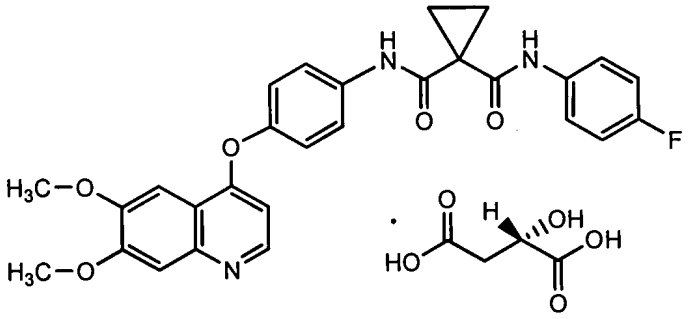
This listing of claims replaces all previous claim listings.

1-39. Cancelled.

40. (Currently amended) A capsule pharmaceutical composition:

Ingredient	$\frac{\textbf{mg/unit dose}}{\textbf{total fill weight}}$ **X 100**	**mg/unit dose**
Compound IB with [[5]] 50 ppm or less of 6,7-dimethoxy-quinoline-4-ol (10 percent drug load formulation)	10	25
Silicified Microcrystalline Cellulose	78.7	196.75
Croscarmellose sodium	5	12.5
Sodium starch glycolate	5	12.5
Fumed Silica	0.3	0.75
Stearic acid	1	2.5
Total fill weight		250

wherein compound IB has the structure:



IB

41. (Previously presented) The capsule pharmaceutical composition of claim 40, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 25 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

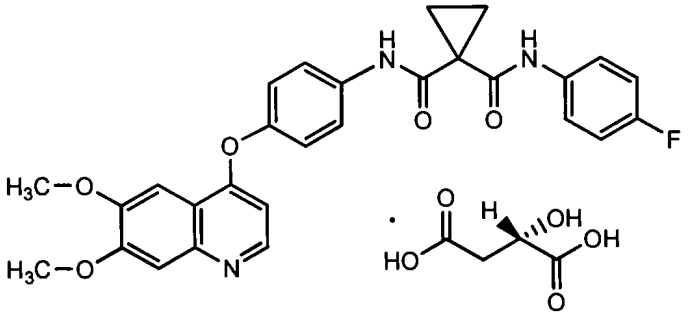
42. (Previously presented) The capsule pharmaceutical composition of claim 40, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 15 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

43. (Previously presented) The capsule pharmaceutical composition of claim 40, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 10 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

44. (Currently amended) A capsule pharmaceutical composition:

Ingredient	$\frac{\textbf{mg/unit dose}}{\textbf{total fill weight}}$ **X 100**	**mg/unit dose**
Compound IB with [[5]] 50 ppm or less of 6,7-dimethoxy-quinoline-4-ol (50 percent drug load formulation)	50	100
Silicified Microcrystalline Cellulose	37.7	75.40
Croscarmellose sodium	5	10.00
Sodium starch glycolate	5	10.00
Fumed Silica	0.3	0.6
Stearic acid	2	4.0
Total fill weight		200

wherein compound IB has the structure:



IB ; and wherein the amount of carriers and excipients used in the capsule pharmaceutical composition can be varied proportionally according to the amount of Compound IB used.

45. (Previously presented) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 25 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

46. (Previously presented) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 15 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

47. (Previously presented) The capsule pharmaceutical composition of claim 44, wherein the formation of 6,7-dimethoxy-quinoline-4-ol in the pharmaceutical formulation is minimized to 10 ppm or less from 0 to 6 months at 25 °C and 60 percent relative humidity.

REMARKS

Claim Status

Claims 1-39 are cancelled.

Claims 40 and 44 are currently amended. The amendments are supported by the claims and specification as originally filed, for example at paragraph [0090]. No new matter is added through the entry of these amendments.

Claims 41-43 and 45-47 are previously presented.

The claim amendments are made in the interest of expediting prosecution. The Applicant does not intend to surrender any range of equivalents to which the Applicant would otherwise be entitled. Further, by the present amendment, it does not follow that the amended claims have become so perfect in their description that no one could devise an equivalent. After amendment, as before, limitations in the ability to describe the present invention in language in the patent claims naturally prevent the Applicant from capturing every nuance of the invention or describing with complete precision the range of its novelty or every possible equivalent. *See* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 62 USPQ2d 1705 (2002). By amending the claims, the Applicant does not concede that patent coverage available to them would not extend as far as the original claim. The Applicant reserves the right to file divisional and/or continuation applications to pursue the breadth of the claims as filed. The Applicant respectfully requests the timely allowance of the amended claims.

REQUEST FOR CONTINUED EXAMINATION

It is believed that the claim amendments submitted herewith satisfy the requirement under 37 C.F.R. § 1.114 for a submission accompanying a Request for Continued Examination. The fee set forth in 37 C.F.R. § 1.17(e)(2) is also submitted herewith.

OTHER C-MET INHIBITOR CASES

The Applicant wishes to make the Examiner aware of the Applicant's other applications related to c-Met inhibitors and their use in the treatment of cancer. For the Examiner's convenience, the Applicant is providing a list of the Applicant's applications directed to the treatment of cancer using c-Met inhibitors. The Applicant understands the Examiner has electronic access to these applications and to the Office Actions that have issued in these

applications, and has therefore not included copies with this Response. The Applicant will gladly provide the applications and Office Actions to the Examiner, however, upon request.

Application Number	Filing or 371 Date	Patent Number	Examiner	Status
10/573,336	09/18/2006		Koontz, Tammy J.	Abandoned
11/571,140	12/21/2006	7,977,345	Moore, Susanna	Issued
11/586,751	10/26/2006	9,174,947	Ward, Paul V.	Issued
11/753,462	05/24/2007	8,178,532	Ward, Paul V.	Issued
11/753,503	05/24/2007	8,476,298	Ward, Paul V.	Issued
11/753,514	05/24/2007	8,067,436	Bernhardt, Emily A.	Issued
12/393,806	02/26/2009	7,579,473	Seaman, D. Margaret M.	Issued
12/911,442	10/25/2010		Ward, Paul, V.	Abandoned
13/087,094	04/14/2011		Chickos, Sarah, J.	Abandoned
13/129,183	05/13/2011		Seaman, D. Margaret M.	Abandoned
13/132,650	06/03/2011		Seaman, D. Margaret M.	Abandoned
13/145,054	10/20/2011	8,877,776	Carter, Kendra D	Issued
13/249,815	09/30/2011	8,497,284	Bernhardt, Emily A.	Issued
13/384,451	07/12/2012	8,673,912	Anderson, Rebecca L.	Issued
13/389,266	07/12/2012		Perreira, Melissa Jean	Abandoned
13/427,093	03/22/2012		Ward, Paul V.	Abandoned
13/438,964	04/04/2012		Brown-Pettigrew, Angela C.	Abandoned
13/634,275	09/12/2012		Anderson, Rebecca L.	Abandoned
13/753,031	01/29/2013		Pagonakis, Anna	Abandoned
13/753,146	01/29/2013		Pagonakis, Anna	Abandoned
13/810,537	08/26/2013		Pallay, Michael B.	Pending
13/810,546	08/27/2013		Branson, Daniel L.	Pending
13/876,290	11/05/2013		Stone, Christopher R.	Abandoned
13/876,306	11/08/2013		Lee, Andrew P.	Abandoned
13/876,318	10/25/2013		Karol, Jody Lynn	Abandoned
13/888,592	05/07/2013		Ward, Paul V.	Abandoned
13/928,977	06/27/2013		Bernhardt, Emily A.	Abandoned
14/021,614	09/09/2013		Matos Negron, Taina Del Mar	Pending
14/115,236	02/28/2014		Anderson, James D.	Pending
14/166,545	01/28/2014		Not Yet Assigned	Abandoned
14/173,973	02/06/2014		Johannsen, Diana B.	Abandoned
14/340,871	07/25/2014		Carter, Kendra D.	Pending
14/346,570	03/21/2014		Calvillo, Y. Jeanmarie Z.	Pending
14/353,251	04/21/2014		Murray, Jeffrey H.	Issued
14/356,927	05/08/2014		Baek, Bong-sook	Pending
14/356,938	05/08/2014		Cerioni, Daniel Lee	Pending
14/398,188	10/31/2014		Henley III, Raymond J.	Pending
14/426,580	03/06/2015		Jean-Louis, Samira J.M.	Pending
14/518,733	10/20/2014		Chickos, Sarah J.	Pending

Application Number	Filing or 371 Date	Patent Number	Examiner	Status
14/668,312	03/25/2015		Brown-Pettigrew, Angela C.	Abandoned
14/699,683	04/29/2015		Perreira, Melissa Jean	Pending
14/776,337	09/14/2015		Reese, Heidi L.	Pending
14/782,493	10/05/2015		Grazier, Nyeemah A.	Pending
14/782,537	10/05/2015		Not Yet Assigned	Pending
14/843,480	09/02/2015		Stone, Christopher R.	Pending
14/847,801	09/08/2015		Ward, Paul V.	Pending
14/933,801	11/05/2015		Brown-Pettigrew, Angela C.	Pending
15/066,872	03/10/2016		Not Yet Assigned	Pending
15/133,708	04/20/2016		Not Yet Assigned	Pending

CONCLUSION

It is believed that due for this submission are the $850.00 fee set forth in 37 C.F.R. § 1.17(e)(2) for a small entity filing a second Request for Continued Examination under § 1.114 and the $70.00 petition fee set forth in § 1.17(h) for a petition to withdraw from issue under § 1.313. The Applicant authorizes the Office to charge this total of $920.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Respectfully submitted,

Date: November 29, 2016

/Meghan M. Klaric/

Meghan M. Klaric
Reg. No. 71,226
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Ste. 300
Kalamazoo, MI 49007-3800
Direct (269) 337-7840
Fax (269) 337-7841

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

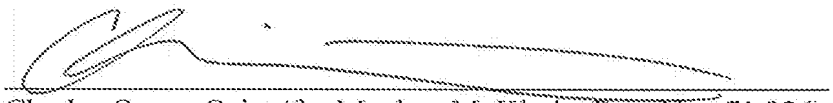
Inventors:	Jo Ann Wilson, et al.	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8(a)

The undersigned hereby certifies that the following documents are being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4) on this 29th day of November, 2016:

1. Cover Letter to the Commissioner for Patents;
2. Petition under 37 C.F.R. § 1.313(c) to Withdraw Application from Issue after Payment of the Issue Fee;
3. Request for Continued Examination under 37 C.F.R. § 1.114;
4. Request for Continued Examination Transmittal (PTO/SB/30); and
5. This Certificate of Transmission under 37 C.F.R. § 1.8(a).



Charles Gregg-Geist (for Meghan M. Klaric, Reg. No.: 71,226)

Electronic Patent Application Fee Transmittal

Application Number:	13984559
Filing Date:	20-Mar-2014
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Filer:	Meghan Mary Klaric/Charles Gregg-Geist
Attorney Docket Number:	224990/10-039C-US/343999

Filed as Small Entity

Filing Fees for U.S. National Stage under 35 USC 371

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
PETITION FEE-37CFR 1.17(H) (GROUP II)	2464	1	70	70
RCE- 2ND AND SUBSEQUENT REQUEST	2820	1	850	850
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**920**

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Decision Date : November 29, 2016

In re Application of :

Jo Ann Wilson

DECISION ON PETITION

UNDER CFR 1.313(c)(2)

Application No : 13984559

Filed : 20-Mar-2014

Attorney Docket No : 224990/10-039C-US/343999

This is an electronic decision on the petition under 37 CFR 1.313(c)(2), filed November 29, 2016, to withdraw the above-identified application from issue after payment of the issue fee.

The petition is **GRANTED.**

The above-identified application is withdrawn from issue for consideration of a submission under 37 CFR 1.114 (request for continued examination). See 37 CFR 1.313(c)(2).

Petitioner is advised that the issue fee paid in this application cannot be refunded. If, however, this application is again allowed, petitioner may request that it be applied towards the issue fee required by the new Notice of Allowance.

Telephone inquiries concerning this decision should be directed to the Patent Electronic Business Center (EBC) at 866-217-9197.

This application file is being referred to Technology Center AU 1625 for processing of the request for continuing examination under 37 CFR 1.114 .

Office of Petitions

Electronic Acknowledgement Receipt

EFS ID:	27636685
Application Number:	13984559
International Application Number:	
Confirmation Number:	6725
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Customer Number:	91684
Filer:	Meghan Mary Klaric/Charles Gregg-Geist
Filer Authorized By:	Meghan Mary Klaric
Attorney Docket Number:	224990/10-039C-US/343999
Receipt Date:	29-NOV-2016
Filing Date:	20-MAR-2014
Time Stamp:	17:21:57
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$920
RAM confirmation Number	113016INTEFSW00004876503145
Deposit Account	
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	EX10-039C-US_RCE_Transmittal_PTO-SB-30.PDF	811299 5a16e7e95078b3fefd613f160c6a19389afa7ad8	no	3
Warnings:					
Information:					
2	Petition automatically granted by EFS	petition-request.pdf	31745 fb132313c5597acf669745146f407040a84065fd	no	2
Warnings:					
Information:					
3		EX10-039_Submission.pdf	1103614 d3de295b6bd6208d88b6ae1d2c91152524db0848	yes	12

Multipart Description/PDF files in .zip description

Document Description	Start	End
Transmittal Letter	1	2
Transmittal Letter	3	4
Amendment Submitted/Entered with Filing of CPA/RCE	5	5
Claims	6	8
Applicant Arguments/Remarks Made in an Amendment	9	11
Transmittal Letter	12	12

Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	32483 c59e1be499fb8cb764dee6ef630c8ed615cb964e	no	2

Warnings:	
Information:	
Total Files Size (in bytes):	1979141

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/984,559	Filing Date 03/20/2014	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT **11/29/2016**

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 8	Minus	** 34	= 0	X $40 =	0
Independent (37 CFR 1.16(h))	* 2	Minus	***15	= 0	X $210 =	0
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	0

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
GOIGA DUCKETT

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 08/10/2016
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	11/10/2016

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Honigman Miller Schwartz and Cohn LLP
2 Heidi M. Berven, Ph.D.
3 Jonathan P. O'Brien, Ph.D.

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Exelixis, Inc.
(B) RESIDENCE: (CITY and STATE OR COUNTRY): San Francisco, CA

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
☒ Issue Fee
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☒ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 503145 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
☐ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
☐ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
☐ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Meghan M. Klaric/ Date November 10, 2016
Typed or printed name Meghan M. Klaric Registration No. 71,226

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8(a)

The undersigned hereby certifies that the following documents are being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4) on this 10th day of November, 2016:

1. This Cover Letter to the Commissioner for Patents;
2. Part B Fee(s) Transmittal (PTOL-85); and
3. Certificate of Transmission under 37 C.F.R. § 1.8(a).

/Amy L. Peters/

Amy L. Peters (for Meghan M. Klaric, Reg. No.: 71,226)

Electronic Patent Application Fee Transmittal

Application Number:	13984559
Filing Date:	20-Mar-2014
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Filer:	Meghan Mary Klaric/Amy Peters
Attorney Docket Number:	224990/10-039C-US/343999

Filed as Small Entity

Filing Fees for U.S. National Stage under 35 USC 371

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
UTILITY APPL ISSUE FEE	2501	1	480	480

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**480**

Electronic Acknowledgement Receipt

EFS ID:	27477770
Application Number:	13984559
International Application Number:	
Confirmation Number:	6725
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Customer Number:	91684
Filer:	Meghan Mary Klaric/Amy Peters
Filer Authorized By:	Meghan Mary Klaric
Attorney Docket Number:	224990/10-039C-US/343999
Receipt Date:	10-NOV-2016
Filing Date:	20-MAR-2014
Time Stamp:	16:40:03
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$480
RAM confirmation Number	111416INTEFSW00003573503145
Deposit Account	
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		2016_11_10_16_31_30.pdf	183220 cec9fa63c263d28e1f845f4a716757cb358adb64	yes	3

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Miscellaneous Incoming Letter	1	1
	Issue Fee Payment (PTO-85B)	2	2
	Transmittal Letter	3	3

Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30652 3208233591f329d9796adadb0f40c328ec2e5dbf	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	213872		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

HONIGMAN

Honigman Miller Schwartz and Cohn LLP
Attorneys and Counselors

Meghan M. Klaric

(269) 337-7840
Fax: (269) 337-7841
mklaric@honigman.com

Via EFS

November 10, 2016

Commissioner for Patents
United States Patent and Trademark Office
P. O. Box 1450
Alexandria, VA 22313

Re: ***Application No.: 13/984,559***
Inventor: Jo Ann Wilson
Filing Date: March 20, 2014
Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
Confirmation No.: 6725
Attorney Docket No.: 224990/10-039C-US/343999

Dear Sir or Madam:

Enclosed for filing please find the following documents:

1. This Cover Letter to the Commissioner for Patents;
2. Part B Fee(s) Transmittal (PTOL-85); and
3. Certificate of Transmission under 37 C.F.R. § 1.8(a).

The Applicant believes that due for this submission is the $480.00 Issue Fee. The Applicant authorizes the Office to charge this $480.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Very truly yours,

HONIGMAN MILLER SCHWARTZ AND COHN LLP

/Meghan M. Klaric/

Meghan M. Klaric
Reg. No. 71,226

MMK/ayp
Enclosures

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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NOTICE OF ALLOWANCE AND FEE(S) DUE

91684 7590 08/10/2016

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 08/10/2016

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	11/10/2016

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 08/10/2016
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

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nonprovisional	SMALL	$480	$0	$0	$480	11/10/2016

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29 — NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

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EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	**PAPER NUMBER**
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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 13/984,559	Applicant(s) WILSON ET AL.	
	Examiner TIMOTHY R. ROZOF	Art Unit 1625	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *August 4, 2016, RCE*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *40-47*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/TIMOTHY R ROZOF/
Primary Examiner, Art Unit 1625

UNITED STATES PATENT AND TRADEMARK OFFICE

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BIB DATA SHEET

CONFIRMATION NO. 6725

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/984,559	03/20/2014	514	1625	224990/10-039C-US/343999

APPLICANTS

INVENTORS

Jo Ann Wilson, San Francisco, CA;
Khalid Shah, South San Francisco, CA;

**** CONTINUING DATA ***************************

This application is a 371 of PCT/US12/24591 02/10/2012
which claims benefit of 61/441,520 02/10/2011
and claims benefit of 61/441,527 02/10/2011

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED **** ** SMALL ENTITY **

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☐ No Verified and Acknowledged /TIMOTHY R ROZOF/ Examiner's Signature	☐ Met after Allowance TRR Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		CA	0	25	6

ADDRESS

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800
UNITED STATES

TITLE

PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

FILING FEE RECEIVED		
3890	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	13984559
Filing Date	2014-03-20
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	Timothy R. Rozof
Attorney Docket Number	224990/10-039C-US/343999

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	7579473		2009-08-25	EXELIXIS, INC.	
	2	7977345		2011-07-12	EXELIXIS, INC.	
	3	7999006		2011-08-16	EXELIXIS, INC.	
	4	8067436		2011-11-29	EXELIXIS, INC.	
	5	8178532		2012-05-15	EXELIXIS, INC.	
	6	8314232		2012-11-20	EXELIXIS, INC.	
	7	8476298		2013-07-02	EXELIXIS, INC.	
	8	8497284		2013-07-30	EXELIXIS, INC.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

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	Application Number	13984559
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	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	9	8673912		2014-03-18	EXELIXIS, INC.	
	10	8877776		2014-11-04	EXELIXIS, INC.	
	11	9174947		2015-11-03	EXELIXIS, INC.	
	12	9365516		2016-06-14	EXELIXIS, INC.	

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20080161305		2008-07-03	EXELIXIS, INC.	
	2	20090274693		2009-11-05	EXELIXIS, INC.	
	3	20110077233		2011-03-31	EXELIXIS, INC.	
	4	20120070368		2012-03-22	EXELIXIS, INC.	
	5	20120184523		2012-07-19	EXELIXIS, INC.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

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	First Named Inventor	Jo Ann Wilson
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	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	6	20120252840		2012-10-04	EXELIXIS, INC.	
	7	20120282179		2012-11-08	EXELIXIS, INC.	
	8	20130030172		2013-01-31	EXELIXIS, INC.	
	9	20130142790		2013-01-31	EXELIXIS, INC.	
	10	20130143881		2013-01-31	EXELIXIS, INC.	
	11	20130150363		2013-06-06	EXELIXIS, INC.	
	12	20130197230		2013-06-06	EXELIXIS, INC.	
	13	20130252940		2013-06-13	EXELIXIS, INC.	
	14	20130252956		2013-08-01	EXELIXIS, INC.	
	15	20130330377		2013-09-26	EXELIXIS, INC.	
	16	20130337015		2013-09-26	EXELIXIS, INC.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

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	Attorney Docket Number	224990/10-039C-US/343999

	17	20140057943		2013-12-12	EXELIXIS, INC.	
	18	20140057908		2013-12-19	EXELIXIS, INC.	
	19	20140066444		2014-02-27	EXELIXIS, INC.	
	20	20140155396		2014-02-27	EXELIXIS, INC.	
	21	20140179736		2014-03-06	EXELIXIS, INC.	
	22	20140200242		2014-06-05	EXELIXIS, INC.	
	23	20140228401		2014-06-26	EXELIXIS, INC.	
	24	20140302012		2014-07-17	EXELIXIS, INC.	
	25	20140323522		2014-08-14	EXELIXIS, INC.	
	26	20150057310		2014-10-09	EXELIXIS, INC.	
	27	20150196545		2014-10-30	EXELIXIS, INC.	

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	28	20150202196		2015-02-26	EXELIXIS, INC.	
	29	20150376133		2015-07-16	EXELIXIS, INC.	
	30	20160000772		2015-07-23	EXELIXIS, INC.	
	31	20160051532		2015-12-31	EXELIXIS, INC.	
	32	20160185725		2016-01-07	EXELIXIS, INC.	
	33	20050209247		2005-09-22	CHIRON CORPORATION	
	34	20070078159		2007-04-05	MATSUSHIMA, et al.	
	35	20110059081		2011-03-10	QUINTILES TRANSNATIONAL CORP.	

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

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	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

NON-PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Kurzrock R et al. "379 POSTER A phase I study of XL 184, a MET, VEGFR2, and RET kinase inhibitor, administered orally to patients (pts) with advanced malignancies, including a subgroup of pts with medullary thyroid cancer (MTC)." Eropean journal of cancer. supplement, vol 6, no 12, 2008-10-01, 119.	☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE			
Examiner Signature	/TIMOTHY R ROZOF/	Date Considered	08/05/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1]See Kind Codes of USPTO Patent Documents at www.USPTO.GOVor MPEP 901.04. [2]Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3]For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4]Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5]Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	Meghan M. Klaric	Date (YYYY-MM-DD)	2016-08-04
Name/Print	Meghan M. Klaric	Registration Number	71,226

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

CPC						
Symbol					**Type**	**Version**
A61K		31	/	47	F	2013-01-01
C07D		215	/	233	I	2013-01-01
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CPC Combination Sets								
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	08/05/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
		A	6	1	K	31 / 47 (2006.01.01)						
CROSS REFERENCE(S)		C	0	7	D	215 / 233 (2006.0)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)											

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	08/05/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

☒ **Claims renumbered in the same order as presented by applicant** ☐ **CPA** ☐ **T.D.** ☐ **R.1.47**

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	40														
2	41														
3	42														
4	43														
5	44														
6	45														
7	46														
8	47														

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	08/05/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1927	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L2	7246	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:36
L3	5493	L2 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L4	495	L3 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L5	96	L4 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L6	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:36
L7	757	L3 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L8	12	L5 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L9	1927	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L10	7246	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:36
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L13	96	L12 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
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L16	12	L13 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	ON	2016/08/05 11:36

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L18	7246	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:36
L19	5493	L18 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
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L21	96	L20 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L22	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:36
L23	757	L19 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L24	12	L21 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L25	1927	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L26	7246	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:36
L27	5493	L26 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
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L29	96	L28 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
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L32	12	L29 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:36
L33	0	((A61K31/47.cpc.) or (C07D215/233.cpc.)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L34	6123	A61K31/47.cpc. C07D215/233.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L35	4231	L34 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	ON	2016/08/05 11:37

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L36	566	L35 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L37	82	L36 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L38	1927	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L39	7246	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L40	5493	L39 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L41	495	L40 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L42	96	L41 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L43	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L44	757	L40 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L45	12	L42 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L46	1927	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L47	7246	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L48	5493	L47 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L49	495	L48 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L50	96	L49 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L51	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L52	757	L48 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L53	12	L50 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L54	1927	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	ON	2016/08/05 11:37

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L55	7246	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L56	5493	L55 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L57	495	L56 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L58	96	L57 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L59	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L60	757	L56 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L61	12	L58 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L62	1927	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L63	7246	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L64	5493	L63 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L65	495	L64 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L66	96	L65 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L67	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L68	757	L64 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L69	12	L66 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L70	0	((A61K31/47.cpc.) or (C07D215/233.cpc.)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/08/05 11:37
L71	6123	A61K31/47.cpc. C07D215/233.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L72	4231	L71 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
L73	566	L72 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	ON	2016/08/05 11:37

			DERWENT			
L74	82	L73 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/08/05 11:37
S1	1868	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 13:11
S2	6107	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2014/10/04 13:12
S3	4920	S2 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 13:12
S4	476	S3 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 13:14
S5	88	S4 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 13:14
S6	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2014/10/04 13:14
S7	735	S3 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 15:14
S8	11	S5 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2014/10/04 15:15
S10	1907	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S11	6748	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2015/06/03 13:56
S12	5294	S11 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S13	492	S12 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S14	96	S13 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S15	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2015/06/03 13:56
S16	748	S12 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S17	12	S14 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2015/06/03 13:56
S19	1924	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S20	7064	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	OFF	2016/01/07 13:23

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S21	5473	S20 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S22	494	S21 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S23	96	S22 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S24	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:23
S25	755	S21 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S26	12	S23 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S27	1924	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S28	7064	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:23
S29	5473	S28 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S30	494	S29 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S31	96	S30 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S32	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:23
S33	755	S29 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S34	12	S31 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:23
S35	0	((A61K31/47.cpc.) or (C07D215/233.cpc.)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/01/07 13:33
S36	5706	A61K31/47.cpc. C07D215/233.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:33
S37	4165	S36 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:33
S38	546	S37 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/01/07 13:34
S39	81	S38 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	ON	2016/01/07 13:34

			DERWENT			
S42	1925	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S43	7164	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S44	5481	S43 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S45	494	S44 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S46	96	S45 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S47	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S48	756	S44 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S49	12	S46 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S50	1925	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S51	7164	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S52	5481	S51 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S53	494	S52 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S54	96	S53 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S55	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S56	756	S52 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S57	12	S54 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S58	1925	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S59	7164	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S60	5481	S59 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO;	OR	ON	2016/04/28 12:34

			DERWENT			
S61	494	S60 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S62	96	S61 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S63	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S64	756	S60 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S65	12	S62 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S66	1925	546/153	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S67	7164	((546/153) or (514/312)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S68	5481	S67 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S69	494	S68 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S70	96	S69 and ((c$met) or (Ret))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S71	2	("20070054928").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S72	756	S68 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S73	12	S70 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S74	0	((A61K31/47.cpc.) or (C07D215/233.cpc.)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2016/04/28 12:34
S75	5906	A61K31/47.cpc. C07D215/233.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S76	4191	S75 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S77	550	S76 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34
S78	81	S77 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2016/04/28 12:34

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S9	1	((546/153) or (514/312)).CCLS.		OR	OFF	2014/10/04 13:43
S18	1	((546/153) or (514/312)).CCLS.		OR	OFF	2015/06/03 13:56
S40	0	((546/153) or (514/312)).CCLS.		OR	OFF	2016/01/07 13:23
S41	0	((546/153) or (514/312)).CCLS.		OR	OFF	2016/01/07 13:23

8/ 5/ 2016 11:41:29 AM
C:\ Users\ trozof\ Documents\ EAST\ Workspaces\ 13984559.wsp

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON, JO ANN
	Examiner	Art Unit
	TIMOTHY R ROZOF	1625

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
Class, inventor, and EAST search	8/5/2016	TRR

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
A61K	31/47	8/5/2016	TRR
C07D	215/233	8/5/2016	TRR

	/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CONTINUED EXAMINATION UNDER 37 C.F.R. § 1.114

This Request for Continued Examination under 37 C.F.R. § 1.114 is submitted in response to the Notice of Allowance dated May 4, 2016. A submission and fee in support of the Applicant's Request is enclosed.

Remarks begin on page 2.

REMARKS

REQUEST FOR CONTINUED EXAMINATION

It is believed that the Information Disclosure Statement submitted herewith satisfies the requirement under § 1.114 for a submission accompanying a Request for Continued Examination. The fee set forth in 37 C.F.R. § 1.17(e)(2) is also submitted herewith.

INFORMATION DISCLOSURE STATEMENT

The Applicant notes that the filing of the enclosed Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement qualifies as prior art under 35 U.S.C. §§ 102 or 103, or is considered to be material to patentability as defined in 37 C.F.R § 1.56(b). The Applicant believes that the fee set forth in 37 C.F.R. § 1.17(p) is not required at this time pursuant to § 1.97(b)(4).

OTHER C-MET INHIBITOR CASES

The Applicant wishes to make the Examiner aware of the Applicant's other applications related to c-Met inhibitors and their use in the treatment of cancer. For the Examiner's convenience, the Applicant is providing a list of the Applicant's applications directed to the treatment of cancer using c-Met inhibitors. The Applicant understands the Examiner has electronic access to these applications and to the Office Actions that have issued in these applications, and has therefore not included copies with this Response. The Applicant will gladly provide the applications and Office Actions to the Examiner, however, upon request.

Application Number	Filing or 371 Date	Patent Number	Examiner	Status
10/573,336	09/18/2006		Koontz, Tammy J.	Abandoned
11/571,140	12/21/2006	7,977,345	Moore, Susanna	Issued
11/586,751	10/26/2006	9,174,947	Ward, Paul V.	Issued
11/753,462	05/24/2007	8,178,532	Ward, Paul V.	Issued
11/753,503	05/24/2007	8,476,298	Ward, Paul V.	Issued
11/753,514	05/24/2007	8,067,436	Bernhardt, Emily A.	Issued
12/393,806	02/26/2009	7,579,473	Seaman, D. Margaret M.	Issued
12/911,442	10/25/2010		Ward, Paul, V.	Abandoned
13/087,094	04/14/2011		Chickos, Sarah, J.	Abandoned
13/129,183	05/13/2011		Seaman, D. Margaret M.	Abandoned
13/132,650	06/03/2011		Seaman, D. Margaret M.	Abandoned
13/145,054	10/20/2011	8,877,776	Carter, Kendra D	Issued

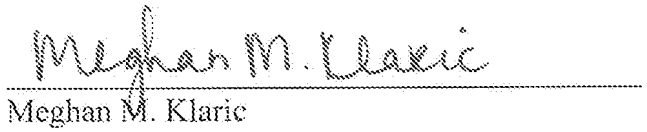
Application Number	Filing or 371 Date	Patent Number	Examiner	Status
13/249,815	09/30/2011	8,497,284	Bernhardt, Emily A.	Issued
13/384,451	07/12/2012	8,673,912	Anderson, Rebecca L.	Issued
13/389,266	07/12/2012		Perreira, Melissa Jean	Abandoned
13/427,093	03/22/2012		Ward, Paul V.	Abandoned
13/438,964	04/04/2012		Brown-Pettigrew, Angela C.	Abandoned
13/634,275	09/12/2012		Anderson, Rebecca L.	Abandoned
13/753,031	01/29/2013		Pagonakis, Anna	Abandoned
13/753,146	01/29/2013		Pagonakis, Anna	Abandoned
13/810,537	08/26/2013		Pallay, Michael B.	Pending
13/810,546	08/27/2013		Branson, Daniel L.	Pending
13/876,290	11/05/2013		Stone, Christopher R.	Abandoned
13/876,306	11/08/2013		Lee, Andrew P.	Abandoned
13/876,318	10/25/2013		Karol, Jody Lynn	Abandoned
13/888,592	05/07/2013		Ward, Paul V.	Abandoned
13/928,977	06/27/2013		Bernhardt, Emily A.	Abandoned
14/021,614	09/09/2013		Matos Negron, Taina Del Mar	Pending
14/115,236	02/28/2014		Anderson, James D.	Pending
14/166,545	01/28/2014		Not Yet Assigned	Abandoned
14/173,973	02/06/2014		Johannsen, Diana B.	Abandoned
14/340,871	07/25/2014		Carter, Kendra D.	Pending
14/346,570	03/21/2014		Calvillo, Y. Jeanmarie Z.	Pending
14/353,251	04/21/2014		Murray, Jeffrey H.	Issued
14/356,927	05/08/2014		Baek, Bong-sook	Pending
14/356,938	05/08/2014		Cerioni, Daniel Lee	Pending
14/398,188	10/31/2014		Henley III, Raymond J.	Pending
14/426,580	03/06/2015		Jean-Louis, Samira J.M.	Pending
14/518,733	10/20/2014		Chickos, Sarah J.	Pending
14/668,312	03/25/2015		Brown-Pettigrew, Angela C.	Abandoned
14/699,683	04/29/2015		Perreira, Melissa Jean	Pending
14/776,337	09/14/2015		Reese, Heidi L.	Pending
14/782,493	10/05/2015		Grazier, Nyeemah A.	Pending
14/782,537	10/05/2015		Not Yet Assigned	Pending
14/843,480	09/02/2015		Stone, Christopher R.	Pending
14/847,801	09/08/2015		Ward, Paul V.	Pending
14/933,801	11/05/2015		Brown-Pettigrew, Angela C.	Pending
15/066,872	03/10/2016		Not Yet Assigned	Pending
15/133,708	04/20/2016		Not Yet Assigned	Pending

CONCLUSION

It is believed that due for this submission is the $850.00 fee set forth in 37 C.F.R. § 1.17(e)(2) for a small entity filing a second Request for Continued Examination under § 1.114. The Applicant authorizes the Office to charge this $850.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Respectfully submitted,

Date: August 4, 2016



Meghan M. Klaric
Reg. No. 71,226
Honigman Miller Schwartz and Cohn LLP
350 East Michigan Avenue, Ste. 300
Kalamazoo, MI 49007-3800
Direct (269) 337-7840
Fax (269) 337-7841

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	13984559
Filing Date	2014-03-20
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	Timothy R. Rozof
Attorney Docket Number	224990/10-039C-US/343999

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	7579473		2009-08-25	EXELIXIS, INC.	
	2	7977345		2011-07-12	EXELIXIS, INC.	
	3	7999006		2011-08-16	EXELIXIS, INC.	
	4	8067436		2011-11-29	EXELIXIS, INC.	
	5	8178532		2012-05-15	EXELIXIS, INC.	
	6	8314232		2012-11-20	EXELIXIS, INC.	
	7	8476298		2013-07-02	EXELIXIS, INC.	
	8	8497284		2013-07-30	EXELIXIS, INC.	

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	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	9	8673912		2014-03-18	EXELIXIS, INC.	
	10	8877776		2014-11-04	EXELIXIS, INC.	
	11	9174947		2015-11-03	EXELIXIS, INC.	
	12	9365516		2016-06-14	EXELIXIS, INC.	

If you wish to add additional U.S. Patent citation information please click the Add button.

U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20080161305		2008-07-03	EXELIXIS, INC.	
	2	20090274693		2009-11-05	EXELIXIS, INC.	
	3	20110077233		2011-03-31	EXELIXIS, INC.	
	4	20120070368		2012-03-22	EXELIXIS, INC.	
	5	20120184523		2012-07-19	EXELIXIS, INC.	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	6	20120252840		2012-10-04	EXELIXIS, INC.	
	7	20120282179		2012-11-08	EXELIXIS, INC.	
	8	20130030172		2013-01-31	EXELIXIS, INC.	
	9	20130142790		2013-01-31	EXELIXIS, INC.	
	10	20130143881		2013-01-31	EXELIXIS, INC.	
	11	20130150363		2013-06-06	EXELIXIS, INC.	
	12	20130197230		2013-06-06	EXELIXIS, INC.	
	13	20130252940		2013-06-13	EXELIXIS, INC.	
	14	20130252956		2013-08-01	EXELIXIS, INC.	
	15	20130330377		2013-09-26	EXELIXIS, INC.	
	16	20130337015		2013-09-26	EXELIXIS, INC.	

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	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	17	20140057943		2013-12-12	EXELIXIS, INC.	
	18	20140057908		2013-12-19	EXELIXIS, INC.	
	19	20140066444		2014-02-27	EXELIXIS, INC.	
	20	20140155396		2014-02-27	EXELIXIS, INC.	
	21	20140179736		2014-03-06	EXELIXIS, INC.	
	22	20140200242		2014-06-05	EXELIXIS, INC.	
	23	20140228401		2014-06-26	EXELIXIS, INC.	
	24	20140302012		2014-07-17	EXELIXIS, INC.	
	25	20140323522		2014-08-14	EXELIXIS, INC.	
	26	20150057310		2014-10-09	EXELIXIS, INC.	
	27	20150196545		2014-10-30	EXELIXIS, INC.	

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	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	28	20150202196		2015-02-26	EXELIXIS, INC.	
	29	20150376133		2015-07-16	EXELIXIS, INC.	
	30	20160000772		2015-07-23	EXELIXIS, INC.	
	31	20160051532		2015-12-31	EXELIXIS, INC.	
	32	20160185725		2016-01-07	EXELIXIS, INC.	
	33	20050209247		2005-09-22	CHIRON CORPORATION	
	34	20070078159		2007-04-05	MATSUSHIMA, et al.	
	35	20110059081		2011-03-10	QUINTILES TRANSNATIONAL CORP.	

If you wish to add additional U.S. Published Application citation information please click the Add button.

FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

NON-PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Kurzrock R et al. "379 POSTER A phase I study of XL 184, a MET, VEGFR2, and RET kinase inhibitor, administered orally to patients (pts) with advanced malignancies, including a subgroup of pts with medullary thyroid cancer (MTC)." Eropean journal of cancer. supplement, vol 6, no 12, 2008-10-01, 119.	☐

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE			
Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1]See Kind Codes of USPTO Patent Documents at www.USPTO.GOVor MPEP 901.04. [2]Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3]For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4]Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5]Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	Meghan M. Klaric	Date (YYYY-MM-DD)	2016-08-04
Name/Print	Meghan M. Klaric	Registration Number	71,226

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Doc code: RCEX
Doc description: Request for Continued Examination (RCE)

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	13/984,559	Filing Date	2014-03-20	Docket Number (if applicable)	224990/10-039C-US/343999	Art Unit	1625
First Named Inventor	Jo Ann Wilson			Examiner Name	Timothy R. Rozof		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☒ Enclosed

- ☐ Amendment/Reply
- ☒ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

☒ **The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.**
The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 503145

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature
☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Signature of Registered U.S. Patent Practitioner			
Signature	Meghan M. Kleric	Date (YYYY-MM-DD)	2016-08-04
Name	Meghan M. Kleric	Registration Number	71226

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

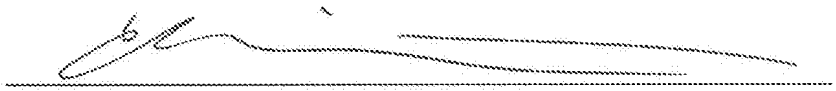
Inventor:	Jo Ann Wilson	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8(a)

The undersigned hereby certifies that the following documents are being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4) on this 4th day of August, 2016:

1. Cover Letter to the Commissioner for Patents;
2. Request for Continued Examination under 37 C.F.R. § 1.114;
3. Request for Continued Examination Transmittal (PTO/SB/30);
4. Information Disclosure Statement (PTO/SB/08A);
5. Non-Patent Literature (1 Document); and
6. This Certificate of Transmission under 37 C.F.R. § 1.8(a).



Charles Gregg-Geist (for Meghan M. Klaric, Reg. No.: 71,226)

Electronic Patent Application Fee Transmittal

Application Number:	13984559
Filing Date:	20-Mar-2014
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Filer:	Meghan Mary Klaric/Charles W. Gregg-Geist
Attorney Docket Number:	224990/10-039C-US/343999

Filed as Small Entity

Filing Fees for U.S. National Stage under 35 USC 371

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
RCE- 2nd and Subsequent Request	2820	1	850	850
		Total in USD ($)		**850**

Electronic Acknowledgement Receipt

EFS ID:	26552844
Application Number:	13984559
International Application Number:	
Confirmation Number:	6725
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Customer Number:	91684
Filer:	Meghan Mary Klaric/Charles W. Gregg-Geist
Filer Authorized By:	Meghan Mary Klaric
Attorney Docket Number:	224990/10-039C-US/343999
Receipt Date:	04-AUG-2016
Filing Date:	20-MAR-2014
Time Stamp:	17:16:01
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$850
RAM confirmation Number	080516INTEFSW00004318503145
Deposit Account	503145
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		EX10-039C-US_RCE.pdf	2596180 d1de1247fd54c7cf578d14f4a52a27e33351244f	yes	16

Multipart Description/PDF files in .zip description

Document Description	Start	End
Transmittal Letter	1	2
Request for Continued Examination (RCE)	3	6
Information Disclosure Statement (IDS) Form (SB08)	7	13
Transmittal Letter	14	15
Transmittal Letter	16	16

Warnings:

Information:

2	Non Patent Literature	Kurzrock_2011_ActivityOfXL184.PDF	854829 ec11031cb1159dad22fed9fae49c672d5e8fd00a	no	7

Warnings:

Information:

3	Fee Worksheet (SB06)	fee-info.pdf	30841 b0bd6cf8a124857d2c2e3e0c9a7aaf5d1a002085	no	2

Warnings:

Information:

Total Files Size (in bytes):	3481850

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

HONIGMAN

Honigman Miller Schwartz and Cohn LLP
Attorneys and Counselors

Meghan M. Klaric

(269) 337-7840
Fax: (269) 337-7841
mklaric@honigman.com

Via EFS

August 4, 2016

Commissioner for Patents
United States Patent and Trademark Office
P. O. Box 1450
Alexandria, VA 22313

Re: ***Application No.: 13/984,559***
Inventor: Jo Ann Wilson
Filing Date: March 20, 2014
Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
Confirmation No.: 6725
Attorney Docket No.: 224990/10-039C-US/343999

Dear Sir or Madam:

Enclosed for filing please find the following documents:

1. This Cover Letter to the Commissioner for Patents;
2. Request for Continued Examination under 37 C.F.R. § 1.114;
3. Request for Continued Examination Transmittal (PTO/SB/30);
4. Information Disclosure Statement (PTO/SB/08A);
5. Non-Patent Literature (1 Document); and
6. Certificate of Transmission under 37 C.F.R. § 1.8(a).

The Applicant notes that the filing of the enclosed Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement qualifies as prior art under 35 U.S.C. §§ 102 or 103, or is considered to be material to patentability as defined in 37 C.F.R § 1.56(b).

It is believed that due for this submission is the $850.00 fee set forth in 37 C.F.R. § 1.17(e)(2) for a small entity filing a second Request for Continued Examination under § 1.114. The Applicant authorizes the Office to charge this $850.00 to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999. It is believed that no additional fees are due at this time. However, if there are any other fees required for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Very truly yours,

HONIGMAN MILLER SCHWARTZ AND COHN LLP

Meghan M. Klaric

Meghan M. Klaric
Reg. No. 71,226

MMK/cwg

Enclosures

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

91684 7590 05/04/2016

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 05/04/2016

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	08/04/2016

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 05/04/2016
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	08/04/2016

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29 — NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

91684 7590 05/04/2016

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 05/04/2016

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 13/984,559	Applicant(s) WILSON ET AL.	
	Examiner TIMOTHY R. ROZOF	Art Unit 1625	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *April 20, 2016, RCE*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *40-47*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/TIMOTHY R ROZOF/
Primary Examiner, Art Unit 1625

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13984559
Filing Date	2014-03-20
First Named Inventor	Jo Ann Wilson
Art Unit	1625
Examiner Name	Timothy R. Rozof
Attorney Docket Number	224990/10-039C-US/343999

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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U.S.PATENT APPLICATION PUBLICATIONS

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2009136663	WO		2009-11-12	TAKEDA PHARMACEUTICAL COMPANY LIMITED		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button

NON-PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13984559
	Filing Date	2014-03-20
	First Named Inventor	Jo Ann Wilson
	Art Unit	1625
	Examiner Name	Timothy R. Rozof
	Attorney Docket Number	224990/10-039C-US/343999

	1		☐

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EXAMINER SIGNATURE

Examiner Signature	/TIMOTHY R ROZOF/	Date Considered	04/28/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1]See Kind Codes of USPTO Patent Documents at www.USPTO.GOVor MPEP 901.04. [2]Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3]For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4]Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5]Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /T.R.R/

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON, JO ANN
	Examiner	Art Unit
	TIMOTHY R ROZOF	1625

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
Class, inventor, STN and EAST search	4/28/2016	TRR

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
A61K	31/47	4/28/2016	TRR
C07D	215/233	4/28/2016	TRR

	/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

CPC							
Symbol						**Type**	**Version**
A61K		31	/	47		F	2013-01-01
C07D		215	/	233		I	2013-01-01
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CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	04/28/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
		A	6	1	K	31 / 47 (2006.01.01)						
CROSS REFERENCE(S)		C	0	7	D	215 / 233 (2006.0)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)											

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625	04/28/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON ET AL.
	Examiner	**Art Unit**
	TIMOTHY R ROZOF	1625

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	40														
2	41														
3	42														
4	43														
5	44														
6	45														
7	46														
8	47														

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 8	
/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625 (Primary Examiner)	04/28/2016 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure NONE

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NEWS 12 JAN 11 PatentPak Now available to STN Express 8.6 and STN on the Web customers
NEWS 13 JAN 11 CAplus Family of Files Updated with New Data to Support PatentPak in STN
NEWS 14 JAN 14 The Derwent World Patents Index (DWPI): Latest Manual Code Revision is now live
NEWS 15 FEB 9 Emtree in Classic STN Updated for 2016 with Additional Thesaurus Fields and Expanded Terminology
NEWS 16 MAR 23 CHEMLIST Content Expanded with the Addition of Information from Vermont
NEWS 17 APR 26 Data Quality Improved in CNFULL and FRFULL

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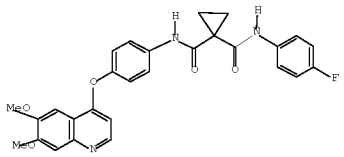
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REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

CAplus includes complete International Patent Classification (IPC) reclassification data for the first quarter of 2016.

CAplus now includes the comprehensive Cooperative Patent Classification (CPC). See HELP CPC for details.

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L4 383 L3

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L4 ANSWER 1 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:559516 CAPLUS full-text
TITLE: Cabozantinib is selectively cytotoxic in acute myeloid leukemia cells with FLT3-internal tandem duplication (FLT3-ITD)
AUTHOR(S): Lu, Jeng-Wei; Wang, An-Ni; Liao, Heng-An; Chen, Chien-Yuan; Hou, Hsin-An; Hu, Chung-Yi; Tien, Hwei-Fan; Ou, Da-Liang; Lin, Liang-In
CORPORATE SOURCE: Department of Clinical Laboratory Sciences and Medical Biotechnology, National Taiwan University, Taipei, Taiwan
SOURCE: Cancer Letters (New York, NY, United States) (2016), 376(2), 218-225
CODEN: CALEDQ; ISSN: 0304-3835
DIGITAL OBJECT ID: 10.1016/j.canlet.2016.04.004
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is an oral multikinase inhibitor that exhibits anti-tumor activity in several cancers. We found that cabozantinib was significantly cytotoxic to MV4-11 and Molm-13 cells that harbored FLT3-ITD, resulting in IC50 values of 2.4 nM and 2.0 nM, resp. However, K562, OCI-AML3 and THP-1 (leukemia cell lines lacking FLT3-ITD) were resistant to cabozantinib, showing IC50 values in the micromolar range. Cabozantinib arrested MV4-11 cell growth at the G0/G1 phase within 24 h, which was associated with decreased phosphorylation of FLT3, STAT5, AKT and ERK. Addnl., cabozantinib induced MV4-11 cell apoptosis in a dose-dependent manner (as indicated by annexin V staining and high levels of cleaved caspase 3 and PARP-1), down-regulated the anti-apoptotic protein survivin and up-regulated the

pro-apoptotic protein Bak. Thus, cabozantinib is selectively cytotoxic to leukemia cells with FLT3-ITD, causing cell-cycle arrest and apoptosis. In mouse xenograft model, cabozantinib significantly inhibited MV4-11 and Molm-13 tumor growth at a dosage of 10 mg/kg and showed longer survival rate. Clin. trials evaluating the efficacy of cabozantinib in acute myeloid leukemia (AML) with FLT3-ITD are warranted.

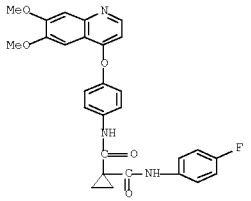
IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib

RL: BSU (Biological study, unclassified); BIOL (Biological study) (cabozantinib as selectively cytotoxic in acute myeloid leukemia cells with FLT3-internal tandem duplication)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:552052 CAPLUS Full-text

DOCUMENT NUMBER: 164:447096

TITLE: Pharmaceutical compositions comprising tyrosine kinase inhibitors for treating enveloped viruses

INVENTOR(S): Einav, Shirit; Neveu, Gregory; Barouch-Bentov, Rina

PATENT ASSIGNEE(S): The Leland Stanford Junior University, USA

SOURCE: PCT Int. Appl., 38pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016054468	A1	20160407	WO 2015-US53638	20151002

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62057037 P 20140929

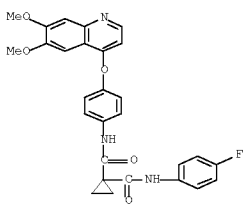
AB Provided herein are methods for identifying and treating cancers that are resistant to PARP inhibition. Methods for sensitizing cancers to a PARP inhibitor therapy are also provided. In some aspects, PARP inhibitor cancers are treated with a PARP inhibitor therapy in combination with a c-Met inhibitor therapy.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prediction of response to PARP inhibitors and combinational therapy of cancer targeting c-met and PARP1 and treatment with other therapy)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62059449 P 20141003

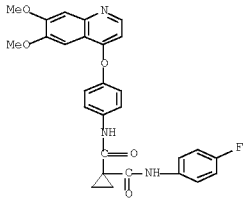
AB Described are compns. such as tyrosine kinase inhibitors (e.g. erlotinib, sunitinib) and methods for treating an enveloped virus in a patient in need thereof. Exemplary enveloped viruses are those in the family Filoviridae and include Ebola virus.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. comprising tyrosine kinase inhibitors for treating enveloped viruses)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 3 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:551762 CAPLUS Full-text

TITLE: Prediction of response to PARP inhibitors and combinational therapy of cancer targeting c-Met and PARP1

INVENTOR(S): Hung, Mien-Chie; Du, Yi

PATENT ASSIGNEE(S): Board of Regent, The University of Texas System, USA

SOURCE: PCT Int. Appl., 103pp.
CODEN: PIXXD2

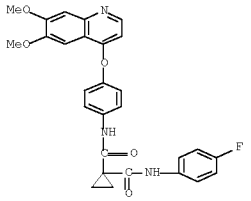
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

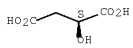
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016054055	A1	20160407	WO 2015-US52966	20150929



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 4 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:534801 CAPLUS Full-text

TITLE: Quick-release medicine phosphatide compound and pharmaceutical composition thereof

INVENTOR(S): Li, Xinsong; Du, Yawei; Ling, Longbing; He, Ruiyu

PATENT ASSIGNEE(S): Southeast University, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 54pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105457038	A	20160406	CN 2015-10756327	20151109

PRIORITY APPLN. INFO.: CN 2015-10756327 20151109

AB The invention discloses a quick-release medicine phosphatide compd. and pharmaceutical composition thereof. In this compound I, medicine Y1 and Y2 are connected with quick-release hydrophobic spacer arm and enhancement type hydrophobic spacer arm through chemical bond. Two kinds of the spacer arms collaborate with each other and strengthen hydrophobic action to form hydrophobic lipophilic chain. Two hydrophobic chains are connected with phospholipid hydrophilic head to constitute amphipathic mol. Pharmaceutical composition is quick-release medicine phosphatide compound or combined medicinal combination of this compound and pharmaceutically acceptable

carrier. The quick-release medicine phosphatide compound and lipidosome nanoparticle thereof can be used as liquid preparation, solid preparation, semi-solid preparation, sterilized preparation and sterile preparation with low toxicity, and can be used for the efficient treatment of diseases such as various tumors.

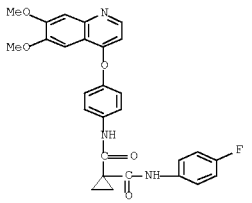
IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quick-release medicine phosphatide compound and pharmaceutical composition thereof)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 5 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:501826 CAPLUS Full-text

DOCUMENT NUMBER: 164:433336

TITLE: Prediction of effect of a c-met inhibitor using mutation of KRAS or BRAF

INVENTOR(S): Shim, Seon Hui; Jung, Soo Yeon; Kim, Kyung Ah

PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea

SOURCE: U.S. Pat. Appl. Publ., 126pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160090635	A1	20160331	US 2015-14869563	20150929
KR 2016037666	A	20160406	KR 2014-130560	20140929
PRIORITY APPLN. INFO.:			KR 2014-130560 A	20140929

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

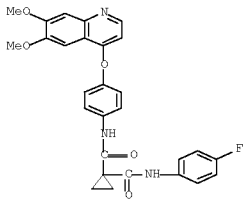
AB A method for predicting and/or monitoring the efficacy of a c-Met inhibitor using a biomarker; a method for selecting a subject suitable for the application of a c-Met inhibitor using a biomarker; and a method for preventing and/or treating cancer comprising administering a c-Met inhibitor to the selected subject. In particular embodiments, provided are biomarkers for use in predicting and/or monitoring the therapeutic effect of a c-Met inhibitor or selecting a subject suitable for the application of a c-Met inhibitor, including IL-8, bIG-H3, KRAS or BRAF and nucleic acids encoding the proteins. Another embodiment provides a c-Met inhibitor or a pharmaceutical composition including a c-Met inhibitor, for use in inhibiting c-Met and/or treating a cancer in a subject, wherein the subject has a higher level of IL-8 or bIG-H3 compared to a reference sample in which a c-Met inhibitor is not effective, and/or has a mutation of KRAS and/or BRAF. KRAS protein comprises at least one amino acid mutation selected from the group consisting of G12A, G12D, G12R, G12C, G12S, G12V, A146T, A59T, L23R, G13N, G13D, I24F, Q61L, Q61H, G13C, and Q61K; and BRAF protein comprises at least one amino acid mutation selected from the group consisting of G596R, V600E, V600K, V600R, K601E, D594G, K601E, G469A, V600M, G469A, V600L, G466V, V600D, G469V, D594G, D594N, N581S, L597V, L597S, L597Q, K601N, G466V, G466E, G464V, and G469E.

IT 849217-68-1, Cabozantinib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prediction of effect of a c-met inhibitor in cancer therapy using mutation of KRAS or BRAF)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 6 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:467583 CAPLUS Full-text

DOCUMENT NUMBER: 164:424395

TITLE: Combination therapies for treatment of cancer

INVENTOR(S): Janes, Matthew Robert; Patricelli, Matthew Peter; Li, Liansheng; Ren, Pingda; Liu, Yi

PATENT ASSIGNEE(S): Araxes Pharma LLC, USA

SOURCE: PCT Int. Appl., 397pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016044772	A1	20160324	WO 2015-US51030	20150918

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.:	US 2014-62052332	P 20140918
	US 2015-62195633	P 20150722

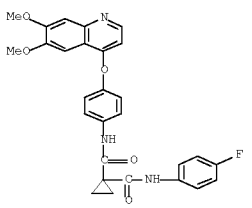
AB Combination therapies for treatment of cancers assocd. with mutations in the KRAS gene are provided. Compns. comprising therapeutic agents for treatment of cancers associated with mutations in the KRAS gene are also provided.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapies for treatment of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:448327 CAPLUS Full-text

TITLE: Expression profiling of small intestinal neuroendocrine tumors identifies subgroups with clinical relevance, prognostic markers and therapeutic targets

AUTHOR(S): Andersson, Ellinor; Arvidsson, Yvonne; Swaerd, Christina; Hofving, Tobias; Waengberg, Bo; Kristiansson, Erik; Nilsson, Ola

CORPORATE SOURCE: Sahlgrenska Cancer Center, Department of Pathology, Institute of Biomedicine, Sahlgrenska Academy at the University of Gothenburg, Goeteborg, Swed.

SOURCE: Modern Pathology (2016) Ahead of Print
CODEN: MODPEO; ISSN: 0893-3952

DIGITAL OBJECT ID: 10.1038/modpathol.2016.48

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We wanted to define the transcriptome of small intestinal neuroendocrine tumors in order to identify clin. relevant subgroups of tumors, prognostic markers and novel targets for treatment. Genome-wide expression profiling was conducted on tumor biopsies from 33 patients with well-differentiated neuroendocrine tumors of the distal ileum and metastatic disease at the time of diagnosis. Unsupervised hierarchical clustering anal. identified three groups of tumors. The largest group, comprising half of the tumors, was characterized by longer patient survival and higher expression of neuroendocrine markers, including SSTR2. Tumors with higher grade (G2/3) or gain of chromosome 14 were associated with shorter patient survival and increased expression of cell cycle-promoting genes. Pathway anal. predicted the prostaglandin E receptor 2 (PTGER2) as the most significantly activated regulator in tumors of higher grade, whereas Forkhead box M1 (FOXM1) was the most significantly activated regulator in tumors with gain of chromosome 14. Druggable genes identified from expression profiles included clin. proven SSTR2 and also novel targets, for example, receptor tyrosine kinases (RET, FGFR1/3, PDGFRB and FLT1), epigenetic regulators, mol. chaperones and signal transduction mols. Evaluation of candidate drug targets on neuroendocrine tumors cells (GOT1) showed significant inhibition of tumor cell growth after treatment with tyrosine kinase inhibitors or inhibitors of HDAC, HSP90 and AKT. In conclusion, we have defined the transcriptome of small intestinal neuroendocrine tumors and identified novel subgroups with clin. relevance. We found specific gene expression patterns associated with tumor grade and chromosomal alterations. Our data also suggest novel prognostic biomarkers and therapies for these patients.

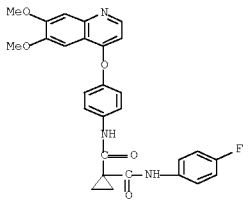
IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression profiling of small intestinal neuroendocrine tumors identifies subgroups with clin. relevance, prognostic markers and therapeutic targets)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:381187 CAPLUS Full-text
DOCUMENT NUMBER: 164:368125
TITLE: Biomarker for predicting sensitivity to protein kinase inhibitor and use thereof
INVENTOR(S): Kim, Tae Won; Jin, Dong Hoon; Hong, Seung Woo; Moon, Jai Hee; Shin, Jae Sik; Lee, Ha Reum; Choi, Eun Kyoung; Kim, Seung Mi; Jung, Soo A.; Ha, Seung Hee; Jung, Ha Na; Lee, Dae Hee; Jung, Seang Hwan; Lee, Jung Shin; Choi, Eun Kyung; Lee, Jae Lyun; Hong, Yong Sang; Kim, Kyu Pyo; Kim, Jeong Eun; Park, Seong Joon; Kim, Bong Choel
PATENT ASSIGNEE(S): CJ HealthCare Corporation, S. Korea
SOURCE: PCT Int. Appl., 60pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016036172	A1	20160310	WO 2015-KR9322	20150903

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

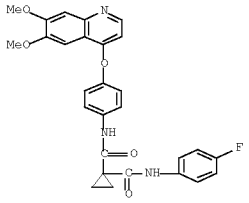
KR 2016028399	A	20160311	KR 2015-125055	20150903

PRIORITY APPLN. INFO.: KR 2014-116787 A 20140903

AB The present invention relates to a biomarker for predicting the sensitivity of cells to a protein kinase inhibitor and a use thereof, a composition, a kit, and a prediction method. The biomarker comprises splicing variant or mutant of RON gene. According to the present invention, an effect of predicting sensitivity to a protein kinase inhibitor is excellent, and thus the present invention can be useful for cancer treatment.
IT 1140909-48-3, XL-184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active RON-containing biomarker for predicting cell sensitivity to protein kinase inhibitor)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

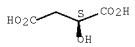
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

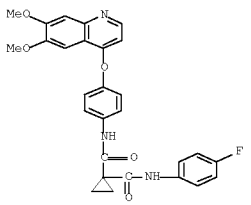
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:352953 CAPLUS Full-text
TITLE: Delineation of Polypharmacology across the Human Structural Kinome Using a Functional Site Interaction Fingerprint Approach
AUTHOR(S): Zhao, Zheng; Xie, Li; Xie, Lei; Bourne, Philip E.
CORPORATE SOURCE: National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, MD, 20894, USA
SOURCE: Journal of Medicinal Chemistry (2016) Ahead of Print
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/acs.jmedchem.5b02041
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

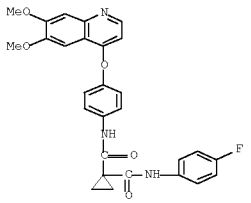
AB Targeted polypharmacol. of kinases has emerged as a promising strategy to design efficient and safe therapeutics. Here, we perform a systematic study of kinase-ligand binding modes for the human structural kinome at scale (208 kinases, 1777 unique ligands, and their complexes) by integrating chemical genomics and structural genomics data and by introducing a functional site interaction fingerprint (Fs-IFP) method. New insights into kinase-ligand binding modes were obtained. We establish relationships between the features of binding modes, the ligands, and the binding pockets, resp. We also drive the intrinsic binding specificity and which correlation with amino acid conservation. Third, we explore the landscape of the binding modes and highlight the regions of "selectivity pocket" and "selectivity entrance". Finally, we demonstrate that Fs-IFP similarity is directly correlated to the exptl. determined profile. These improve our understanding of kinase-ligand interactions and contribute to the design of novel polypharmacol. therapies targeting kinases.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delineation of polypharmacol. across structural kinome using functional site interaction fingerprint approach)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

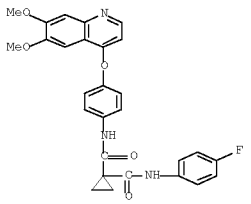
L4 ANSWER 10 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:342498 CAPLUS Full-text
DOCUMENT NUMBER: 164:380608
TITLE: Exploiting Temporal Collateral Sensitivity in Tumor Clonal Evolution
AUTHOR(S): Zhao, Boyang; Sedlak, Joseph C.; Srinivas, Raja; Creixell, Pau; Pritchard, Justin R.; Tidor, Bruce; Lauffenburger, Douglas A.; Hemann, Michael T.
CORPORATE SOURCE: Computational and Systems Biology Program, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SOURCE: Cell (Cambridge, MA, United States) (2016), 165(1), 234-246
CODEN: CELLB5; ISSN: 0092-8674
DIGITAL OBJECT ID: 10.1016/j.cell.2016.01.045
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB The prevailing approach to addressing secondary drug resistance in cancer focuses on treating the resistance mechanisms at relapse. However, the dynamic nature of clonal evolution, along with potential fitness costs and cost compensations, may present exploitable vulnerabilities-a notion that we term "temporal collateral sensitivity.". Using a combined pharmacol. screen and drug resistance selection approach in a murine model of Ph+ acute lymphoblastic leukemia, we indeed find that temporal and/or persistent collateral sensitivity to non-classical BCR-ABL1 drugs arises in emergent tumor subpopulations during the evolution of resistance toward initial treatment with BCR-ABL1-targeted inhibitors. We determined the sensitization mechanism via genotypic, phenotypic, signaling, and binding measurements in combination with computational models and demonstrated significant overall survival extension in mice. Addnl. stochastic math. models and small-mol. screens extended our insights, indicating the value of focusing on evolutionary trajectories and pharmacol. profiles to identify new strategies to treat dynamic tumor vulnerabilities.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exploiting temporal collateral sensitivity in tumor clonal evolution)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



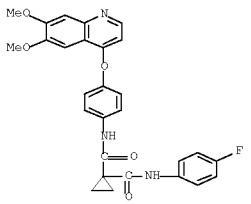
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:333433 CAPLUS Full-text
TITLE: Population pharmacokinetic/pharmacodynamic modeling of tumor growth kinetics in medullary thyroid cancer patients receiving cabozantinib
AUTHOR(S): Miles, Dale R.; Wada, David R.; Jumbe, Nelson L.; Lacy, Steven A.; Nguyen, Linh T.
CORPORATE SOURCE: Exelixis Inc., San Francisco, CA, USA
SOURCE: Anti-Cancer Drugs (2016), 27(4), 328-341
CODEN: ANTDEV; ISSN: 0959-4973
DIGITAL OBJECT ID: 10.1097/CAD.0000000000000330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Nonlinear mixed effects models were developed to describe the relationship between cabozantinib exposure and target lesion tumor size in a phase III study of patients with progressive metastatic medullary thyroid cancer. These models used cabozantinib exposure ests. from a previously published population pharmacokinetic model for cabozantinib in cancer patients that was updated with data from healthy-volunteer studies. Semi-mechanistic models predict well for tumors with static, increasing, or decreasing growth over time, but they were not considered adequate for predicting tumor sizes in medullary thyroid cancer patients, among whom an early reduction in tumor size was followed by a late stabilization phase in those receiving cabozantinib. A semi-empirical tumor model adequately predicted tumor profiles that were assumed to have a net growth rate constant that was piecewise continuous in the regions of 0-110 and 110-280 days. Emax models relating average concentration to average change in tumor size predicted that an average concentration of 79 and 58 ng/mL, resp., would yield 50% of the maximum possible tumor reduction during the first 110 days of dosing and during the subsequent 110-280 days of dosing. Simulations of tumor responses showed that daily doses of 60 mg or greater are expected to provide a similar tumor reduction Both model evaluation of observed data and simulation results suggested that the two protocol-defined cabozantinib dose redns. from 140 to 100 mg/day and from 100 to 60 mg/day are not projected to result in a marked reduction in target lesion regrowth.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (population pharmacokinetic/pharmacodynamic modeling of tumor growth kinetics in medullary thyroid cancer patients receiving cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



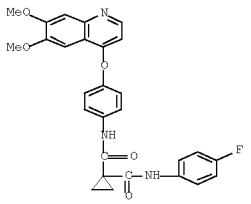
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:249149 CAPLUS Full-text
DOCUMENT NUMBER: 164:320714
TITLE: The discovery of 2-substituted phenol quinazolines as potent RET kinase inhibitors with improved KDR selectivity
AUTHOR(S): Newton, Rebecca; Bowler, Katherine A.; Burns, Emily M.; Chapman, Philip J.; Fairweather, Emma E.; Fritzl, Samantha J. R.; Goldberg, Kristin M.; Hamilton, Niall M.; Holt, Sarah V.; Hopkins, Gemma V.; Jones, Stuart D.; Jordan, Allan M.; Lyons, Amanda J.; Nikki March, H.; McDonald, Neil Q.; Maguire, Laura A.; Mould, Daniel P.; Purkiss, Andrew G.; Small, Helen F.; Stowell, Alexandra I. J.; Thomson, Graeme J.; Waddell, Ian D.; Waszkowycz, Bohdan; Watson, Amanda J.; Ogilvie, Donald J.
CORPORATE SOURCE: Cancer Research UK Manchester Institute, Drug Discovery Unit, University of Manchester, Withington, M20 4BX, UK
SOURCE: European Journal of Medicinal Chemistry (2016), 112, 20-32
CODEN: EJMCA5; ISSN: 0223-5234
DIGITAL OBJECT ID: 10.1016/j.ejmech.2016.01.039
PUBLISHER: Elsevier Masson SAS
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Deregulation of the receptor tyrosine kinase RET has been implicated in medullary thyroid cancer, a small percentage of lung adenocarcinomas, endocrine-resistant breast cancer and pancreatic cancer. There are several clin. approved multi-kinase inhibitors that target RET as a secondary pharmacol. but addnl. activities, most notably inhibition of KDR, lead to dose-limiting toxicities. There is, therefore, a clin. need for more specific RET kinase inhibitors. Herein we report our efforts towards identifying a potent and selective RET inhibitor using vandetanib 1 as the starting point for structure-based drug design. Phenolic anilinoquinazolines exemplified by 6 showed improved affinities towards RET but, unsurprisingly, suffered from high metabolic clearance. Efforts to mitigate the metabolic liability of the phenol led to the discovery that a flanking substituent not only improved the hepatocyte stability, but could also impart a significant gain in selectivity. This culminated in the identification of 36; a potent RET inhibitor with much improved selectivity against KDR.
IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (phenol quinazolines preparation as RET kinase inhibitors with improved KDR selectivity and potential as antitumor agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:237680 CAPLUS Full-text
TITLE: Patterns in target-directed breast cancer research
AUTHOR(S): Torres, Sofia; Simmons, Christine; Boileau, Jean-Francois; McLeod, Deanna; Martins, Ilidio; Trudeau, Maureen
CORPORATE SOURCE: Sunnybrook Health Sciences Centre, Toronto, ON, M4N 3M5, Can.
SOURCE: SpringerPlus (2016), 5(1), 1-15
CODEN: SPRIFB; ISSN: 2193-1801
DIGITAL OBJECT ID: 10.1186/s40064-016-1736-1
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB We undertake an anal. of ongoing BC targeted therapy trials registered to CT.gov to describe patterns of ongoing clin. research, highlight gaps in current research programs and identify ways of optimizing ongoing initiatives. A search of clinicaltrials.gov was conducted on Sept. 4, 2013 to identify ongoing randomized phase II and III trials of targeted therapies in BC. A total of 280 trials were analyzed, the majority conducted in either human epidermal growth factor receptor 2 (HER2)-pos. (n = 79, 28.2 %) or hormone receptor (HR)-pos. (n = 104, 37.1 %) populations. Less than half of all trials were conducted in populations selected to match the agent under investigation (n = 126, 45 %). HER2-directed therapy is the single most investigated class of targeted agents (n = 73, 26.1 %), but trials investigating anti-angiogenic agents are also common (n = 49, 17.5 %). The most common new classes of agents under investigation in HR-pos. and triple neg. (TN)/BRCA-pos. disease, are non-receptor protein kinase-inhibitors (n = 12; 11.5 %) and poly (ADP-ribose) polymerase inhibitors (n = 6; 30 %), resp. The majority of regimens combine new targeted agents with either chemotherapy (n = 164, 58.6 %) or endocrine therapy (n = 113, 40.4 %); a total of 8 trials (2.8 %) investigated peptide-drug conjugates. The most frequently utilized end-points were pathol. complete response in the neo-adjuvant setting (n = 36, 52.9 %) and time-to-event end-points in the adjuvant and advanced settings (77.3 and 72.6 %, resp.). Our findings suggest a need for more target-matched agent development, maintenance of a value-based focus in research and a need for the clin. development of agents to treat TN/BRCA-pos. and HR-pos. BC.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (patterns in target-directed breast cancer research)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



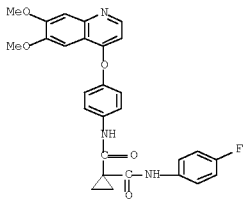
REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:226918 CAPLUS Full-text
TITLE: Chemical Proteomics Reveals Ferrochelatase as a Common Off-target of Kinase Inhibitors
AUTHOR(S): Klaeger, Susan; Gohlke, Bjoern; Perrin, Jessica; Gupta, Vipul; Heinzlmeir, Stephanie; Helm, Dominic; Qiao, Huichao; Bergamini, Giovanna; Handa, Hiroshi; Savitski, Mikhail M.; Bantscheff, Marcus; Medard, Guillaume; Preissner, Robert; Kuster, Bernhard
CORPORATE SOURCE: Chair of Proteomics and Bioanalytics, Technical University of Munich, Freising, Germany
SOURCE: ACS Chemical Biology (2016) Ahead of Print
CODEN: ACBCCT; ISSN: 1554-8929
DIGITAL OBJECT ID: 10.1021/acschembio.5b01063
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Many protein kinases are valid drug targets in oncol. because they are key components of signal transduction pathways. The number of clin. kinase inhibitors is on the rise, but these mols. often exhibit polypharmacol., potentially eliciting desired and toxic effects. Therefore, a comprehensive assessment of a compound's target space is desirable for a better understanding of its biol. effects. The enzyme ferrochelatase (FECH) catalyzes the conversion of protoporphyrin IX into heme and was recently found to be an off-target of the BRAF inhibitor Vemurafenib, likely explaining the phototoxicity associated with this drug in melanoma patients. This raises the question of whether FECH binding is a more general feature of kinase inhibitors. To address this, we applied a chemical proteomics approach using kinobeads to evaluate 226 clin. kinase inhibitors for their ability to bind FECH. Surprisingly, low or submicromolar FECH binding was detected for 29 of all compds. tested and isothermal dose response measurements confirmed target engagement in cells. We also show that Vemurafenib, Linsitinib, Neratinib, and MK-2461 reduce heme levels in K562 cells, verifying that drug binding leads to a loss of FECH activity. Further biochem. and docking expts. identified the protoporphyrin pocket in FECH as one major drug binding site. Since the genetic loss of FECH activity leads to photosensitivity in humans, our data strongly suggest that FECH inhibition by kinase inhibitors is the mol. mechanism triggering photosensitivity in patients. We therefore suggest that a FECH assay should generally be part of the preclin. mol. toxicol. package for the development of kinase inhibitors.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical proteomics reveals ferrochelatase as a common off-target of kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:224790 CAPLUS Full-text
DOCUMENT NUMBER: 164:293822
TITLE: Drug combinations to treat multiple myeloma
INVENTOR(S): Aftab, Dana T.; Lamb, Peter
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016022697	A1	20160211	WO 2015-US43825	20150805

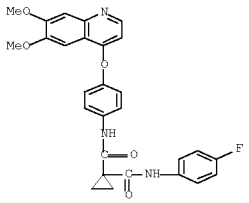
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62033386 P 20140805
OTHER SOURCE(S): MARPAT 164:293822

AB This invention relates to the combination of a C-Met inhibitor and a proteasome inhibitor to treat cancer, particularly multiple myeloma.

IT 849217-68-1P
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug combinations to treat multiple myeloma)

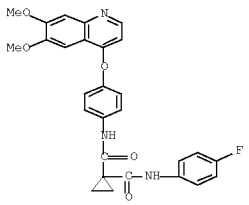
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P 1365530-43-3P 1634653-27-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug combinations to treat multiple myeloma)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

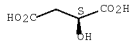
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

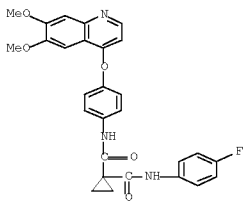
Absolute stereochemistry. Rotation (-).



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

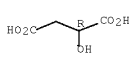
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

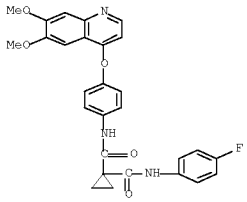


RN 1634653-27-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

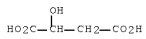
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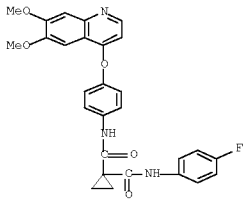


CM 2

CRN 6915-15-7
CMF C4 H6 O5

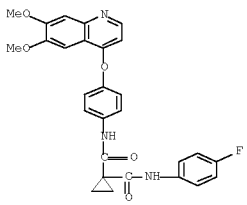


IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations to treat multiple myeloma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

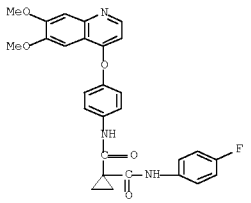
L4 ANSWER 17 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:219788 CAPLUS Full-text
TITLE: Phase 1 dose escalation trial of the safety and pharmacokinetics of cabozantinib concurrent with temozolomide and radiotherapy or temozolomide after radiotherapy in newly diagnosed patients with high-grade gliomas
AUTHOR(S): Schiff, David; Desjardins, Annick; Cloughesy, Timothy; Mikkelsen, Thomas; Glantz, Michael; Chamberlain, Marc C.; Reardon, David A.; Wen, Patrick Y.
CORPORATE SOURCE: Department of Neurology, Neuro-Oncology Center, University of Virginia Medical Center, Charlottesville, VA, USA
SOURCE: Cancer (Hoboken, NJ, United States) (2016), 122(4), 582-587
CODEN: CANCAR; ISSN: 0008-543X
DIGITAL OBJECT ID: 10.1002/cncr.29798
PUBLISHER: Wiley-Blackwell



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:222043 CAPLUS Full-text
DOCUMENT NUMBER: 164:270659
TITLE: Interaction of new kinase inhibitors cabozantinib and tofacitinib with human serum alpha-1 acid glycoprotein. A comprehensive spectroscopic and molecular Docking approach
AUTHOR(S): Ajmal, Mohammad Rehan; Abdelhameed, Ali Saber; Alam, Parvez; Khan, Rizwan Hasan
CORPORATE SOURCE: Interdisciplinary Biotechnology Unit, Aligarh Muslim University, Aligarh, 202002, India
SOURCE: Spectrochimica Acta, Part A: Molecular and Biomolecular Spectroscopy (2016), 159, 199-208
CODEN: SAMCAS; ISSN: 1386-1425
DIGITAL OBJECT ID: 10.1016/j.saa.2016.01.049
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In the current study we have investigated the interaction of newly approved kinase inhibitors namely Cabozantinib (CBZ) and Tofacitinib (TFB) with human Alpha-1 acid glycoprotein (AAG) under simulated physiol. conditions using fluorescence quenching measurements, CD, dynamic light scattering and mol. docking methods. CBZ and TFB binds to AAG with significant affinity and the calculated binding constant for the drugs lie in the order of 104. With the increase in temperature the binding constant values decreased for both CBZ and TFB. The fluorescence resonance energy transfer (FRET) from AAG to CBZ and TFB suggested the fluorescence intensity of AAG was quenched by the two studied drugs via the formation of a non-fluorescent complex in the static manner. The mol. distance r value calculated from FRET is around 2 nm for both drugs, fluorescence spectroscopy data was employed for the study of thermodn. parameters, standard Gibbs free energy change at 300K was calculated as - 5.234 kcal mol- 1 for CBZ-AAG interaction and - 6.237 kcal mol- 1 for TFB-AAG interaction, standard enthalpy change and standard entropy change for CBZ-AAG interaction are - 9.553 kcal mol- 1 and - 14.618 cal mol- 1K- 1 resp. while for AAG-TFB interaction, standard enthalpy and standard entropy change was calculated as 4.019 kcal mol- 1 and 7.206 cal mol- 1K- 1 resp. Protein binding of the two drugs caused the tertiary structure alterations. Dynamic light scattering measurements demonstrated the reduction in the hydrodynamic radii of the protein. Furthermore mol. docking results suggested the Hydrophobic interaction and hydrogen bonding were the interactive forces in the binding process of CBZ to AAG while in case of TFB only hydrophobic interactions were found to be involved, overlap of the binding site for two studied drugs on the AAG mol. was revealed by docking results.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor drugs cabozantinib and tofacitinib interaction with serum α1-acid glycoprotein)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

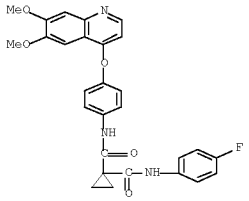
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB BACKGROUND : Cabozantinib inhibits mesenchymal-epithelial transition factor (MET) and vascular endothelial growth factor receptor 2 (VEGFR2) and has demonstrated activity in patients with recurrent glioblastoma, warranting evaluation of the addition of cabozantinib to radiotherapy (RT) and temozolomide (TMZ) for patients with newly diagnosed high-grade glioma. METHODS : Cabozantinib doses of 40 mg and 60 mg were explored. Patients on the concurrent treatment arm received cabozantinib daily with standard TMZ and after RT continued cabozantinib daily with adjuvant TMZ. In the maintenance arm, patients who completed RT and ≥1 adjuvant cycle of TMZ continued adjuvant TMZ with added cabozantinib (3 schedules: days 1-28, days 1-14, or days 8-21). RESULTS : A total of 26 patients (25 with recurrent glioblastoma and 1 patient with anaplastic astrocytoma) aged 30 to 72 years were enrolled (10 to the concurrent arm and 16 to the maintenance arm). The median number of post-RT TMZ cycles was 4.5 (range, 0-14 cycles) in the concurrent arm and 5.5 (range, 1-12 cycles) in the maintenance arm. Cabozantinib at a dose of 60 mg daily was the maximum administered dose and a dose of 40 mg daily was determined to be the maximum tolerated dose for both treatment arms (schedule of days 1-28). The most frequent grade 3/4 adverse events were thrombocytopenia (31% of patients), leukopenia (27% of patients, including 5 patients with neutropenia), and deep vein thrombosis and/or pulmonary embolism (23% of patients) (adverse events were graded according to the National Cancer Institute Common Terminol. Criteria for Adverse Events [version 3.0]). CONCLUSIONS : Cabozantinib at a dose of 40 mg daily with RT plus TMZ and post-RT TMZ for patients with newly diagnosed high-grade glioma was generally well tolerated, and demonstrated no pharmacokinetic interactions with concurrent TMZ. Given the strong theor. rationale for combining anti-VEGF and anti-MET activity with standard therapy, cabozantinib at a dose of 40 mg daily warrants evaluation in combination with standard therapy for patients with newly diagnosed glioblastoma. Cancer 2016;122:582-587. © 2015 American Cancer Society.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phase 1 dose escalation trial of safety and pharmacokinetics of cabozantinib concurrent with temozolomide and radiotherapy or temozolomide after radiotherapy in newly diagnosed patients with high-grade gliomas)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 18 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:196080 CAPLUS Full-text
DOCUMENT NUMBER: 164:318691
TITLE: Hydrophilic drug phospholipid, its pharmaceutical composition and application
INVENTOR(S): Li, Xinsong; Xu, Chen; Du, Yawei; Ling, Longbing; Hou, Yongpeng
PATENT ASSIGNEE(S): Southeast University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 38pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105288648	A	20160203	CN 2015-10661316	20151014

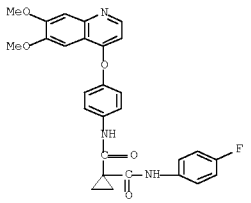
PRIORITY APPLN. INFO.: CN 2015-10661316 20151014
OTHER SOURCE(S): MARPAT 164:318691
AB The present invention discloses a hydrophilic drug phospholipid, its pharmaceutical composition and application. the pharmaceutical composition is hydrophilic drug phospholipid or the composition of the combination drug of hydrophilic drug phospholipid and pharmacodynamic acceptable carrier, it can be liquid formulation, solid prepns., semi-solid formulation, capsules, granules, gels, injection. the pharmaceutical composition is liposomal nanoparticle formed by hydrophilic drug phospholipid or hydrophilic drug phospholipid and additives, the particle size is 10-1000 nm. the hydrophilic drug phospholipid and its liposomal nanoparticles can be used as the liquid formulations, solid prepns., semi-solid formulation, sterilized prepns. and sterile preparation, have low toxicity, can be used effective treatment for various tumors.
IT 849217-68-1, Cabozantinib
RL: NANO (Nanomaterial); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic drug phospholipid, its pharmaceutical composition and application)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 19 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:193681 CAPLUS Full-text
DOCUMENT NUMBER: 164:245721
TITLE: Use of HSP90 as marker for predicting efficacy of c-Met inhibitor in treatment of cancer
INVENTOR(S): Lee, Ji Min; Kim, Bo Gyou; Oh, Seung Ja; Kim, Kyung Ah; Lee, Saet Byoul; Hwang, Jae Woong
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 94pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160030559	A1	20160204	US 2015-14814278	20150730
KR 2016015076	A	20160212	KR 2014-97560	20140730

PRIORITY APPLN. INFO.: KR 2014-97560 A 20140730
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention relates to the use of heat shock protein 90 (Hsp90) as marker for predicting an efficacy of a c-Met inhibitor, selecting a subject for application of a c-Met inhibitor, or monitoring an efficacy of a c-Met inhibitor, and a relevant method of using Hsp90 for treatment of cancer.
IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of HSP90 as marker for predicting efficacy of c-Met inhibitor in treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



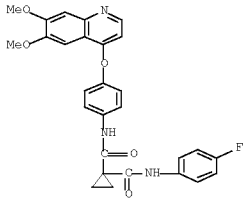
L4 ANSWER 20 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:188602 CAPLUS Full-text
DOCUMENT NUMBER: 164:277127
TITLE: Preparation of acetylcyclopentylmethylaminopyridopyrimidinone derivatives for use as CDK small-molecule inhibitors
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 117pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015597	A1	20160204	WO 2015-CN84983	20150723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294681	A	20160203	CN 2015-10439329	20150723
CN 105294682	A	20160203	CN 2015-10439488	20150723
CN 105294736	A	20160203	CN 2015-10443167	20150724

PRIORITY APPLN. INFO.: CN 2014-10361634 A 20140726
CN 2015-10076030 A 20150212
OTHER SOURCE(S): MARPAT 164:277127
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [B = Ph, pyridazinyl, pyrimidinyl, pyrazinyl, etc.; L = bond, CH2, CH2CH2, CH2NHCH2, etc.; R1 and R2 independently = H, F, Cl, Br, OH, alkyl, etc.; R3 = H, heteroaryl, cycloalkyl, heterocyclyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as CDK small-mol. inhibitors. Thus, e.g., II was prepared by a multistep procedure (preparation given). Select I were evaluated in CDK4 and CDK6 enzymic inhibition activity assays, e.g., II demonstrated IC50 values of 18 nM and 35 nM, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of acetylcyclopentylmethylaminopyridopyrimidinone derivs. for use as CDK small-mol. inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



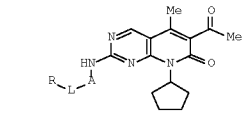
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:186216 CAPLUS Full-text
DOCUMENT NUMBER: 164:277126
TITLE: 2-Aminopyrido[2,3-d]pyrimidin-7(8H)-one derivatives as
CDK inhibitors and their preparation
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

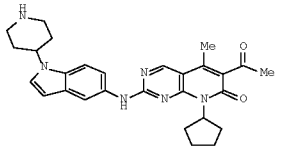
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015598	A1	20160204	WO 2015-CN84984	20150723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294681	A	20160203	CN 2015-10439329	20150723
CN 105294682	A	20160203	CN 2015-10439488	20150723
CN 105294736	A	20160203	CN 2015-10443167	20150724
PRIORITY APPLN. INFO.:			CN 2014-10361634 A	20140726
			CN 2015-10076030 A	20150212

OTHER SOURCE(S): MARPAT 164:277126
GI



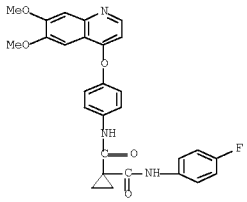
I



II

AB The invention provides substituted 2-aminopyrido[2,3-d]pyrimidin-7(8H)-one compds. of formula I, which can be used for treating inflammation and cell proliferation diseases. The compound of the invention is a powerful cyclin-dependent kinase 4 (CDK 4) or cyclin-dependent kinase 6 (CDK 6) inhibitor. Compds. of formula I wherein L is a bond, (un)substituted C0-4 alkylene, (un)substituted amino-C0-4 alkyl, (un)substituted O-C0-4 alkyl, etc.; A is bicyclic heteroaryl, and bicyclic heterocyclyl; R is H, C3-9 cycloalkyl, C1-9 heteroaryl, C2-9 heterocyclyl, etc.; and stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). The invention compds. were evaluated for their CDK inhibitory activity. From the assay, it was determined that compound II exhibited IC50 values of 6.8 nM and 29.2 nM toward CDK4 and CDK6, resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of aminopyridopyrimidinone derivs. as CDK inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

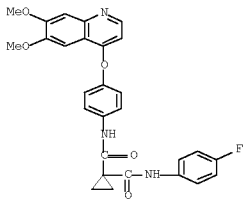


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:185751 CAPLUS Full-text
DOCUMENT NUMBER: 164:277125
TITLE: 6-[2-(Pyridinyl-2-ylamino)pyrimidin-4-yl]imidazole compounds as CDK inhibitors and their preparation
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 278pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015605	A1	20160204	WO 2015-CN85036	20150724
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294683	A	20160203	CN 2015-10444529	20150724
CN 105294655	A	20160203	CN 2015-10447867	20150724
PRIORITY APPLN. INFO.:			CN 2014-10362374 A	20140726
			CN 2015-10015255 A	20150113

OTHER SOURCE(S): MARPAT 164:277125
GI



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:185021 CAPLUS Full-text
DOCUMENT NUMBER: 164:264663
TITLE: Preparation of isopropylmethylbenzoimidazolylpyrimidine derivatives for use as CDK small-molecule inhibitors
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 125pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

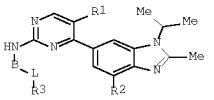
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015604	A1	20160204	WO 2015-CN85034	20150724
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294683	A	20160203	CN 2015-10444529	20150724
CN 105294655	A	20160203	CN 2015-10447867	20150724
PRIORITY APPLN. INFO.:			CN 2014-10362374 A	20140726
			CN 2015-10015255 A	20150113

OTHER SOURCE(S): MARPAT 164:264663
GI

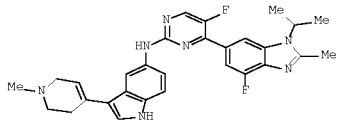
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides substituted 6-[2-(pyridinyl-2-ylamino)pyrimidin-4-yl]imidazole compds. of formula I, which can be used for treating inflammation and cell proliferation diseases. The compound of the invention is a powerful cyclin-dependent kinase 4 (CDK 4) or cyclin-dependent kinase-6 (CDK 6) inhibitor. Compds. of formula I wherein R1 and R2 are independently H, F, Cl, Br, OH, C1-4 alkyl, etc.; L1 is a bond, (un)substituted C0-4 alkylene, (un)substituted C0-4 alkoxy-C0-4 alkylene, (un)substituted C0-4 alkylamino-C0-4 alkyl, etc.; R3 is (spiro/bridge/fused) C5-12 heterobicyclyl, C1-9 heteroaryl, C6-12 aryl, etc.; and stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). The invention compds. were evaluated for their CDK inhibitory activity (some data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of [(pyridinylamino)pyrimidinyl]benzimidazoles as CDK inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



I



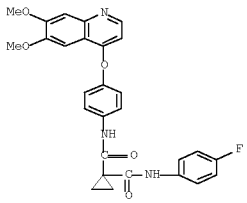
II

AB Title compds. I [B = Ph, pyridazinyl, pyrimidinyl, pyrazinyl, etc.; L = bond, CH2, CH2CH2, CH2NHCH2, etc.; R1 and R2 independently = H, F, Cl, Br, OH, alkyl, etc.; R3 = H, heteroaryl, cycloalkyl, heterocyclyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as CDK small-mol. inhibitors. Thus, e.g., II was prepared by amination of 6-(2-chloro-5-fluoropyrimidin-4-yl)-4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazole with 3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1H-indol-5-amine. Select I were evaluated in enzymic inhibition activity assays (data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of isopropylmethylbenzoimidazolylpyrimidine derivs. for use as CDK small-mol. inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:184907 CAPLUS Full-text

DOCUMENT NUMBER: 164:251528

TITLE: Method of preparing fluorine-18 labeled cabozantinib and its analogs

INVENTOR(S): Xu, Wei; Donnelly, David J.; Chow, Patrick L.; Henley, Benjamin J.

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016019285	A1	20160204	WO 2015-US43195	20150731

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62031471 P 20140731

OTHER SOURCE(S): MARPAT 164:251528

GI

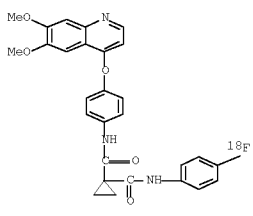
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a method of prepg. compds. of I [wherein R1 and R2 = independently alkoxy or haloalkoxy; R3 = H, F, Cl, etc.; R4 = F, 18F, Cl, etc.] such as cabozantinib II, R4 = F, and [18F]-II, R4 = 18F, comprising the reaction of 4-aminophenol with 4-chloro-6,7-dimethoxyquinoline yielding the ether intermediate, III, which undergoes coupling with 1-carboxycyclopropanecarbonyl chloride providing IV, followed by amidation of IV with 4-fluoroaniline or [18F]-4-fluoroaniline under microwave heating yielding cabozantinib or [18F]-labeled cabozantinib. [18F]-II was administered to mice implanted with U87 tumors (glioblastoma) and to tumor-free animals. PET imaging resulted in visualization of the tumors in the brains of the tumor bearing animals and little or no uptake of [18F]-II in control animals suggesting [18F]-II does not cross the blood brain barrier in tumor-free mice but has significant uptake in U87 implanted mice.

IT 1870906-64-1P
RL: DGN (Diagnostic use); IMF (Industrial manufacture); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of preparing fluorine-18 labeled cabozantinib and its analogs)

RN 1870906-64-1 CAPLUS

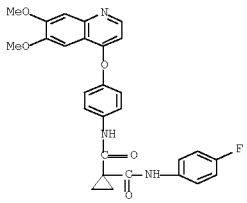
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[4-(fluoro-18F)phenyl]- (CA INDEX NAME)



IT 849217-68-1P, Cabozantinib
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of preparing fluorine-18 labeled cabozantinib and its analogs)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:145922 CAPLUS Full-text

TITLE: A Phase II Trial of the Multitargeted Tyrosine Kinase Inhibitor Lenvatinib (E7080) in Advanced Medullary Thyroid Cancer

AUTHOR(S): Schlumberger, Martin; Jarzab, Barbara; Cabanillas, Maria E.; Robinson, Bruce; Pacini, Furio; Ball, Douglas W.; McCaffrey, Judith; Newbold, Kate; Allison, Roger; Martins, Renato G.; Licitra, Lisa F.; Shah, Manisha H.; Bodenner, Donald; Elisei, Rossella; Burmeister, Lynn; Funahashi, Yasuhiro; Ren, Min; O'Brien, James P.; Sherman, Steven I.

CORPORATE SOURCE: Department of Nuclear Medicine and Endocrine Oncology, Institut Gustave-Roussy and University Paris-Sud, Villejuif, Fr.

SOURCE: Clinical Cancer Research (2016), 22(1), 44-53
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-1127

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: Pos. results of phase I studies evaluating lenvatinib in solid tumors, including thyroid cancer, prompted a phase II trial in advanced medullary thyroid carcinoma (MTC). Exptl. Design: Fifty-nine patients with unresectable progressive MTC per Response Evaluation Criteria In Solid Tumors (RECIST) v1.0 within the prior 12 mo received lenvatinib (24-mg daily, 28-day cycles) until disease progression, unmanageable toxicity, withdrawal, or death. Prior anti-VEGFR therapy was permitted. The primary endpoint was objective response rate (ORR) by RECIST v1.0 and independent imaging review. Results: Lenvatinib ORR was 36% [95% confidence interval (CI), 24%-49%]; all partial responses. ORR was comparable between patients with (35%) or without (36%) prior anti-VEGFR therapy. Disease control rate (DCR) was 80% (95% CI, 67%-89%); 44% had stable disease. Among responders, median time to response (TTR) was 3.5 mo (95% CI, 1.9-3.7). Median progression-free survival (PFS) was 9.0 mo (95% CI, 7.0-not evaluable). Common toxicity criteria grade 3/4 treatment-emergent adverse events included diarrhea (14%), hypertension (7%), decreased appetite (7%),

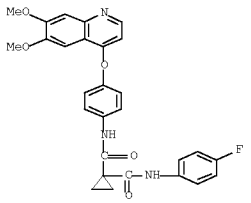
fatigue, dysphagia, and increased alanine aminotransferase levels (5% each). Ret proto-oncogene status did not correlate with outcomes. Low baseline levels of angiopoietin-2, hepatocyte growth factor, and IL8 were associated with tumor reduction and prolonged PFS. High baseline levels of VEGF, soluble VEGFR3, and platelet-derived growth factor BB, and low baseline levels of soluble Tie-2, were associated with tumor reduction Conclusions: Lenvatinib had a high ORR, high DCR, and a short TTR in patients with documented progressive MTC. Toxicities were managed with dose modifications and medications. Clin Cancer Res; 22(1); 44-53. ©2015 AACR.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(efficacy and safety of multitargeted tyrosine kinase inhibitor lenvatinib was evaluated for treatment of advanced medullary thyroid cancer in patients)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:145903 CAPLUS Full-text

TITLE: Integrating Murine and Clinical Trials with Cabozantinib to Understand Roles of MET and VEGFR2 as Targets for Growth Inhibition of Prostate Cancer

AUTHOR(S): Varkaris, Andreas; Corn, Paul G.; Parikh, Nila U.; Efstathiou, Eleni; Song, Jian H.; Lee, Yu-Chen; Aparicio, Ana; Hoang, Anh G.; Gaur, Sanchaika; Thorpe, Lynnelle; Maity, Sankar N.; Bar Eli, Menashe; Czerniak, Bogdan A.; Shao, Yiping; Alauddin, Mian; Lin, Sue-Hwa; Logothetis, Christopher J.; Gallick, Gary E.

CORPORATE SOURCE: Department of Genitourinary Medical Oncology, David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

SOURCE: Clinical Cancer Research (2016), 22(1), 107-121
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-0235

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

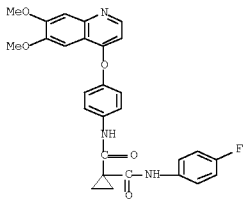
AB Purpose: We performed parallel investigations in cabozantinib-treated patients in a phase II trial and simultaneously in patient-derived xenograft (PDX) models to better understand the roles of MET and VEGFR2 as targets for prostate cancer therapy. Exptl. Design: In the clin. trial, radiog. imaging and serum markers were examined, as well as mol. markers in tumors from bone biopsies. In mice harboring PDX intrafemurally or s.c., cabozantinib effects on tumor growth, MET, PDX in which MET was silenced, VEGFR2, bone turnover, angiogenesis, and resistance were examined Results: In responsive patients and PDX, islets of viable pMET-pos. tumor cells persisted, which rapidly regrew after drug withdrawal. Knockdown of MET in PDX did not affect tumor growth in mice nor did it affect cabozantinib-induced growth inhibition but did lead to induction of FGFR1. Inhibition of VEGFR2 and MET in endothelial cells reduced the vasculature, leading to necrosis. However, each islet of viable cells surrounded a VEGFR2-neg. vessel. Reduction of bone turnover was observed in both cohorts. Conclusions: Our studies demonstrate that MET in tumor cells is not a persistent therapeutic target for metastatic castrate-resistant prostate cancer (CRPC), but inhibition of VEGFR2 and MET in endothelial cells and direct effects on osteoblasts are responsible for cabozantinib-induced tumor inhibition. However, vascular heterogeneity represents one source of primary therapy resistance, whereas induction of FGFR1 in tumor cells suggests a potential mechanism of acquired resistance. Thus, integrated cross-species investigations demonstrate the power of combining preclin. models with clin. trials to understand mechanisms of activity and resistance of investigational agents. Clin Cancer Res; 22(1); 107-21. ©2015 AACR.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib treatment-induced inhibition of VEGFR2, FGFR1 and MET signaling which responsible for tumor inhibition in in-vitro human prostate cancer cells and in in-vivo mouse model)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:126388 CAPLUS Full-text

DOCUMENT NUMBER: 164:244992

TITLE: AutoT&T v.2: An Efficient and Versatile Tool for Lead Structure Generation and Optimization

AUTHOR(S): Li, Yan; Zhao, Zhixiong; Liu, Zhihai; Su, Minyi; Wang, Renxiao

CORPORATE SOURCE: State Key Laboratory of Bioorganic and Natural Products Chemistry, Collaborative Innovation Center of Chemistry for Life Sciences, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China

SOURCE: Journal of Chemical Information and Modeling (2016), 56(2), 435-453
CODEN: JCISD8; ISSN: 1549-9596

DIGITAL OBJECT ID: 10.1021/acs.jcim.5b00691

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal; (online computer file)

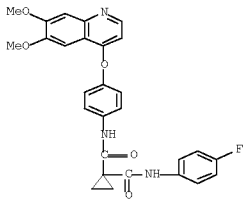
LANGUAGE: English

AB In structure-based drug design, automated de novo design methods are helpful tools for lead discovery as well as lead optimization. In a previous study the authors reported a new de novo design method, namely, Automatic Tailoring and Transplanting (AutoT&T). It overcomes some intrinsic problems in conventional fragment-based buildup methods. In this study, the authors describe an upgraded version, namely, AutoT&T2. Structural operations conducted by AutoT&T2 have been largely optimized by introducing several new algorithms. As a result, its overall speed in multiround optimization jobs has been improved by a few thousand fold. With this improvement, it is now practical to conduct structural crossover among multiple lead mols. using AutoT&T2. Three different test cases are described in this study that demonstrate the new features and versatile applications of AutoT&T2. The AutoT&T2 software suite is available to the public. Besides, a Web portal for running AutoT&T2 online is provided at http://www.sioc-ccbg.ac.cn/software/att2 for testing.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AutoT&T v.2 is efficient and versatile tool for lead structure generation and optimization)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:125847 CAPLUS Full-text

TITLE: Research advances of FLT3 inhibitors in treatment of acute myeloid leukemia

AUTHOR(S): Li, Tonghui; Guo, Hao; Lu, Tao; Wang, Yue; Lu, Shuai; Tang, Weifang

CORPORATE SOURCE: Department of Organic Chemistry, China Pharmaceutical University, Nanjing, 211198, Peop. Rep. China

SOURCE: Zhongguo Yaoke Daxue Xuebao (2015), 46(2), 153-161
CODEN: ZHYXE9; ISSN: 1000-5048

DIGITAL OBJECT ID: 10.11665/j.issn.1000-5048.20150203

PUBLISHER: Zhongguo Yaoke Daxue

DOCUMENT TYPE: Journal; General Review

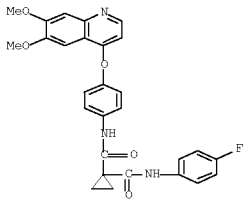
LANGUAGE: Chinese

AB A review with 69 ref. is given on research advances of FLT3 inhibitors in treatment of acute myeloid leukemia. Acute myeloid leukemia (AML) is one of the most common acute leukemia in adults. Those patients with FLT3 mutations have a particularly poor prognosis. Recently, the emergence of a variety of targeted inhibitors has shown the capability of suppressing FLT3 signaling in vivo, which provided a new way to treat AML. In this paper, we reviewed those inhibitors based on their structures, which include indolone-related inhibitors, indolocarbazo-related inhibitors, benzimidazole/benzopyrazole-related inhibitors, quinoline/quinoxaline/quinazoline-related inhibitors, tricyclic inhibitors, pyrimidine-related inhibitors and others.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(research advances of FLT3 inhibitors in treatment of acute myeloid leukemia)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

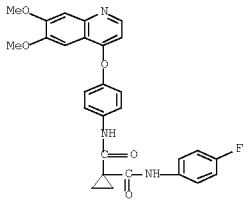


L4 ANSWER 29 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:118025 CAPLUS Full-text
DOCUMENT NUMBER: 164:355574
TITLE: Novel polymorph's of cabozantinib-S-malate
INVENTOR(S): Jetti, Ramakoteswara Rao; Indukuri, Anjaneyaraju; Punde, Dnyandeo; Bohra, Chandersingh; Gadakar, Mahesh Kumar; Gore, Vinayak
PATENT ASSIGNEE(S): Mylan Laboratories Ltd., India
SOURCE: Indian Pat. Appl., 54pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2014CH02561	A	20160115	IN 2014-CH2561	20140523
WO 2015177758	A1	20151126	WO 2015-IB53765	20150522

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

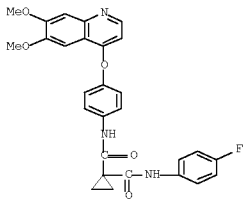
PRIORITY APPLN. INFO.: IN 2014-CH2561 A 20140523
AB The present disclosure provides novel cryst. forms of cabozantinib (S)-malate, designated as form-M1, M2, M3 and M4 and novel crystalline forms of cabozantinib free base, form-M1, M2 and M3 and methods of their production The present disclosure also provides processes for the preparation of crystalline cabozantinib (S)-malate form N-1.
IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(novel polymorph's of cabozantinib-S-malate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P, Cabozantinib (S)-malate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(novel polymorph's of cabozantinib-S-malate)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

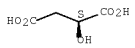
CRN 849217-68-1
CMF C28 H24 F N3 O5



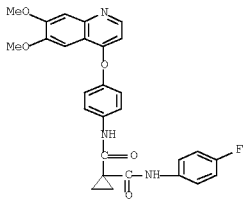
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 30 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:117601 CAPLUS Full-text
DOCUMENT NUMBER: 164:421210
TITLE: A photoactivable multi-inhibitor nanoliposome for tumour control and simultaneous inhibition of treatment escape pathways
AUTHOR(S): Spring, Bryan Q.; Bryan Sears, R.; Zheng, Lei Zak; Mai, Zhiming; Watanabe, Reika; Sherwood, Margaret E.; Schoenfeld, David A.; Pogue, Brian W.; Pereira, Stephen P.; Villa, Elizabeth; Hasan, Tayyaba
CORPORATE SOURCE: Wellman Center for Photomedicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Nature Nanotechnology (2016), 11(4), 378-387
CODEN: NNAABX; ISSN: 1748-3387
DIGITAL OBJECT ID: 10.1038/nnano.2015.311
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Nanoscale drug delivery vehicles can facilitate multimodal therapies of cancer by promoting tumor-selective drug release. However, few are effective because cancer cells develop ways to resist and evade treatment. Here, we introduce a photoactivable multi-inhibitor nanoliposome (PMIL) that imparts light-induced cytotoxicity in synchrony with a photoinitiated and sustained release of inhibitors that suppress tumor regrowth and treatment escape signaling pathways. The PMIL consists of a nanoliposome doped with a photoactivable chromophore (benzoporphyrin derivative, BPD) in the lipid bilayer, and a nanoparticle containing cabozantinib (XL184)-a multikinase inhibitor-encapsulated inside. Near-IR tumor irradiation, following i.v. PMIL administration, triggers photodynamic damage of tumor cells and microvessels, and simultaneously initiates release of XL184 inside the tumor. A single PMIL treatment achieves prolonged tumor reduction in two mouse models and suppresses metastatic escape in an orthotopic pancreatic tumor model. The PMIL offers new prospects for cancer therapy by enabling spatiotemporal control of drug release while reducing systemic drug exposure and associated toxicities.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photoactivable multi-inhibitor nanoliposome for tumor control and simultaneous inhibition of treatment escape pathways)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

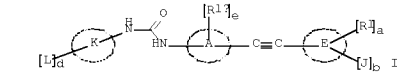


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

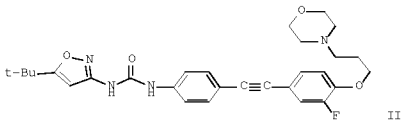
L4 ANSWER 31 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:112224 CAPLUS Full-text
DOCUMENT NUMBER: 164:213920
TITLE: Preparation of substituted urea derivatives as protein kinase modulators
INVENTOR(S): Cheng, Changchung; Zhang, Yingjun; Liu, Bing; Long, Bohua; Chen, Yu; Cheng, Zhixin
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 182pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016008433	A1	20160121	WO 2015-CN84253	20150716
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105272930	A	20160127	CN 2015-10422604	20150716
PRIORITY APPLN. INFO.:			CN 2014-10342509 A	20140717
OTHER SOURCE(S):		MARPAT 164:213920		

GI



I



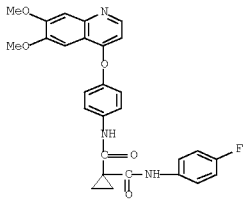
II

AB The title compds. I [ring A and ring E = (independently) C6-10 aryl or C1-12 heteroaryl; each J = G(CH2)nR2;each G = (independently) O, S(O)t, S, C(O), etc.; R1, R1a = H, F, Cl, Br, etc.; R2 = alkyl, cycloalkyl, heterocyclyl, etc.; ring K = 5-6 membered heteroaryl;each L = (independently) NH2, NO2, alkylthio, alkyl, etc.; each a and e = (independently) 0-4; each n, d and b = (independently) 1-4; and each t = (independently) 0-2], useful for preventing, managing, treating or lessening a proliferative disease, and modulating the activity of protein kinase, were prepared and claimed. E.g., a multi-step synthesis of the urea II, starting from 2-fluoro-4-iodophenol and N-(3-chloropropyl)morpholine, was described. Exemplified compds. I were tested for their activity against FLT3 kinase (data given for representative compds. I). Pharmaceutical compns. comprising compound I, alone or in combination with other therapeutic agents, were disclosed.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. as protein kinase modulators)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2015:2073656 CAPLUS Full-text
TITLE:	Hepatocyte growth factor and Met in drug discovery
AUTHOR(S):	Sakai, Katsuya; Aoki, Shunsuke; Matsumoto, Kunio
CORPORATE SOURCE:	Division of Tumor Dynamics and Regulation, Cancer Research Institute, Kanazawa University, Kanazawa, 920-1192, Japan
SOURCE:	Journal of Biochemistry (2015), 157(5), 271-284 CODEN: JOBIAO; ISSN: 0021-924X
DIGITAL OBJECT ID:	10.1093/jb/mvv027
PUBLISHER:	Oxford University Press
DOCUMENT TYPE:	Journal
LANGUAGE:	English

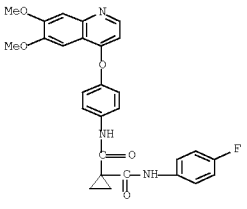
AB Activation of the hepatocyte growth factor (HGF) -Met pathway evokes dynamic biol. responses that support the morphogenesis, regeneration and survival of cells and tissues. A characterization of conditional Met knockout mice indicates that the HGF-Met pathway plays important roles in the regeneration, protection and homeostasis of cells such as hepatocytes, renal tubular cells and neurons. Preclin. studies in disease models have indicated that recombinant HGF protein and expression plasmid for HGF are biol. drug candidates for the treatment of patients with diseases or injuries that involve impaired tissue function. The phase-I and phase-I/II clin. trials of the intrathecal administration of HGF protein for the treatment of patients with amyotrophic lateral sclerosis and spinal cord injury, resp., are ongoing. Biol. actions of HGF that promote the dynamic movement, morphogenesis and survival of cells also closely participate in invasion-metastasis and resistance to the mol.-targeted drugs in tumor cells. Different types of HGF-Met pathway inhibitors are now in clin. trials for treatment of malignant tumors. Basic research on HGF and Met has lead to drug discoveries in regenerative medicine and tumor biol.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hepatocyte growth factor and Met in drug discovery)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2015:2060169 CAPLUS Full-text
TITLE:	Cabozantinib Inhibits Abiraterone's Upregulation of IGFIR Phosphorylation and Enhances Its Anti-Prostate Cancer Activity
AUTHOR(S):	Wang, Xiaodong; Huang, Ying; Christie, Amanda; Bowden, Michaela; Lee, Gwo-Shu Mary; Kantoff, Philip W.; Sweeney, Christopher J.
CORPORATE SOURCE:	Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SOURCE:	Clinical Cancer Research (2015), 21(24), 5578-5587 CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID:	10.1158/1078-0432.CCR-15-0824
PUBLISHER:	American Association for Cancer Research
DOCUMENT TYPE:	Journal
LANGUAGE:	English

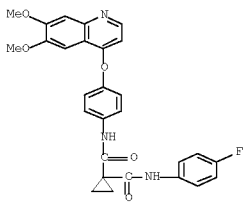
AB Purpose: Abiraterone improves the overall survival of men with metastatic castration-resistant prostate cancer. However, de novo or adaptive resistance to abiraterone limits its activity. Rational combinations of drugs with different mechanisms of action that overcome resistance mechanisms may improve the efficacy of therapy. To that end, we studied the mol. and phenotypic effects of the combination of cabozantinib plus abiraterone. Exptl. Design: Three prostate cancer cell lines were used to interrogate the in vitro mol. and antiproliferative effects of the single agents and combination of cabozantinib and abiraterone. The in vivo impact of the combination was assessed using the LAPC4-CR xenograft mouse model. Results: In vitro proliferation studies demonstrated single-agent doses between 2 μmol/L and 10 μmol/L for abiraterone and cabozantinib inhibit prostate cancer cell proliferation in a dose-dependent manner, and the anticancer activity of abiraterone is enhanced when combined with cabozantinib. In vivo LAPC4-CR xenograft mouse studies also showed that cabozantinib can improve the antitumor activity of abiraterone. Cabozantinib, a multiple receptor tyrosine kinase inhibitor, enhances the ability of abiraterone to inhibit AR activity in a cell line-dependent manner. In addition, our cell line studies demonstrate abiraterone-stimulated insulin-like growth factor I receptor (IGFIR) phosphorylation with downstream activation of MEK1/2 and ERK1/2, and that this potential adaptive resistance mechanism was inhibited by cabozantinib. Conclusions: Cabozantinib can enhance the efficacy of abiraterone by blocking multiple compensatory survival mechanisms, including IGFIR activation, and supports the assessment of the combination in a clin. trial. Clin Cancer Res; 21(24); 5578-87. ©2015 AACR.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib inhibits abiraterone's upregulation of IGFIR phosphorylation and enhances its anti-prostate cancer activity in LAPC4-CR xenograft mouse model)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2015:2059342 CAPLUS Full-text
DOCUMENT NUMBER:	164:119066
TITLE:	Methods and devices for treating posterior ocular disorders
INVENTOR(S):	Noronha, Glenn; Brooks, Christopher John; Andino, Rafael Victor; Patel, Samirkumar; White, Daniel
PATENT ASSIGNEE(S):	Clearside Biomedical, Inc., USA
SOURCE:	PCT Int. Appl., 175pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015195842	A1	20151223	WO 2015-US36299	20150617

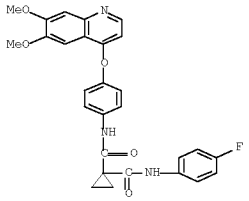
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.:
US 2014-62013209 P 20140617
US 2014-62018148 P 20140627
US 2014-62063792 P 20141014
US 2015-61155367 P 20150430
US 2015-62156802 P 20150504

AB The present invention relates to a methods and devices for treating uveitis, macular edema associated with uveitis and macular edema associated with retinal vein occlusion in a human subject in need thereof. In certain aspects, devices provided herein include a medicament container defining a lumen configured to contain a medicament, a distal end portion of the medicament container including a coupling portion configured to be removably coupled to a needle assembly, a proximal end portion of the medicament container including a flange and a longitudinal shoulder; a piston assembly including a distal end portion movably disposed within the lumen of the medicament container; and a handle coupled to a proximal end portion of the piston assembly.

IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(methods and devices for treating posterior ocular disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:2015841 CAPLUS Full-text
DOCUMENT NUMBER: 164:99265
TITLE: Anti-human Tumor endothelial marker TEM8 antibodies and other molecularly targeted agent for combination therapy of cancer
INVENTOR(S): Saha, Saurabh; Zhang, Xiaoyan M.; Dimitrov, Dimiter; Zhu, Zhongyu; St. Croix, Brad; Zudaire, Enrique
PATENT ASSIGNEE(S): Biomed Valley Discoveries, Inc., USA; Untied States Dept. of Health and Human Services
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015191610	A2	20151217	WO 2015-US34941	20150609
WO 2015191610	A3	20160204		

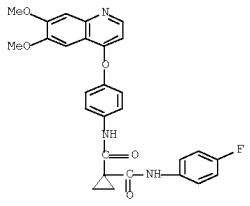
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62009371 P 20140609

AB The present invention provides, inter alia, methods for treating or ameliorating the effects of a disease, such as cancer, in a subject. The methods include: administering to a subject in need thereof (a) a therapeutically effective amount of a molecularly targeted agent; and (b) a therapeutically effective amount of a monoclonal antibody or antigen binding fragment thereof, wherein the monoclonal antibody contains: (i) a heavy chain variable region (VH), which includes an amino acid sequence selected from SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, and SEQ ID NO:7; and (ii) a light chain variable region (VL), which includes an amino acid sequence selected from SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8. Compns., including pharmaceutical compns., and kits for treating diseases, such as cancer, are also provided herein.

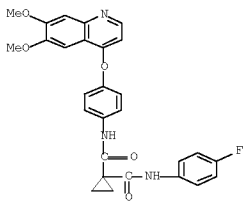
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human Tumor endothelial marker TEM8 antibodies and other molecularly targeted agent for combination therapy of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 36 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:2008346 CAPLUS Full-text
DOCUMENT NUMBER: 164:136379
TITLE: Bioluminescent kinase strips: A novel approach to targeted and flexible kinase inhibitor profiling
AUTHOR(S): Hennek, J.; Alves, J.; Yao, E.; Goueli, S. A.; Zegzouti, H.
CORPORATE SOURCE: R&D Department, Promega Corporation, Madison, WI, 53711, USA
SOURCE: Analytical Biochemistry (2016), 495, 9-20
CODEN: ANBCA2; ISSN: 0003-2697
DIGITAL OBJECT ID: 10.1016/j.ab.2015.11.007
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB In addn. to target efficacy, drug safety is a major requirement during the drug discovery process and is influenced by target specificity. Therefore, it is imperative that every new drug candidate be profiled against various liability panels that include protein kinases. Here, an effective methodol. to streamline kinase inhibitor profiling is described. An accessible standardized profiling system for 112 protein kinases covering all branches of the kinome was developed. This approach consists of creating different sets of kinases and their corresponding substrates in multi-tube strips. The kinase stocks are pre-standardized for optimal kinase activity and used for inhibitor profiling using a bioluminescent ADP detection assay. The authors show that these strips can routinely generate inhibitor selectivity profiles for small or broad kinase family panels. Lipid kinases were also assembled in strip format and profiled together with protein kinases. The authors identified two specific PI3K inhibitors that have off-target effects on CK2 that were not reported before and would have been missed if compds. were not profiled against lipid and protein kinases simultaneously. To validate the accuracy of the data generated by this method, the authors confirmed that the inhibition potencies observed are consistent with published values produced by more complex technologies such as radioactivity assays.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioluminescent kinase strips as novel approach to targeted and flexible kinase inhibitor profiling)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



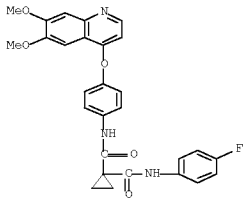
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 37 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1965343 CAPLUS Full-text
TITLE: Repurposing of anticancer drugs: in vitro and in vivo activities against Schistosoma mansoni
AUTHOR(S): Cowan, Noemi; Keiser, Jennifer
CORPORATE SOURCE: Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, CH-4002, Switz.
SOURCE: Parasites & Vectors (2015), 8, 1-9
CODEN: PVAEAK; ISSN: 1756-3305
DIGITAL OBJECT ID: 10.1186/s13071-015-1023-y
PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

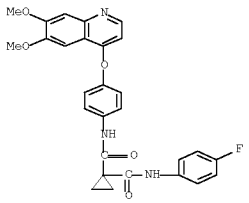
AB Background: Drug discovery for the neglected tropical disease schistosomiasis has a high priority. Anticancer drugs, especially protein kinase inhibitors, might serve as a starting point for drug discovery owing to the importance of protein kinases in helminth growth and development. Furthermore, the Schistosoma mansoni genome encodes several genes for targets of drugs marketed for human use, including several anticancer drugs. Methods: In this study, we screened the approved oncol. drug set of the National Cancer Institute's Developmental Therapeutic Program for antischistosomal activity. Drugs were tested in vitro against the larval and adult stage of S. mansoni. IC50 values and albumin binding were determined for active compds. Lead compds. were tested in the chronic S. mansoni mouse model. Results: Eleven of the 114 compds. tested revealed IC50 values ≤ 10 μM against both S. mansoni stages. Five of these lost activity against adult S. mansoni in the presence of serum albumin. Of 6 compds. studied in vivo, the highest activity was observed from two kinase inhibitors trametinib, and vandetanib, which reduced worm burden by 63.6 and 48.1 % resp., after a single oral dose of 400 mg/kg body weight Conclusion: Our study has confirmed that oncol. drugs possess antischistosomal activity. There is space for further investigation, including elucidation of the mechanisms of action of schistosome-active cancer drugs, application of different treatment courses, and structure-activity relationship studies for improving drug potency.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro drug testing against larval and adult stage of Schistosoma mansoni and determination of IC50 values and albumin binding for active compds., also lead compds. were tested in chronic Schistosoma mansoni mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1916188 CAPLUS Full-text
TITLE: Clinical observation of liver cancer patients treated with axitinib and cabozantinib after failed sorafenib treatment: a case report and literature review
AUTHOR(S): Zhang, Bin; Zhang, Xia; Zhou, Tao; Liu, Jiwei
CORPORATE SOURCE: Department of Oncology, The First Affiliated Hospital of Dalian Medical University, Dalian, Peop. Rep. China
SOURCE: Cancer Biology & Therapy (2015), 16(2), 215-218
CODEN: CBTAAO; ISSN: 1555-8576
DIGITAL OBJECT ID: 10.4161/15384047.2014.962318
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

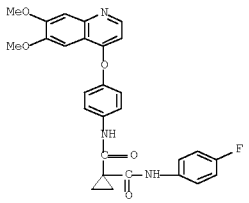
AB A review. Hepatocellular carcinoma (HCC) is a major pathol. type of primary liver cancer. Sorafenib has demonstrated definite efficacy in targeted therapy for HCC. However, when treatment with sorafenib fails, suitable drugs must be found for further treatment. This article reports a case of an HCC patient who was treated with angiogenesis inhibitor axitinib and c-Met inhibitor cabozantinib following treatment with sorafenib. The report focuses on clin. treatment and toxicity. Rational application of targeted therapy is also explored.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(clin. observation of liver cancer patients treated with axitinib and cabozantinib after failed sorafenib treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

ACCESSION NUMBER: 2015:1955534 CAPLUS Full-text
TITLE: Defining the Schistosoma haematobium kinome enables the prediction of essential kinases as anti-schistosome drug targets
AUTHOR(S): Stroehlein, Andreas J.; Young, Neil D.; Jex, Aaron R.; Sternberg, Paul W.; Tan, Patrick; Boag, Peter R.; Hofmann, Andreas; Gasser, Robin B.
CORPORATE SOURCE: Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Parkville, Australia
SOURCE: Scientific Reports (2015), 5, 17759
CODEN: SRCEC3; ISSN: 2045-2322
DIGITAL OBJECT ID: 10.1038/srep17759
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB The blood fluke Schistosoma haematobium causes urogenital schistosomiasis, a neglected tropical disease (NTD) that affects more than 110 million people. Treating this disease by targeted or mass administration with a single chemical, praziquantel, carries the risk that drug resistance will develop in this pathogen. Therefore, there is an imperative to search for new drug targets in S. haematobium and other schistosomes. In this regard, protein kinases have potential, given their essential roles in biol. processes and as targets for drugs already approved by the US Food and Drug Administration (FDA) for use in humans. In this context, we defined here the kinome of S. haematobium using a refined bioinformatic pipeline. We classified, curated and annotated predicted kinases, and assessed the developmental transcription profiles of kinase genes. Then, we prioritised a panel of kinases as potential drug targets and inferred chems. that bind to them using an integrated bioinformatic pipeline. Most kinases of S. haematobium are very similar to those of its congener, S. mansoni, offering the prospect of designing chems. that kill both species. Overall, this study provides a global insight into the kinome of S. haematobium and should assist the repurposing or discovery of drugs against schistosomiasis.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(defining Schistosoma haematobium kinome enables prediction of essential kinases as anti-schistosome drug targets)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



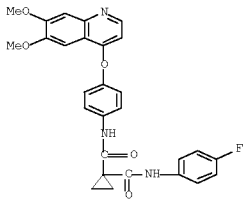
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1897715 CAPLUS Full-text
TITLE: Cabozantinib: an orphan drug for thyroid cancer
AUTHOR(S): Viola, D.; Cappagli, V.; Matrone, A.; Mazzeo, S.; Elisei, R.
CORPORATE SOURCE: Endocrine Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56124, Italy
SOURCE: Expert Opinion on Orphan Drugs (2015), 3(12), 1469-1477
CODEN: EOODAJ; ISSN: 2167-8707
DIGITAL OBJECT ID: 10.1517/21678707.2015.1112789
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Until recently, no therapeutic options were available for the treatment of advanced medullary thyroid cancer (MTC). Cabozantinib (XL184) is a novel tyrosine kinase inhibitor (TKI) that inhibits several tyrosine kinase receptors, in particular those coded by MET, VEGFR-2 and RET oncogenes that are considered to be involved in the pathogenesis of MTC. This article provides an overview of the phase I and III trials that demonstrated the efficacy of cabozantinib in two cohorts of advanced MTC patients who were naive or previously treated with other TKIs. The benefits in terms of progression-free survival (PFS), overall survival (OS) and the demog. clin. and mutational status of the two cohorts of MTC patients are reported and discussed. The possibility to have a therapeutic option for the treatment of patients with advanced and progressive MTC and, in particular, the evidence that the drug can be active also in those patients who already experienced disease progression while taking another TKI is a great opportunity as demonstrated in cases treated with cabozantinib after vandetanib such as the one reported in this paper.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib, an orphan drug for thyroid cancer)

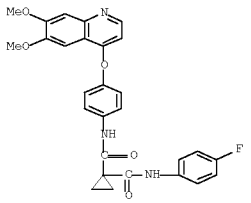
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 41 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1892326 CAPLUS Full-text
DOCUMENT NUMBER: 163:709974
TITLE: Novel polymorphs of cabozantinib (S)-malate and cabozantinib free base
INVENTOR(S): Jetti, Ramakoteswara Rao; Indukuri, Anjaneyaraju; Punde, Dnyandeo; Bohra, Chandersingh; Gadakar, Mahesh Kumar; Gore, Vinayak
PATENT ASSIGNEE(S): Mylan Laboratories Ltd., India
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

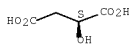
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015177758	A1	20151126	WO 2015-IB53765	20150522
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IN 2014CH02561 A		20160115	IN 2014-CH2561	20140523



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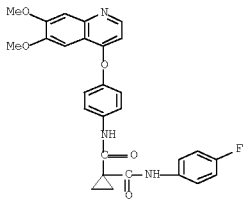
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



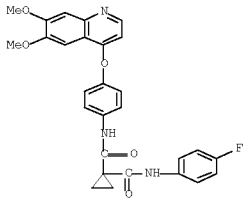
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 42 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1833484 CAPLUS Full-text
DOCUMENT NUMBER: 164:370558
TITLE: Identification of Bone-Derived Factors Conferring De Novo Therapeutic Resistance in Metastatic Prostate Cancer
AUTHOR(S): Lee, Yu-Chen; Lin, Song-Chang; Yu, Guoyu; Cheng, Chien-Jui; Liu, Bin; Liu, Hsuan-Chen; Hawke, David H.; Parikh, Nila U.; Varkaris, Andreas; Corn, Paul; Logothetis, Christopher; Satcher, Robert L.; Yu-Lee, Li-Yuan; Gallick, Gary E.; Lin, Sue-Hwa
CORPORATE SOURCE: Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Cancer Research (2015), 75(22), 4949-4959
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-15-1215
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Resistance to currently available targeted therapies significantly hampers the survival of patients with prostate cancer with bone metastasis. Here we demonstrate an important resistance mechanism initiated from tumor-induced bone. Studies using an osteogenic patient-derived xenograft, MDA-PCa-118b, revealed that tumor cells resistant to cabozantinib, a Met and VEGFR-2 inhibitor, reside in a "resistance niche" adjacent to prostate cancer-induced bone. We performed secretome anal. of the conditioned medium from tumor-induced bone to identify proteins (termed "osteocrines") found within this resistance niche. In accordance with previous reports demonstrating that activation of integrin signaling pathways confers therapeutic resistance, 27 of the 90 osteocrines identified were integrin ligands. We found that following cabozantinib treatment, only tumor cells positioned adjacent to the newly formed woven bone remained viable and expressed high levels of pFAK-Y397 and pTalin-S425, mediators of integrin signaling. Accordingly, treatment of C4-2B4 cells with integrin ligands resulted in increased pFAK-Y397 expression and cell survival, whereas targeting integrins with FAK inhibitors PF-562271 or defactinib inhibited FAK phosphorylation and reduced the survival of PC3-mm2 cells. Moreover, treatment of MDA-PCa-118b tumors with PF-562271 led to decreased tumor growth, irresp. of initial tumor size. Finally, we show that upon treatment cessation, the combination of PF-562271 and cabozantinib delayed tumor recurrence in contrast to cabozantinib treatment alone. Our studies suggest that identifying paracrine de novo resistance mechanisms may significantly contribute to the generation of a broader set of potent therapeutic tools that act combinatorially to inhibit metastatic prostate cancer. Cancer Res; 75(22); 4949-59. ©2015 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(paracrine de novo resistance factors significantly contribute to generation of bone formation, therapeutic resistance and inhibit metastatic prostate cancer cells and in human and mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 43 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1818418 CAPLUS Full-text
TITLE: Advances in receptor tyrosine kinase inhibitors taking
PRIORITY APPLN. INFO.: IN 2014-CH2561 A 20140523
AB The present disclosure provides novel cryst. forms of cabozantinib (S)-malate, designated as form-M1, M2, M3 and M4 and novel crystalline forms of cabozantinib free base, form-M1, M2 and M3 and methods of their production The present disclosure also provides processes for the preparation of crystalline cabozantinib (S)-malate form N-1. Formula (I).
IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(novel polymorphs of cabozantinib (S)-malate and cabozantinib free base)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

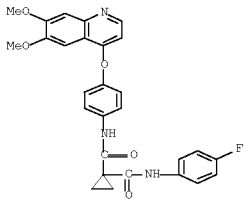


IT 1140909-48-3P, Cabozantinib (S)-malate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(novel polymorphs of cabozantinib (S)-malate and cabozantinib free base)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

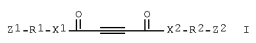
c-Met as anti-tumor target
AUTHOR(S): Zhang, Yuan; Cheng, Yulan; Zhou, Jinpei; Zhang, Huibin
CORPORATE SOURCE: Dept. of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2015), 46(1), 16-27
CODEN: ZHYXE9; ISSN: 1000-5048
DIGITAL OBJECT ID: 10.11665/j.issn.1000-5048.20150102
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 52 refs. on the c-Met signaling pathway and the resistance of kinase inhibitors caused by the cross-talk between c-Met and other membrane receptors and the progress of single-target and multi-target c-Met inhibitors.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reviewing the advances in receptor tyrosine kinase inhibitors taking c-Met as anti-tumor target)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



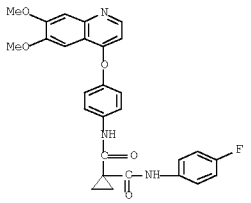
L4 ANSWER 44 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1805828 CAPLUS Full-text
DOCUMENT NUMBER: 163:694481
TITLE: Acetylenedicarboxyl linkers and their uses in specific conjugation of a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: U.S. Pat. Appl. Publ., 80pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150322155	A1	20151112	US 2015-14799666	20150715
PRIORITY APPLN. INFO.:			US 2015-14799666	20150715

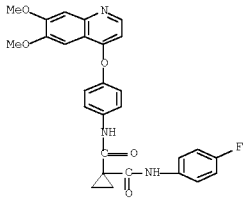
OTHER SOURCE(S): CASREACT 163:694481; MARPAT 163:694481
GI



AB Provided are novel acetylenedicarboxyl linkers used for the specific conjugation of compds./cytotoxic agents to a cell-binding mol., through bridge linking pairs of thiols on the cell-binding mol. Also provided are methods of making such linkers, and of using such linkers in making homogeneous conjugates, as well as of application of the conjugates in treatment of cancers, infections and autoimmune disorders. Particularly provided is a bridge linker compound of the Formula (I), wherein:The acetylenedicarboxyl group is capable of reacting with a pair of sulfur atoms of the cell-binding agent; Z1 and Z2 are the same or different a function group that enables to react with a cytotoxic drug; R1 and R2 are the same or different linear alkyl; X1 and X2 are independently selected from NH, N(R3), O, S or CH2; R3 is H, linear alkyl.
IT 849217-68-1, Cabozan-tinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-therapy with; acetylenedicarboxyl linkers and their uses in specific conjugation of cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

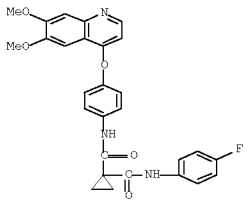


L4 ANSWER 45 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1783974 CAPLUS Full-text
TITLE: New molecularly targeted therapies against advanced hepatocellular carcinoma: From molecular pathogenesis to clinical trials and future directions
AUTHOR(S): Chuma, Makoto; Terashita, Katsumi; Sakamoto, Naoya
CORPORATE SOURCE: Department of Gastroenterology and Hepatology, Hokkaido University, Sapporo, Japan
SOURCE: Hepatology Research (2015), 45(10), E1-E11
CODEN: HPRSFM; ISSN: 1386-6346
DIGITAL OBJECT ID: 10.1111/hepr.12459
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Hepatocellular carcinoma (HCC) can be lethal due to its aggressive course and lack of effective systemic therapies for advanced disease. Sorafenib is the only systemic therapy that has demonstrated an overall survival benefit in patients with advanced HCC, and new agents for treatment of advanced HCC are needed. The multiple pathways involved in HCC oncogenesis, proliferation and survival provide many opportunities for the development of molecularly targeted therapies. Mol. targets of interest have expanded from angiogenesis to cancer cell-directed oncogenic signaling pathways for treatment of advanced HCC. Agents targeting vascular endothelial growth factor receptor, epidermal growth factor receptor, fibroblast growth factor receptor, platelet-derived growth factor receptor, c-mesenchymal-epithelial transition factor-1 and mammalian target of rapamycin signaling have been actively explored. This article focuses on the evaluation of mol. agents targeting pathogenic HCC and provides a review of recently completed phase III drug studies (e.g. involving sorafenib, sunitinib, brivanib, linifanib, erlotinib, everolimus, ramucirumab or orantinib) and ongoing drug studies (e.g. involving lenvatinib, regorafenib, tivantinib or cabozantinib) of molecularly targeted agents in advanced HCC, including a brief description of the biol. rationale behind these agents.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of sorafenib, sunitinib, brivanib, linifanib, erlotinib, everolimus, ramucirumab/orantinib and lenvatinib, regorafenib, tivantinib/cabozantinib of molecularly targeted agents in patients with advanced hepatocellular carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 46 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1783428 CAPLUS Full-text
DOCUMENT NUMBER: 163:681013
TITLE: Cabozantinib for the treatment of progressive metastatic medullary thyroid cancer
AUTHOR(S): Krajewska, Jolanta; Olczyk, Tomasz; Jarzab, Barbara
CORPORATE SOURCE: Nuclear Medicine and Endocrine Oncology Department, M.Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Pol.
SOURCE: Expert Review of Clinical Pharmacology (2016), 9(1), 69-79
CODEN: ERCPAG; ISSN: 1751-2433
DIGITAL OBJECT ID: 10.1586/17512433.2016.1102052
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (XL-184) is a potent inhibitor of MET, VEGFR 2/KDR, RET and other receptor tyrosine kinases, such as KIT, AXL and FLT3. Its efficacy against MTC has been demonstrated in a prospective, randomized, placebo-controlled study (EXAM). Cabozantinib comparing to placebo significantly prolonged progression free survival both in hereditary and sporadic MTC, 11.2 vs. 4.0 mo, resp. Final anal. showed no global differences in overall survival (OS) between cabozantinib and placebo. However, in a subgroup with RET M918T mutation the difference in OS was significant: 44.3 vs. 18.9 mo, resp. Among the most frequent cabozantinib-related adverse events (AEs), observed in >30% of patients were diarrhea, palmar-plantar erythrodysesthesia, decreased weight, decreased appetite, nausea, fatigue, dysgeusia, hair color changes and hypertension. Expert Commentary: Cabozantinib constitutes an effective treatment option with acceptable toxicity in MTC patients showing either germinal or sporadic tumor RET M918T mutation as the drug prolonged OS in these subjects.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of progressive metastatic medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 47 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1726025 CAPLUS Full-text
DOCUMENT NUMBER: 163:628844
TITLE: Method of treating lung adenocarcinoma
INVENTOR(S): Aftab, Dana T.; Yu, Peiwen
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

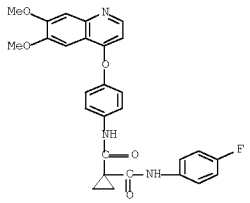
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015164869	A1	20151029	WO 2015-US27800	20150427

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61984599 P 20140425
OTHER SOURCE(S): CASREACT 163:628844; MARPAT 163:628844

AB This invention is directed to the treatment of cancer in a patient, particularly a patient with lung adenocarcinoma, and more particularly a patient with SLC34A2-ROS1, CD74-ROS1, or FIG-ROS1 fusion-pos. non-small cell lung cancer, with an inhibitor of MET, VEGFR2, and ROS1.

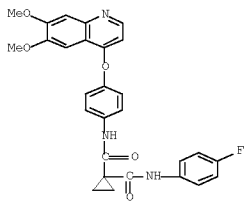
IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(treating lung adenocarcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treating lung adenocarcinoma)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

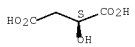
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

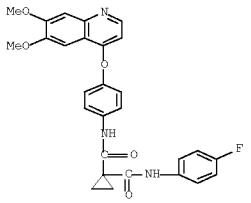
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating lung adenocarcinoma)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

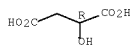
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 48 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1723003 CAPLUS Full-text
DOCUMENT NUMBER: 163:632038
TITLE: Hepatocyte growth factor as marker of prognosis in small cell lung cancer (SCLC)
INVENTOR(S): Arriola Aperribay, Edurne; Canadas Castillo, Israel; Rovira Guerin, Ana; Albanell Mestres, Joan
PATENT ASSIGNEE(S): Fundacio Institut Mar d'Investigacions Mediques (IMIM), Spain
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

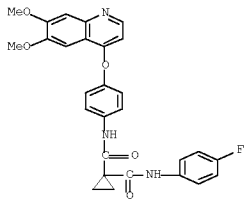
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015161885	A1	20151029	WO 2014-EP58375	20140424

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2014-EP58375 20140424

AB The invention relates to a new marker, the hepatocyte growth factor (HGF) in serum or plasma for the prognosis of small-cell lung cancer (SCLC). The invention also provides methods for selecting subjects suffering from SCLC that are candidate to respond to certain substances inhibiting certain kinases expressed in the tumors. There are also encompassed the use of immunoassay and nucleic acid reagents for detecting HGF in serum or plasma, said reagents for carrying out the prognostic method.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatocyte growth factor in serum or plasma as prognostic marker of small-cell lung cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 49 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1694942 CAPLUS Full-text
DOCUMENT NUMBER: 163:596944
TITLE: Methods for treating cancer using TOR kinase inhibitor combination therapy
INVENTOR(S): Fultz, Kimberly Elizabeth; Tran, Tam Minh; Xu, Shuichan; Xu, Weiming; Trowe, Torsten; Filvaroff, Ellen
PATENT ASSIGNEE(S): Signal Pharmaceuticals, LLC, USA
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

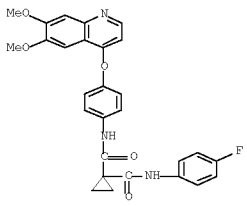
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015160868	A1	20151022	WO 2015-US25843	20150415
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
NZ 629860	A	20160129	NZ 2014-629860	20140902
US 20150297590	A1	20151022	US 2015-14686872	20150415

PRIORITY APPLN. INFO.: US 2014-61980124 P 20140416
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided are methods for treating or preventing cancer, comprising administering an effective amount of a 3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one TOR kinase inhibitor and an effective amount of a second active agent to a patient. Cancers treated by the method include solid tumors of the head, neck, breast, lung, ovaries, colon, rectum, stomach, prostate, urinary bladder, uterine, cervix, and other reproductive organs, wherein the tumors include relapsed, refractory or advanced solid tumors.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy using pyrazinopyrazine TOR kinase inhibitors for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

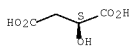
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

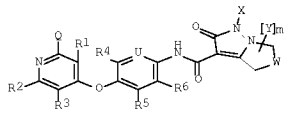


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

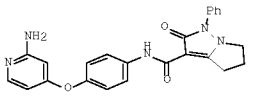
L4 ANSWER 50 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1694572 CAPLUS Full-text
DOCUMENT NUMBER: 163:601731
TITLE: Preparation of bicyclic pyrazolone compounds for inhibiting or modulating the activity of receptor tyrosine kinases
INVENTOR(S): Xi, Ning; Wu, Yanjun
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: U.S. Pat. Appl. Publ., 52pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150299219	A1	20151022	US 2015-14687992	20150416
WO 2015164161	A1	20151029	WO 2015-US26062	20150416
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2014-61982729 P 20140422
OTHER SOURCE(S): CASREACT 163:601731; MARPAT 163:601731
GI

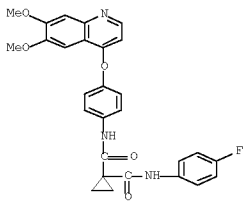


I



II

AB The title compds. I [Q = H, (un)substituted OH, NH2, etc.; U = CR7 or N; X = H, alkyl, cycloalkyl, etc.; Y = alkyl, cycloalkyl, aryl, etc.; m = 0-4; W = (CH2)n, (CH2)nO, (CH2)nNH, (CH2)nS (wherein n = 0-4); R1-R7 = H, F, Cl, Br, etc.; with the provisos], which are used to inhibit or modulate the activity of receptor tyrosine kinases, especially Axl, Mer, c-Met and Ron, were prepared E.g., a multi-step synthesis of II, starting from phenylhydrazine and 4-chlorobutanoyl chloride, was described. Exemplified compds. I were tested for their biol. activity (data given for representative compds. I). The invention also provides pharmaceutical compns. comprising the compound I, and a method of preventing, treating or lessening the severity of a proliferative disorder in a patient with the compds. I or the pharmaceutical compns. comprising I.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of bicyclic pyrazolone compds. for inhibiting or modulating the activity of receptor tyrosine kinases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



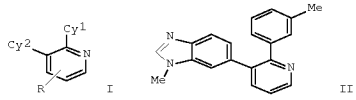
L4 ANSWER 51 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1654358 CAPLUS Full-text
DOCUMENT NUMBER: 163:601695
TITLE: 2,3-Disubstituted pyridine compounds as TGF-beta inhibitors and their preparation
INVENTOR(S): Singh, Rajinder; Bhamidipati, Somasekhar; Ding, Pingyu; Payan, Donald; Gelman, Marina; Kinsella, Todd
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 406pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2015157093	A1	20151015	WO 2015-US24146	20150402
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2014-61976880 P 20140408
US 2014-62019577 P 20140701

OTHER SOURCE(S): MARPAT 163:601695

GI

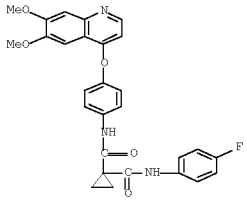


I II

AB The invention described compds. of formula I and a method of treating cancer comprising administering to a subject having cancer one of the compds. in conjunction with another therapeutic treatment of cancer. The compds. I inhibit signaling by a member of the TGF-β superfamily such as nodal or activin. Compds. of formula I wherein Cy1 is (un)substituted Ph, benzofuranyl, (un)substituted C1-3 alkyl, etc.; Cy2 is pyrazolo[1,5-a]pyrimidinyl, benzothiazolyl, imidazo[1,2-a]pyridinyl, (un)substituted phenylsulfonyl, etc.; R is (un)substituted Ph, (un)substituted heteroaryl and (un)substituted heterocycloalkyl; and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by cross-coupling of 2-chloro-2-(3-methylphenyl)pyridine with 1-methyl-1H-benzimidazole-6-boronic acids. The invention compds. were evaluated for their TGF-β inhibitory activity (some data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of disubstituted pyridine compds. as TGF-β inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 52 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1650548 CAPLUS Full-text
DOCUMENT NUMBER: 163:585951
TITLE: Preparation of bridge linkers used for specific conjugation of two or more cytotoxic agents to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin; Zhao, Robert
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 162pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015155753	A2	20151015	WO 2015-IB56083	20150810
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
US 20150284416	A1	20151008	US 2015-14740403	20150616

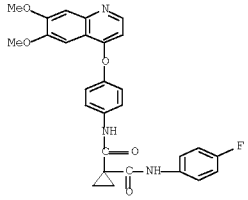
PRIORITY APPLN. INFO.: US 2015-14740403 T0 20150616
OTHER SOURCE(S): MARPAT 163:585951
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to novel linkers contg. a 2,3-disubstituted succinic group, or 2-monosubstituted, or 2,3-disubstituted fumaric or maleic (trans (E)- or cis (Z)-butenedioic) group, e.g., (I), for conjugation of two or more compds./cytotoxic agents per linker to a cell-binding mol., through bridge linking pairs of thiols (reduced from the interchain disulfide bonds of the cell-binding agent by a reducing agent, such as dithiothreitol, dithioerythritol, L-glutathione and tris(2-carboxyethyl)phosphine (TCEP), or/and β-mercaptoethanol) on the cell-binding mol. specifically. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by treating reaction with drugs and to their use for cancers, infections and autoimmune disorders. Thus, linker I was prepared by cyclization of 2,3-dibromosuccinic acid in CH2Cl2 in the presence of P2O5. R1-COCHBrCHBrCO-R (II) was prepared in 3 steps from I and R1-H (preparation given) using R = H (preparation given). A herceptin antibody conjugate with II was prepared by reacting herceptin with and TCEP and II. The resulting conjugate was evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 889 and for SK-OV-3 cell was over 800. Five-week-old female BALB/c Nude mice inoculated s.c. in the area under the right shoulder with N-87 carcinoma cells treated with the conjugate had completely no tumor measurable at day 13 till day 60 (the end of experiment) in an in vivo antitumor activity study.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of two or more cytotoxic agents to a cell-binding mol.)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of two or more cytotoxic agents to a cell-binding mol.

L4 ANSWER 53 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1646639 CAPLUS Full-text
DOCUMENT NUMBER: 163:612041
TITLE: Method for screening antitumor drug biomarkers, and application thereof
INVENTOR(S): Xiong, Lei
PATENT ASSIGNEE(S): HTS Biotechnology (Shanghai) Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 23pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

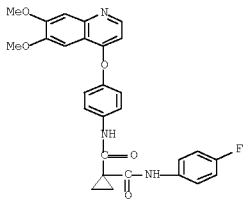
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104975063	A	20151014	CN 2014-10130154	20140401

PRIORITY APPLN. INFO.: CN 2014-10130154 20140401

AB The invention discloses method for screening antitumor drug biomarkers, and application thereof. The method comprises the steps of: (1) providing tumor cells as starting cells, and tumor cells are from identical tumor tissue of the same object, (2) performing passage of the starting cells, establishing cell lines, and detecting genomic information of the cell lines so as to obtain at least 5 tumor cell lines that have genomic differences and are highly homologous, (3) performing antitumor drug sensitivity testing of the tumor cell lines, and typing the tumor cell lines based on the testing results, and (4) based on the typing results, analyzing the genomic information of the tumor cell lines to determine anti-tumor drug biomarkers. The method can maximally reduce background noise between different tumor cell lines, and can help to efficiently and accurately screen biomarkers of antitumor drugs.

IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); BUU (Biological use, unclassified); PAC (Pharmacological activity); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(method for screening antitumor drug biomarkers, and application thereof)

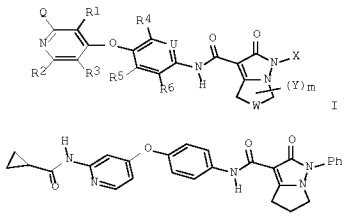
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 54 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1640328 CAPLUS Full-text
DOCUMENT NUMBER: 163:618028
TITLE: Preparation of bicyclopyrazolone compounds as tyrosine kinase inhibitors
INVENTOR(S): Xi, Ning; Wu, Yanjun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 81pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104974162	A	20151014	CN 2015-10167125	20150409
PRIORITY APPLN. INFO.:			CN 2014-10141156 A	20140409

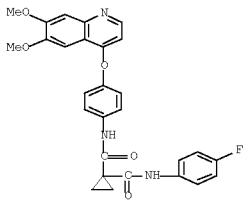
OTHER SOURCE(S): MARPAT 163:618028
GI



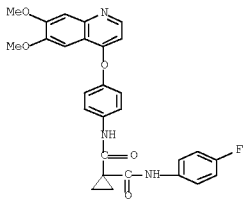
I

II

AB The invention provides bicyclopyrazolone compds. I [wherein Q = H, (un)substituted OH, NH2, etc.; U = (un)substituted CH or N; X = H, alkyl, alkenyl, alkynyl, etc.; Y = independently H, alkyl, alkenyl, etc.; W = (CH2)n, (CH2)nO, (CH2)nNH, or (cH2)nS; n = 0-4; R1-R6 = independently H, F, Cl, Br, CN, N3, etc.; m = 1-4; with provisos], stereoisomers, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts, or prodrugs thereof for suppressing the activity of receptor tyrosine kinase, especially Axl, Mer, c-Met and Ron kinases. The invention also provides pharmaceutical compns. comprising the title compds., and application of the title compds. and pharmaceutical compns. for preventing and treating proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 3 and 26 nM against Mer and c-Met tyrosine kinases, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of bicyclopyrazolone compds. as tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



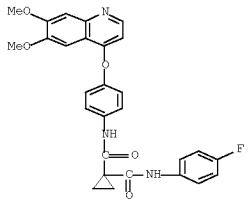
L4 ANSWER 55 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1635205 CAPLUS Full-text
TITLE: Selective targeting of CTNNB1-, KRAS- or MYC-driven cell growth by combinations of existing drugs
AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; Spijkers-Hagelstein, Jill A. P.; de Vetter, Judith R. F.; de Man, Jos; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE: Netherlands Translational Research Center B.V., Oss, Neth.
SOURCE: PLoS One (2015), 10(5), e0125021/1-e0125021/22
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0125021
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The aim of combination drug treatment in cancer therapy is to improve response rate and to decrease the probability of the development of drug resistance. Preferably, drug combinations are synergistic rather than additive, and, ideally, drug combinations work synergistically only in cancer cells and not in non-malignant cells. We have developed a workflow to identify such targeted synergies, and applied this approach to selectively inhibit the proliferation of cell lines with mutations in genes that are difficult to modulate with small mols. The approach is based on curve shift anal., which we demonstrate is a more robust method of determining synergy than combination matrix screening with Bliss-scoring. We show that the MEK inhibitor trametinib is more synergistic in combination with the BRAF inhibitor dabrafenib than with vemurafenib, another BRAF inhibitor. In addition, we show that the combination of MEK and BRAF inhibitors is synergistic in BRAF-mutant melanoma cells, and additive or antagonistic in, resp., BRAF-wild type melanoma cells and non-malignant fibroblasts. This combination exemplifies that synergistic action of drugs can depend on cancer genotype. Next, we used curve shift anal. to identify new drug combinations that specifically inhibit cancer cell proliferation driven by difficult-to-drug cancer genes. Combination studies were performed with compds. that as single agents showed preference for inhibition of cancer cells with mutations in either the CTNNB1 gene (coding for β-catenin), KRAS, or cancer cells expressing increased copy nos. of MYC. We demonstrate that the Wnt-pathway inhibitor ICG-001 and trametinib acted synergistically in Wnt-pathway-mutant cell lines. The ERBB2 inhibitor TAK-165 was synergistic with trametinib in KRAS-mutant cell lines. The EGFR/ERBB2 inhibitor neratinib acted synergistically with the spindle poison docetaxel and with the Aurora kinase inhibitor GSK-1070916 in cell lines with MYC amplification. Our approach can therefore efficiently discover novel drug combinations that selectively target cancer genes.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective targeting of CTNNB1-, KRAS-or MYC-driven human cancer cell growth by combinations of existing drugs)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

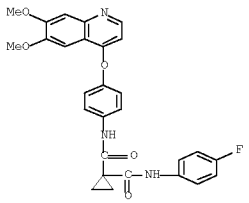
L4 ANSWER 56 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1634096 CAPLUS Full-text
TITLE: Pharmacokinetic interaction study of combining cabozantinib with erlotinib in rats by UPLC-MS/MS
AUTHOR(S): Wang, Zhiyi; Zhang, Qingwei; Zhang, Meiling; Wu, Haiya; Zhang, Yuan
CORPORATE SOURCE: The Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, 325000, Peop. Rep. China
SOURCE: Latin American Journal of Pharmacy (2015), 34(2), 313-318
CODEN: LAJPA9; ISSN: 0326-2383
PUBLISHER: Colegio de Farmaceuticos de la Provincia de Buenos Aires
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study examd. whether oral administration of erlotinib to rats with cabozantinib led to any pharmacokinetic interactions or not. Twenty four rats were randomly divided into 3 groups, cabozantinib group (cabozantinib 30 mg/kg, n = 8), erlotinib group (erlotinib 25 mg/kg, n = 8) and co-administration group (erlotinib 25 mg/kg and cabozantinib 30 mg/kg, n = 8). The concentration of cabozantinib and erlotinib in rat plasma was determined by a sensitive and simple UPLC-MS/MS method. There was statistical pharmacokinetics difference for cabozantinib in the cabozantinib group and co-administration group, when co-oral administration cabozantinib with erlotinib, the AUC(0-t) and Cmax increased ($p < 0.01$). There was statistical pharmacokinetics difference for erlotinib in the erlotinib group and co-administration group, when co-oral administration erlotinib with cabozantinib, the AUC(0-t) increased and CL decreased ($p < 0.05$). These data indicate erlotinib could influence the pharmacokinetic profile of cabozantinib in rats, and vice versa, which might cause drug-drug interactions when using cabozantinib with erlotinib.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmacokinetic interaction study of combining cabozantinib with erlotinib in rats by ultra-performance liquid chromatog.-mass spectrum/mass spectrum)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 57 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1626773 CAPLUS Full-text
TITLE: Evaluation of the effect of food and gastric pH on the single-dose pharmacokinetics of cabozantinib in healthy adult subjects
AUTHOR(S): Nguyen, Linh; Holland, Jaymes; Mamelok, Richard; Laberge, Marie-Kristine; Grenier, Julie; Swearingen, Dennis; Armas, Danielle; Lacy, Steven
CORPORATE SOURCE: Exelixis, Inc., San Francisco, CA, USA
SOURCE: Journal of Clinical Pharmacology (2015), 55(11), 1293-1302
CODEN: JCPCBR; ISSN: 0091-2700
DIGITAL OBJECT ID: 10.1002/jcph.526
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is a small mol. tyrosine kinase inhibitor that has been approved for the treatment of patients with progressive, metastatic medullary thyroid cancer. Cabozantinib exhibits a pH-dependent solubility profile in vitro. Two phase 1 clin. pharmacol. studies were conducted in healthy subjects to evaluate whether factors that may affect cabozantinib solubility and gastric pH could alter cabozantinib bioavailability: a food effect study (study 1) and a drug-drug interaction (DDI) study with the proton pump inhibitor (PPI) esomeprazole (study 2). Following a high-fat meal (study 1), cabozantinib Cmax and AUC were increased (40.5% and 57%, resp.), and the median tmax was delayed by 2 h. Cabozantinib should thus not be taken with food (patients should not eat for at least 2 h before and at least 1 h after administration). In the DDI study (study 2), the 90% confidence intervals (CIs) around the ratio of least-squares means of cabozantinib with esomeprazole vs. cabozantinib alone for AUC0-inf were within the 80%-125% limits; the upper 90%CI for Cmax was 125.1%. Because of the low apparent risk of a DDI, concomitant use of PPIs or weaker gastric pH-altering agents with cabozantinib is not contraindicated.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(evaluation of effect of food and gastric hydrogen ion concentration on single-dose pharmacokinetics of cabozantinib in healthy adult subjects)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



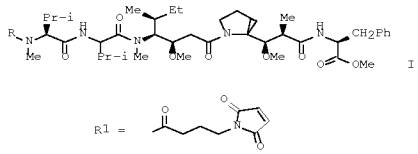
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 58 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623830 CAPLUS Full-text
DOCUMENT NUMBER: 163:553993
TITLE: Preparation of cytotoxic auristatin analogs and their conjugates with cell-binding molecules
INVENTOR(S): Liang, Qingliang; Zhao, Robert Y.; Ye, Hangbo; Gai, Shun; Jia, Junxiang; Huang, Yuanyuan; Li, Xing; Guo, Huihui; Xie, Hongsheng; Li, Wenjun; Zhou, Xiaomai; Yang, Chengyu; Zhuo, Xiaotao; Zhao, Linyao; Cao, Minjun; Lin, Chen; Peng, Jie; Ye, Zhicang; Xu, Jun
PATENT ASSIGNEE(S): Hangzhou DAC Biotech Co, Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 127pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

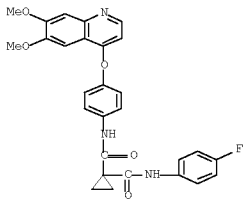
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151079	A2	20151008	WO 2015-IB54653	20150620

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2015-IB54653 20150620
OTHER SOURCE(S): MARPAT 163:553993
GI



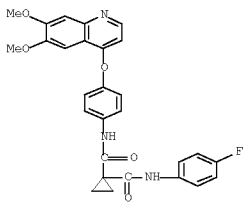
AB The invention is related to the prepn. of cytotoxic auristatin analogs, e.g., I, in particular monomethyl auristatin F (MMAF) conjugates of such cytotoxic agents with a cell-binding agent, methods of using them to arrest or retard abnormal cell growth and /or proliferation and to their use for targeted treatment of cancer, autoimmune disease, and infectious diseases. Thus, I [R = H] was prepared and coupled to 4-maleimidobutyric acid to provide I [R = R1] linker drug conjugate. A herceptin antibody-I [R = R1] conjugate was prepared and evaluated for its in vitro potency against N-87 human gastric carcinoma cells.
IT 849217-68-1, Cabozantinib 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug, synergistic agent; preparation of auristatin analogs and their conjugates with cell-binding mols. useful as antiproliferative and antitumor agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

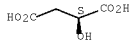
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

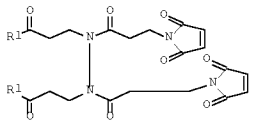
Absolute stereochemistry. Rotation (-).



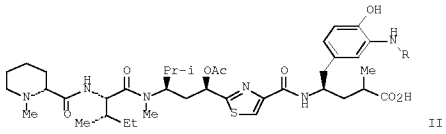
L4 ANSWER 59 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623829 CAPLUS Full-text
DOCUMENT NUMBER: 163:553992
TITLE: Preparation of bridge linkers used for specific conjugation of a cytotoxic agent to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 112pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151081	A2	20151008	WO 2015-IB55264	20150712
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150314017	A1	20151105	US 2015-14799712	20150715
PRIORITY APPLN. INFO.:			WO 2015-IB55264	T0 20150712

OTHER SOURCE(S): CASREACT 163:553992; MARPAT 163:553992
GI



I

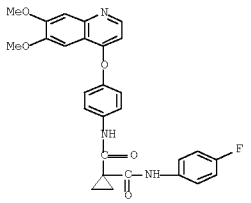


II

AB The invention is related to the prepn. of novel linkers contg. a hydrazine unit, e.g., I, used for the specific conjugation in particular cytotoxic agents to a cell-binding mol., through bridge linking a pair of thiols on the cell-binding mol. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by reaction with drugs and to their use for treating especially cancer. Thus, the linker I [R1 = OH] was prepared by a multi-step synthesis starting from O-benzylhydroxylamine hydrochloride and tert-Bu 3-aminopropanoate and 3-maleimidopropanoic acid. Reaction of I with oxalyl chloride, and treatment of the diacid dichloride with II [R = H] gave I [R1 = II wherein R is absent]. A herceptin antibody-I [R1 = II wherein R is absent] conjugate was prepared and evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 105 and for SK-OV-3 cell was over 3136.

IT **849217-68-1**, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.

L4 ANSWER 60 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623828 CAPLUS Full-text
DOCUMENT NUMBER: 163:585947
TITLE: Preparation of novel bridge linkers containing an acetylenedicarbonyl group for specific conjugation of a cytotoxic agent to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 113pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151080	A2	20151008	WO 2015-IB55051	20150704
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			WO 2015-IB55051	20150704

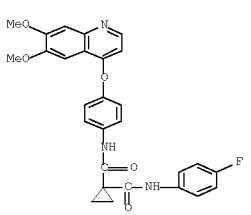
OTHER SOURCE(S): MARPAT 163:585947
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of novel bridge linkers contg. an acetylenedicarboxylic group, e.g., I, to link two drugs to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by reaction with drugs and to their use for treating especially cancer. Thus, I [R = 2,5-dioxopyrrolidin-1-yloxy] was prepared by reacting 13-amino-bis(4,7,10-trioxadodecanoic acid) (preparation given) with bis(2,5-dioxopyrrolidin-1-yl)but-2-ynedioate (preparation given) and treatment of the tetraacid with NHS. Amidation of I [R = 2,5-dioxopyrrolidin-1-yloxy] with tubulysin analog R1-H gave R1-I [R = absent] containing 4 tubulysins analog per bridge linker. A herceptin antibody-R1-I [R = absent] conjugate was prepared and evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 270 (IC50>10/IC50 = 0.037), and for SK-OV-3 cell was over 344.

IT **849217-68-1**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.

L4 ANSWER 61 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1623827 CAPLUS Full-text
DOCUMENT NUMBER: 163:553991
TITLE: Preparation of hydrophilic linkers for the conjugation of a cytotoxic agent or a chromophore to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

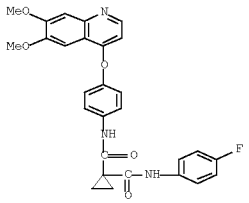
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151078	A2	20151008	WO 2015-IB54521	20150615
WO 2015151078	A3	20160310		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2015-IB54521 20150615
OTHER SOURCE(S): MARPAT 163:553991
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of hydrophilic linkers contg. phosphamide, phosphinate, sulfonamide, sulfonyl, sulfonimide, and/or sulfoxide groups, e.g., I, to link drugs, in particular, cytotoxic agents or a chromophore mols. to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (e.g. cytotoxic agent) conjugates comprising either modification of the drugs with these hydrophilic linkers first, followed by reaction with cell-binding agents; or modification of cell-binding agents with these hydrophilic linkers first, followed by reaction with drugs. Thus, linker I was prepared from N-methylethane-1,2-diamine and succinic anhydride using POCl3, 3-(methylamino)propanoic acid and NHS. Conjugation of I with the tubulysin analog II [R = H] gave the drug-linker conjugate II [R = Rl]. An antiHer2-II [R= Rl] antibody conjugate of was prepared and evaluated for its in vitro cytotoxicity. The specificity of the conjugate for N87 cell was over 1315 (IC50> 50/IC50= 0.038), and for SK-OV-3 cell was over 1560.
IT 849217-68-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)

L4 ANSWER 62 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1617130 CAPLUS Full-text
DOCUMENT NUMBER: 163:553989
TITLE: Preparation of hydrophilic linkers for the conjugation of a cytotoxic agent or a chromophore to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: U.S. Pat. Appl. Publ., 69pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

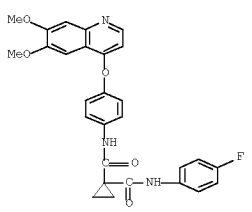
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150284416	A1	20151008	US 2015-14740403	20150616
WO 2015155753	A2	20151015	WO 2015-IB56083	20150810

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-14740403 T0 20150616
OTHER SOURCE(S): CASREACT 163:553989
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of hydrophilic linkers contg. phosphamide, phosphinate, sulfonamide, sulfonyl, sulfonimide, and/or sulfoxide groups, e.g., I, to link drugs, in particular, cytotoxic agents or a chromophore mols. to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (e.g. cytotoxic agent) conjugates comprising either modification of the drugs with these hydrophilic linkers first, followed by reaction with cell-binding agents; or modification of cell-binding agents with these hydrophilic linkers first, followed by reaction with drugs. Thus, linker I was prepared from N-methylethane-1,2-diamine and succinic anhydride using POCl3, 3-(methylamino)propanoic acid and NHS. Conjugation of I with the tubulysin analog II [R = H] gave the drug-linker conjugate II [R = Rl]. An antiHer2-II [R= Rl] antibody conjugate of was prepared and evaluated for its in vitro cytotoxicity. The specificity of the conjugate for N87 cell was over 1315 (IC50> 50/IC50= 0.038), and for SK-OV-3 cell was over 1560.
IT 849217-68-1P, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 63 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1617114 CAPLUS Full-text
DOCUMENT NUMBER: 163:551060
TITLE: Combination therapy comprising anti-angiogenesis agents and OX40 binding agonists
INVENTOR(S): Walsh, Kevin; De Almeida, Patricia; Du, Changchun; Kim, Jeong; Zhu, Jing; Bevers, Jack; Andya, James; Shen, Ye
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 166pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015153514	A1	20151008	WO 2015-US23434	20150330

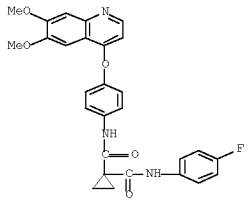
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20150307617	A1	20151029	US 2015-14673792	20150330

PRIORITY APPLN. INFO.:
US 2014-61973193 P 20140331
US 2014-61989448 P 20140506
US 2014-62073873 P 20141031
US 2014-62080171 P 20141114
US 2015-62113345 P 20150206
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

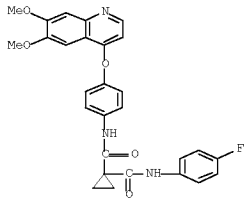
AB The authors disclose a cancer treatment method comprising the administering of an anti-angiogenesis agent and an OX40 binding agonist. In the one example, anti-VEGF antibody treatment resulted in reduced tumor growth, compared to anti-gp120 (control), in a syngeneic mouse colon carcinoma model. Anti-OX40 antibody treatment exhibited little activity alone. Anti-OX40 treatment in combination with anti-VEGF treatment demonstrated superior tumor growth inhibition when compared to single agent administration or anti-gp120 treatment.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-angiogenesis agents in combination with OX40 agonists for treatment of cancer)
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 64 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1606231 CAPLUS Full-text
TITLE: Antitumor Effects and Mechanisms of AZD4547 on FGFR2-Deregulated Endometrial Cancer Cells
AUTHOR(S): Kwak, Yeonui; Cho, Hanna; Hur, Wooyoung; Sim, Taebo
CORPORATE SOURCE: KU-KIST Graduate School of Converging Science and Technology, Korea University, Seoul, S. Korea
SOURCE: Molecular Cancer Therapeutics (2015), 14(10), 2292-2302
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-15-0032
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Uncontrolled activation of FGFRs induces the progression of various cancers. It was recently reported that FGFR2-activating mutants are implicated in about 12% of endometrial carcinomas. AZD4547, a potent pan-FGFR inhibitor, is currently being evaluated in clin. trials for several FGFR-driven cancers. However, AZD4547 has not been examined yet against FGFR2 mutant-driven endometrial cancers. Thus, we evaluated the activity of AZD4547 against four different endometrial cancer cells, including AN3-CA, MFE296, MFE280, and HEC1A, where all but HEC1A cells express distinctive FGFR2 mutations. We found that AZD4547 exhibits potent antiproliferative activity (EC50 = 31 nmol/L) against AN3-CA cells harboring FGFR2-K310R/N550K mutant. Anal. using a phospho-kinase array revealed that AZD4547 blocks FGFR2 downstream signaling, such as p38, ERK1/2, JNK, p70S6K, and PLCγ. Moreover, oral administration of AZD4547 (30 mg/kg, every day) remarkably delayed tumor growth in a mouse xenograft model of AN3-CA cells. Unbiased reporter gene assay showed that AZD4547 antagonizes the aFGF-induced activation of several transcription factors, including EGR1, ELK-1/SRF, AP-1, and NFκB. Genome-wide transcriptome anal. revealed that AZD4547 perturbs a number of transcriptions, and EGR1 was identified as one of the major targets of AZD4547. The significance of the FGFR2-EGR1 axis in endometrial cancer progression has not been reported. In addition, using kinome-wide inhibition profiling anal., we first identified potential new target kinases of AZD4547, including MAP4K3, MAP4K5, IRR, RET, and FLT3. Our study demonstrated that AZD4547 exhibits its therapeutic activity against endometrial cancer cells by perturbing various regulatory mechanisms related to FGFR signaling. Mol Cancer Ther; 14(10); 2292-302. ©2015 AACR.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (antitumor effects and mechanisms of AZD4547 on FGFR2-deregulated endometrial cancer cells)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



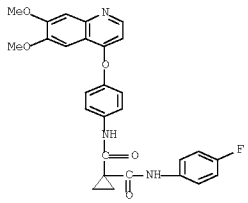
L4 ANSWER 65 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1604658 CAPLUS Full-text
DOCUMENT NUMBER: 163:569777
TITLE: Preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid salt and their crystal forms
INVENTOR(S): Chen, Minhua; Zhang, Yanfeng; Li, Jiaoyang; Zhang, Xiaoyu; Lu, Fei
PATENT ASSIGNEE(S): Crystal Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104961681	A	20151007	CN 2014-10641139	20141113

PRIORITY APPLN. INFO.: CN 2014-10641139 20141113
AB The title N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid salt has higher solubility than N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide malate, and plays important roles in improving the bioavailability, treatment effect, and safety of drug.
IT 1817758-85-8P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure; preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid and their crystal forms)
RN 1817759-89-9 CAPLUS
CN Galactaric acid, compd. with N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

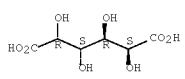
CRN 849217-68-1
CMF C28 H24 F N3 O5



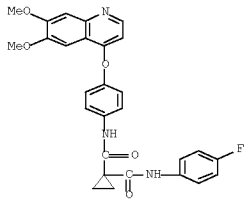
CM 2

CRN 526-99-8
CMF C6 H10 O8

Relative stereochemistry.



IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid and their crystal forms)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

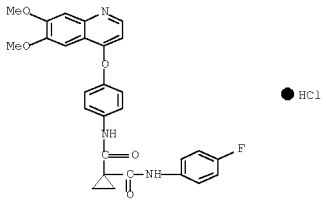


L4 ANSWER 66 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1604653 CAPLUS Full-text
DOCUMENT NUMBER: 163:569776
TITLE: Preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms
INVENTOR(S): Chen, Minhua; Zhang, Yanfeng; Li, Jiaoyang; Zhang, Xiaoyu; Lu, Fei
PATENT ASSIGNEE(S): Crystal Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

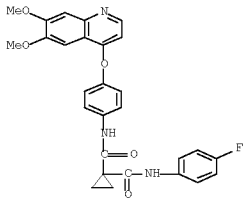
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104961680	A	20151007	CN 2014-10626255	20141107

PRIORITY APPLN. INFO.: CN 2014-10626255 20141107
AB The title N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride has higher solubility than N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide malate, and plays important roles in improving the bioavailability, treatment effect, and safety of drug.
IT 1817759-42-4P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure; preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms)

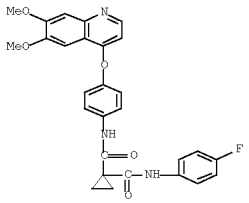
RN 1817759-42-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrochloride (1:1) (CA INDEX NAME)



IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

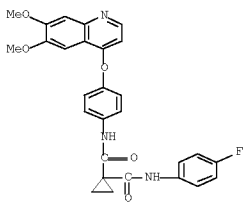


L4 ANSWER 67 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1602738 CAPLUS Full-text
TITLE: TAMing resistance to multi-targeted kinase inhibitors through Axl and Met inhibition
AUTHOR(S): Pinato, D. J.; Chowdhury, S.; Stebbing, J.
CORPORATE SOURCE: Department of Surgery and Cancer, Imperial College London, London, UK
SOURCE: Oncogene (2015) Ahead of Print
CODEN: ONCNES; ISSN: 0950-9232
DIGITAL OBJECT ID: 10.1038/onc.2015.374
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. TAM (Tyro3-Axl-Mer) receptor tyrosine kinases and Met are implicated in several hallmarks of cancer progression including sustained angiogenesis, enhanced motility, tissue invasion and acquisition of metastatic potential through the upregulation of epithelial-to-mesenchymal transition. Increasing evidence has confirmed Axl and Met as emerging central drivers of adaptive resistance to targeted therapies across a wide variety of cancers. In this issue of Oncogene, Zhou et al. describe the mechanisms linking Axl and Met activation to acquired resistance to sunitinib in renal cell carcinoma (RCC), providing a pre-clin. rationale for the development of Axl and Met inhibitors including cabozantinib in anti-angiogenic resistant RCC.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TAMing resistance to multi-targeted kinase inhibitors through Axl and Met inhibition)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



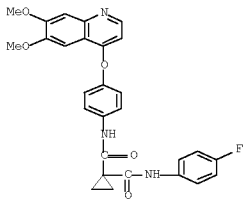
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 68 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1593218 CAPLUS Full-text
DOCUMENT NUMBER: 163:673623
TITLE: Cabozantinib in Thyroid Cancer
AUTHOR(S): Fallahi, Poupak; Ferrari, Silvia M.; Di Bari, Flavia; Materazzi, Gabriele; Benvenga, Salvatore; Miccoli, Paolo; Antonelli, Alessandro
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56126, Italy
SOURCE: Recent Patents on Anti-Cancer Drug Discovery (2015), 10(3), 259-269
CODEN: RPADDY; ISSN: 1574-8928
DIGITAL OBJECT ID: 10.2174/1574892810666150708110816
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib is an oral once-daily multitarget tyrosine kinase inhibitor of MET, VEGFR2, RET, acting against KIT, AXL, FLT3 and Tie-2. Cabozantinib has shown anti-cancer effects in preclin. and clin. models of cancers derived from both epithelial and mesenchymal origins [prostate cancer, non small lung cancer, medullary thyroid cancer (MTC) and differentiated thyroid cancer (DTC), renal cell carcinoma, etc.]. In a Phase III clin. study, cabozantinib improved PFS (11.2 mo vs. 4.0 mo in the placebo group) of patients with MTC (independently of age, bone metastases, RET status and prior treatment). Cabozantinib was approved in 2012 by FDA for metastatic MTC and in 2013 by EMA. Cabozantinib has been also evaluated in metastatic DTC patients, because they have activation on tyrosine kinases, including MET, VEGFR2 and RET, suggesting the possible use of cabozantinib in metastatic DTC. Actually, two Phase II trials of cabozantinib in DTC patients resistant to RAI are ongoing. To increase the antineoplastic effect of cabozantinib, and to overcome the occurrence of drug resistance, combination studies with other anticancer agents are ongoing. In conclusion, cabozantinib has shown to exert an important therapeutic effect in patients with MTC improving PFS. In DTC patients, cabozantinib has shown promising results.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of tyrosine kinase inhibitor cabozantinib in thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



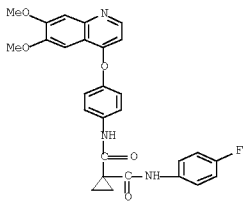
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 152 THERE ARE 152 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 69 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1592351 CAPLUS Full-text
TITLE: Sensitivity of neuroblastoma to the novel kinase inhibitor cabozantinib is mediated by ERK inhibition
AUTHOR(S): Zhang, Linna; Scorsone, Kathleen; Woodfield, Sarah E.; Zage, Peter E.
CORPORATE SOURCE: Department of Pediatrics, Section of Hematology-Oncology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Cancer Chemotherapy and Pharmacology (2015), 76(5), 977-987
CODEN: CCPHDZ; ISSN: 0344-5704
DIGITAL OBJECT ID: 10.1007/s00280-015-2871-z
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Purpose: Children with high-risk neuroblastoma have poor survival rates, and novel therapies are needed. We hypothesized that cabozantinib would be effective against neuroblastoma tumor cells and tumors in preclin. models via inhibition of receptor tyrosine kinase signaling pathways. Methods: We determined neuroblastoma cell viability after treatment with cabozantinib alone and in combination with 13-cis-retinoic acid, topotecan, and temozolomide using MTT assays. Inhibition of RET and intracellular signaling was measured by Western blot anal. of treated and untreated cells. To investigate the efficacy of cabozantinib against neuroblastoma tumors in vivo, neuroblastoma cells were injected orthotopically into immunocompromised mice, and mice were treated with oral cabozantinib. Tumors were evaluated for growth by determination of in vivo luminescence and final tumor wts. Results: All neuroblastoma cell lines were sensitive to cabozantinib, and IC50 values ranged from 1.6 to 16.2 μM. Cabozantinib treatment was synergistic with 13-cis-retinoic acid and chemotherapy agents topotecan and temozolomide. Cabozantinib treatment inhibited RET phosphorylation in all cell lines and ERK phosphorylation in more sensitive neuroblastoma cell lines. In mice with neuroblastoma xenograft tumors, cabozantinib treatment significantly reduced tumor growth. Conclusions: Treatment of neuroblastoma tumor cells with cabozantinib inhibits RET and ERK phosphorylation and is effective against neuroblastoma tumor cell lines alone and in combination with 13-cis-retinoic acid, topotecan, and temozolomide. Cabozantinib treatment is also effective in reducing tumor growth in vivo. Cabozantinib therefore represents a novel therapeutic agent for neuroblastoma, and further preclin. and clin. studies are warranted.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(efficacy of cabozantinib against neuroblastoma tumor cells and tumors in preclin. immunocompromised mouse models via inhibition of receptor tyrosine kinase signaling pathways)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



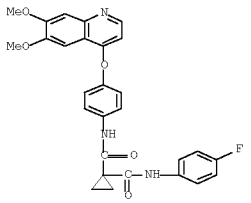
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 70 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1582731 CAPLUS Full-text
TITLE: MET/HGF targeted drugs as potential therapeutic strategies in non-small cell lung cancer
AUTHOR(S): Perez-Ramirez, Cristina; Canadas-Garre, Marisa; Molina, Miguel Angel; Faus-Dader, Maria Jose; Calleja-Hernandez, Miguel Angel
CORPORATE SOURCE: Pharmacogenetics Unit, UGC Provincial de Farmacia de Granada, Instituto de Investigacion Biosanitaria de Granada, Complejo Hospitalario Universitario de Granada, Granada, Spain
SOURCE: Pharmacological Research (2015), 102, 90-106
CODEN: PHMREP; ISSN: 1043-6618
DIGITAL OBJECT ID: 10.1016/j.phrs.2015.09.016
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. This article discusses about MET pathway signaling and dysregulation development of MET inhibitors like tivantinib, cabozantinib, crizotinib and foretinib to block HGF/MET signaling pathway and use of c-Met protein /hepatocyte growth factor targeted drugs as potential therapeutic strategies in non-small cell lung cancer in human and mouse model.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of c-Met protein/hepatocyte growth factor targeted drugs as potential therapeutic strategies in non-small cell lung cancer in human and mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 72 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1577497 CAPLUS Full-text
TITLE: Rapid modification of the bone microenvironment following short-term treatment with Cabozantinib in vivo
AUTHOR(S): Haider, Marie-Therese; Hunter, Keith D.; Robinson, Simon P.; Graham, Timothy J.; Corey, Eva; Dear, T. Neil; Hughes, Russell; Brown, Nicola J.; Holen, Ingunn
CORPORATE SOURCE: Department of Oncology, University of Sheffield, Sheffield, UK
SOURCE: Bone (New York, NY, United States) (2015), 81, 581-592
CODEN: BONEDL; ISSN: 1873-2763
DIGITAL OBJECT ID: 10.1016/j.bone.2015.08.003
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Bone metastasis remains incurable with treatment restricted to palliative care. Cabozantinib (CBZ) is targeted against multiple receptor tyrosine kinases involved in tumor pathobiol., including hepatocyte growth factor receptor (MET) and vascular endothelial growth factor receptor 2 (VEGFR-2). CBZ has demonstrated clin. activity in advanced prostate cancer with resolution of lesions visible on bone scans, implicating a potential role of the bone microenvironment as a mediator of CBZ effects. We characterised the effects of short-term administration of CBZ on bone in a range of in vivo models to determine how CBZ affects bone in the absence of tumor. Studies were performed in a variety of in vivo models including male and female BALB/c nude mice (age 6-17-wk). Animals received CBZ (30 mg/kg, 5 × weekly) or sterile H2O control for 5 or 10 days. Effects on bone integrity (μCT), bone cell activity (PINP, TRAP ELISA), osteoblast and osteoclast number/mm trabecular bone surface, area of epiphyseal growth plate cartilage, megakaryocyte nos. and bone marrow composition were assessed. Effects of longer-term treatment (15-day & 6-wk administration) were assessed in male NOD/SCID and beige SCID mice. CBZ treatment had significant effects on the bone microenvironment, including reduced osteoclast and increased osteoblast nos. compared to control. Trabecular bone structure was altered after 8 administrations. A significant elongation of the epiphyseal growth plate, in particular the hypertrophic chondrocyte zone, was observed in all CBZ treated animals irresp. of administration schedule. Both male and female BALB/c nude mice had increased megakaryocyte nos./mm2 tissue after 10-day CBZ treatment, in addition to vascular ectasia, reduced bone marrow cellularity and extravasation of red blood cells into the extra-vascular bone marrow. All CBZ-induced effects were transient and rapidly lost following cessation of treatment. Short-term administration of CBZ induces rapid, reversible effects on the bone microenvironment in vivo highlighting a potential role in mediating treatment responses.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rapid modification of bone microenvironment following short-term treatment with cabozantinib in vivo)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

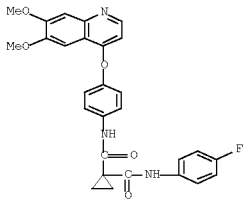


REFERENCE COUNT: 202 THERE ARE 202 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 71 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1579900 CAPLUS Full-text
DOCUMENT NUMBER: 163:512733
TITLE: Cancer treatment with c-MET antagonists and correlation of the latter with HGF expression
INVENTOR(S): Yu, Wei; Shames, David; Koeppen, Hartmut; Phan, See; Rost, Sandra
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 178pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015148531	A1	20151001	WO 2015-US22282	20150324
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2014-61969706 P 20140324
US 2014-61985316 P 20140428
AB The present invention concerns cancer biomarkers. In particular, the invention concerns HGF as a biomarker for patient selection and patient prognosis in cancer, as well as methods of therapeutic treatment, articles of manufacture and methods for making them, diagnostic kits, methods of detection and methods of advertising related thereto. Cancer patients are treated with an anti-c-met antibody in combination with an anti-VEGF antibody.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer treatment with c-MET antagonists and correlation of the latter with HGF expression)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

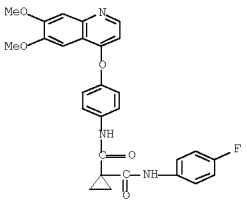
L4 ANSWER 73 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1577278 CAPLUS Full-text
DOCUMENT NUMBER: 164:288433
TITLE: Stromal expression of VEGF-A and VEGFR-2 in prostate tissue is associated with biochemical and clinical recurrence after radical prostatectomy

AUTHOR(S): Nordby, Yngve; Andersen, Sigve; Richardsen, Elin; Ness, Nora; Al-Saad, Samer; Melbo-Jorgensen, Christian; Patel, Hiten R. H.; Donnem, Tom; Busund, Lill-Tove; Bremnes, Roy M.
CORPORATE SOURCE: Department Clinical Medicine, The Arctic University of Norway, Tromso, Norway
SOURCE: Prostate (Hoboken, NJ, United States) (2015), 75(15), 1682-1693
CODEN: PRSTDS; ISSN: 0270-4137
DIGITAL OBJECT ID: 10.1002/pros.23048
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background : There is probably significant overtreatment of patients with prostate cancer due to a lack of sufficient diagnostic tools to predict aggressive disease. Vascular endothelial growth factors (VEGFs) and their receptors (VEGFRs) are potent mediators of angiogenesis and tumor proliferation, but have been examined to a limited extent in large prostate cancer studies. Meanwhile, recent promising results on VEGFR-2 inhibition have highlighted their importance, leading to the need for further investigations regarding their expression and prognostic impact. Design : Using tissue microarray and immunohistochem., the expression of VEGFs (VEGF-A and VEGF-C) and their receptors (VEGFR-2 and VEGFR-3) were measured in neoplastic tissue and corresponding stroma from radical prostatectomy specimens in 535 Norwegian patients. Their expression was evaluated semiquantatively and assocns. with event-free survival were calculated Results : High expression of VEGFR-2 in either stroma or epithelium was independently associated with a higher incidence of prostate cancer relapse (HR = 4.56, P = 0.038). A high combined expression of either VEGF-A, VEGFR-2 or both in stroma was independently associated with a higher incidence of biochem. failure (HR = 1.77, P = 0.011). Conclusions : This large study highlights the prognostic importance of VEGF-A and VEGFR-2 stromal expression. Analyses of these biomarkers may help distinguish which patients will benefit from radical treatment. Together with previous studies showing efficiency of targeting VEGFR-2 in prostate cancer, this study highlights its potential as a target for therapy, and may aid in future selection of prostate cancer patients for novel anti-angiogenic treatment. Prostate 75:1682-1693, 2015. 2015 Wiley Periodicals, Inc.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stromal expression of VEGF-A and VEGFR-2 in prostate tissue was associated with biochem. and clin. recurrence in human after radical prostatectomy)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 74 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1545892 CAPLUS Full-text
DOCUMENT NUMBER: 163:469529
TITLE: Target inhibition map system for combination antitumor therapy design and methods of using same
INVENTOR(S): Pal, Ranadip; Keller, Charles, III; Berlow, Noah E.; Seguin, Bernard
PATENT ASSIGNEE(S): Texas Tech University System, USA; Colorado State University Research Foundation
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

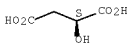
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150269307	A1	20150924	US 2015-14661918	20150318
PRIORITY APPLN. INFO.:			US 2014-61955068 P	20140318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed is a system and method for targeted therapy designs which model a cancer pathway for predicting the effectiveness of targeted anti-cancer drugs. The disclosed system and method includes utilization of a computer processor allowing for the selection of a set of drugs from available drugs using approximation algorithms utilizing cell viability data associated with a testable culture of a patient's tumor for generating a probabilistic target inhibition map (PTIM) from viability data for considering the selection of a set of drugs from available drugs, and further supports a wide variety of scenarios for personalized cancer therapy, related products and services.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(target inhibition map system for combination therapy design and methods of using same)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



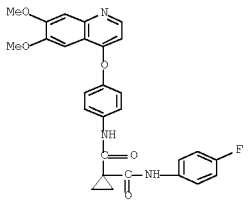
L4 ANSWER 75 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1542977 CAPLUS Full-text
DOCUMENT NUMBER: 163:469542
TITLE: Dosing of cabozantinib formulations
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015142928	A1	20150924	WO 2015-US21072	20150317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2014-61954352 P	20140317
OTHER SOURCE(S):		CASREACT 163:469542		

AB The invention relates to administration of various pharmaceutical formulations of N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1- dicarboxamide, (cabozantinib) a c-Met inhibitor, and its metabolites, to achieve desirable pharmacokinetic and pharmacodynamic effects.

IT 1809822-99-8
RL: ANT (Analyte); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dosing of cabozantinib formulations)

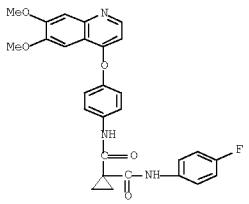
RN 1809822-99-8 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, labeled with carbon-14 (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

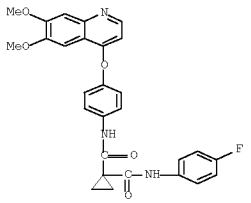
CRN 849217-68-1
CMF C28 H24 F N3 O5



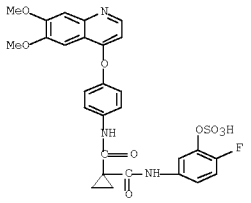
CM 2

CRN 97-67-6
CMF C4 H6 O5

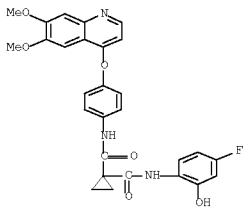
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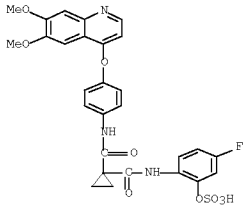
IT 1628530-45-9 1628542-34-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dosing of cabozantinib formulations)
RN 1628530-45-9 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[4-fluoro-3-(sulfooxy)phenyl]- (CA INDEX NAME)



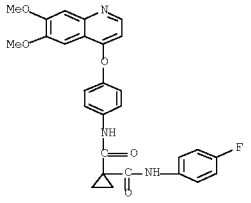
RN 1628542-34-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, monohydroxy deriv. (CA INDEX NAME)



RN 1628530-40-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[4-fluoro-2-(sulfooxy)phenyl]- (CA INDEX NAME)

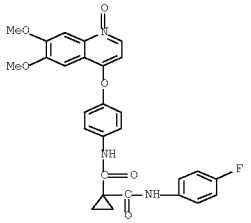


RN 1628530-41-5 CAPLUS
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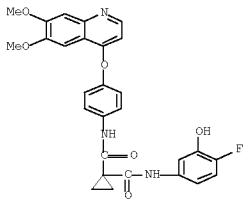


D1—OH

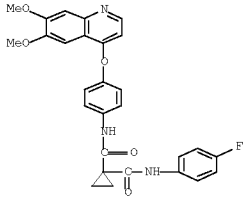
IT 1621681-63-7 1628530-38-0 1628530-40-4
1628530-41-5
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosing of cabozantinib formulations)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 1628530-38-0 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluoro-2-hydroxyphenyl)- (CA INDEX NAME)



IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosing of cabozantinib formulations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

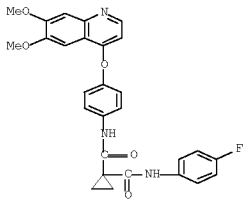
L4 ANSWER 76 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1518424 CAPLUS Full-text
DOCUMENT NUMBER: 163:693610
TITLE: Cabozantinib for the treatment of non-small cell lung cancer with KIF5B-RET fusion. An example of swift repositioning
AUTHOR(S): Song, Minsoo; Kim, Seong-Heon; Yoon, Suk Kyoon
CORPORATE SOURCE: New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Taegu, 701-310, S. Korea
SOURCE: Archives of Pharmacal Research (2015), 38(12),

2120-2123
CODEN: APHRDQ; ISSN: 0253-6269
DIGITAL OBJECT ID: 10.1007/s12272-015-0660-1
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A new chimeric fusion transcript of KIF5B (the kinesin family 5B gene) and the RET (Rearranged during Transcription) oncogene, KIF5B-RET, was found in 1-2 % of lung adenocarcinomas (LADCs) in 2012. Several related clin. trials for non-small cell lung cancer (NSCLC) with KIF5B-RET rearrangements using existing RET inhibitors, such as cabozantinib, lenvatinib, vandetanib, sunitinib, ponatinib, and AUY922, have been swiftly initiated by the discovery of the KIF5B-RET fusion gene. Anti-RET activity and the status of clin. development of cabozantinib for KIF5B-RET fusion-pos. NSCLC are discussed.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of non-small cell lung cancer with KIF5B-RET fusion. An example of swift repositioning)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



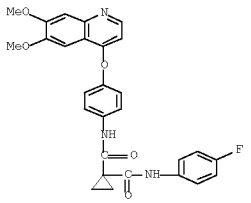
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 77 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1512965 CAPLUS Full-text
TITLE: Design, synthesis and pharmacological evaluation of novel 4-phenoxyquinoline derivatives as potential antitumor agents
AUTHOR(S): Hu, Hao; Jiang, Mingyan; Xie, Lijun; Hu, Gang; Zhang, Cuirong; Zhang, Lixia; Zhou, Shunguang; Zhang, Meihui; Gong, Ping
CORPORATE SOURCE: Key Laboratory of Structure-based Drug Design and Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Chemical Research in Chinese Universities (2015), 31(5), 746-755
CODEN: CRCUED; ISSN: 1005-9040
DIGITAL OBJECT ID: 10.1007/s40242-015-5166-3
PUBLISHER: Jilin University
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB A series of novel 4-phenoxyquinoline derivs. contg. 3-amino-2-cyano-acrylamide framework was designed and synthesized, and the in vitro cytotoxic activities of them against five cancer cell lines(HT-29, H460, A549, MKN-45, and U87MG) were evaluated. Most of the compds. exhibited moderate-to-significant cytotoxicity and high selectivity against one or more cell lines as compared with Foretinib. The studies of their preliminary structure-activity relationships(SARs) indicate that the compds. containing Me groups, especially Me groups at 4-position of the Ph ring(moiety B) are more effective. Among them, compound 36 shows the most potent antitumor activities with IC50 values of 0.04, 0.09, 0.67, 0.39 and 1.10 μmol/L against HT-29, H460, A549, MKN-45 and U87MG cell lines, resp.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(design, synthesis and pharmacol. evaluation of novel 4-phenoxyquinoline derivs. as potential antitumor agents)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



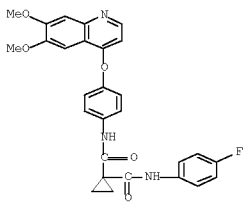
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 78 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1496569 CAPLUS Full-text
TITLE: Oral adverse events in cancer patients treated with VEGFR-directed multitargeted tyrosine kinase inhibitors
AUTHOR(S): Yuan, Anna; Kurtz, Sharyn L.; Barysauskas, Constance M.; Pilotte, Amy P.; Wagner, Andrew J.; Treister, Nathaniel S.
CORPORATE SOURCE: Division of Oral Medicine, Brigham and Women's Hospital, Boston, MA, 02115, USA
SOURCE: Oral Oncology (2015), 51(11), 1026-1033
CODEN: EJCCER; ISSN: 1368-8375
DIGITAL OBJECT ID: 10.1016/j.oraloncology.2015.09.003
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB This study characterized the incidence and clin. features of oral adverse events among cancer patients who received VEGFR-directed multitargeted tyrosine kinase inhibitor (VR-TKI) therapies.Electronic medical records of adult cancer patients treated with sunitinib, sorafenib, regorafenib, pazopanib, cabozantinib, imatinib, and bevacizumab therapy at Dana-Farber Cancer Institute from 2009 to 2012 were reviewed. Data collected included patient characteristics, oral and non-oral adverse events, and time to onset. Time oral adverse event-free was the primary outcome.A total of 747 patients with 806 individual courses of therapy were treated for a median of 3.9 mo with sunitinib (n = 161), sorafenib (n = 172), regorafenib (n = 15), pazopanib (n = 132), cabozantinib (n = 23), imatinib (n = 144), or bevacizumab (n = 159) for lung cancer (21%), gastrointestinal stromal tumor (15%), and metastatic renal cell carcinoma (13%). An oral adverse event was reported in 23.7% of patients at a median of 1.9 mo after starting therapy. The most commonly reported oral adverse event was oral mucosal sensitivity (dysesthesia), occurring in 12% of patients, typically without clin. findings. Multivariate models showed patients who received VR-TKI therapy were at greater risk of any oral adverse event compared with patients treated with imatinib or bevacizumab. Patients receiving VR-TKI therapy who developed an oral adverse event were also at increased risk for hand-foot skin reaction (15.9%).VR-TKI associated oral adverse events are characterized primarily by dysesthesia with lack of clin. signs. Oral dysesthesia is more commonly associated with VR-TKIs than with bevacizumab or imatinib. Management is largely empirical and requires further investigation.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oral adverse events in cancer patients treated with VEGFR-directed multitargeted tyrosine kinase inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



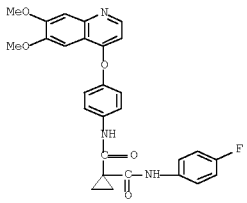
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 79 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1474667 CAPLUS Full-text
DOCUMENT NUMBER: 164:415926
TITLE: Antioxidant and Anticoagulant Status Were Improved by Personalized Dietary Intervention Based on Biochemical and Clinical Parameters in Cancer Patients
AUTHOR(S): Lee, Ga-Yi; Lee, Jong Jyun; Lee, Seung-Min
CORPORATE SOURCE: Program of Clinical Nutrition, Yonsei Graduate School of Human Environmental Sciences, Seoul, S. Korea
SOURCE: Nutrition and Cancer (2015), 67(7), 1083-1092
CODEN: NUCADQ; ISSN: 0163-5581
DIGITAL OBJECT ID: 10.1080/01635581.2015.1073754
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB We investigated whether personalized dietary intervention could improve clin. measurements such as immune cell-mediated cytotoxicity, serum albumin, derivs. of reactive oxygen metabolites (D-ROMS), D-dimer, and fibrinogen. Cancer patients received either a treatment support diet (TD, for those with chemotherapy), or a remission support diet (RD; for those in remission) for at least 3 wk (21-61 days). Both diets were low glycemic, low fat, and high plant protein diets; the diet for the TD group contained an addnl. 0.5 servings of protein. Based on clin. values, addnl. amts. of garlic, onion, tomato, shiitake, rice bran, kale, blueberry, pineapples, and/or turmeric powder were provided in regular meals. Estimated daily intake of protein, plant fat, garlic, onion, allicin, and quercetin was greater in the TD compared to the RD. An increased intake of vitamin A, vitamin C, vitamin E and selenium and a reduction in D-dimer were noted compared to baseline diets in both groups. A decrease in D-ROMS in the RD and an increase in albumin and an increased tendency in cytotoxicity in the TD were observed In conclusion, personalized diets with supplemented functional ingredients improved antioxidant status and/or anticoagulant activity in cancer patients undergoing chemotherapy and in remission.

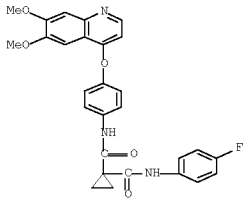
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant and anticoagulant status were improved by personalized dietary intervention based on biochem. and clin. parameters in cancer patients)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

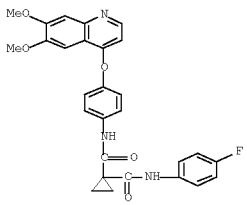
L4 ANSWER 80 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1456151 CAPLUS Full-text
DOCUMENT NUMBER: 163:418831
TITLE: Structural insight into selectivity and resistance profiles of ROS1 tyrosine kinase inhibitors
AUTHOR(S): Davare, Monika A.; Vellore, Nadeem A.; Wagner, Jacob P.; Eide, Christopher A.; Goodman, James R.; Drilon, Alexander; Deininger, Michael W.; O'Hare, Thomas; Druker, Brian J.
CORPORATE SOURCE: Knight Cancer Institute, Oregon Health & Science University, Portland, OR, 97239, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2015), 112(39), E5381-E5390
CODEN: PNASA6; ISSN: 0027-8424
DIGITAL OBJECT ID: 10.1073/pnas.1515281112
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Oncogenic ROS1 fusion proteins are mol. drivers in multiple malignancies, including a subset of non-small cell lung cancer (NSCLC). The phylogenetic proximity of the ROS1 and anaplastic lymphoma kinase (ALK) catalytic domains led to the clin. repurposing of the Food and Drug Administration (FDA)-approved ALK inhibitor crizotinib as a ROS1 inhibitor. Despite the antitumor activity of crizotinib observed in both ROS1- and ALK-rearranged NSCLC patients, resistance due to acquisition of ROS1 or ALK kinase domain mutations has been observed clin., spurring the development of second-generation inhibitors. Here, we profile the sensitivity and selectivity of seven ROS1 and/or ALK inhibitors at various levels of clin. development. In contrast to crizotinib's dual ROS1/ALK activity, cabozantinib (XL-184) and its structural analog foretinib (XL-880) demonstrate a striking selectivity for ROS1 over ALK. Mol. dynamics simulation studies reveal structural features that distinguish the ROS1 and ALK kinase domains and contribute to differences in binding site and kinase selectivity of the inhibitors tested. Cell-based resistance profiling studies demonstrate that the ROS1-selective inhibitors retain efficacy against the recently reported CD74-ROS1G2032R mutant whereas the dual ROS1/ALK inhibitors are ineffective. Taken together, inhibitor profiling and stringent characterization of the structure-function differences between the ROS1 and ALK kinase domains will facilitate future rational drug design for ROS1- and ALK-driven NSCLC and other malignancies.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural insight into selectivity and resistance profiles of ROS1 tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 81 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1433158 CAPLUS Full-text
TITLE: Altiratinib Inhibits Tumor Growth, Invasion, Angiogenesis, and Microenvironment-Mediated Drug Resistance via Balanced Inhibition of MET, TIE2, and VEGFR2
AUTHOR(S): Smith, Bryan D.; Kaufman, Michael D.; Leary, Cynthia B.; Turner, Benjamin A.; Wise, Scott C.; Ahn, Yu Mi; Booth, R. John; Caldwell, Timothy M.; Ensinger, Carol L.; Hood, Molly M.; Lu, Wei-Ping; Patt, Tristan W.; Patt, William C.; Rutkoski, Thomas J.; Samarakoon, Thiwanka; Telikepalli, Hanumaiah; Vogeti, Lakshminarayana; Vogeti, Subha; Yates, Karen M.; Chun, Lawrence; Stewart, Lance J.; Clare, Michael; Flynn, Daniel L.
CORPORATE SOURCE: Deciphera Pharmaceuticals, Lawrence, KS, USA
SOURCE: Molecular Cancer Therapeutics (2015), 14(9), 2023-2034
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-14-1105
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Altiratinib (DCC-2701) was designed based on the rationale of engineering a single therapeutic agent able to address multiple hallmarks of cancer (1). Specifically, altiratinib inhibits not only mechanisms of tumor initiation and progression, but also drug resistance mechanisms in the tumor and microenvironment through balanced inhibition of MET, TIE2 (TEK), and VEGFR2 (KDR) kinases. This profile was achieved by optimizing binding into the switch control pocket of all three kinases, inducing type II inactive conformations. Altiratinib durably inhibits MET, both wild-type and mutated forms, in vitro and in vivo. Through its balanced inhibitory potency vs. MET, TIE2, and VEGFR2, altiratinib provides an agent that inhibits three major evasive (re)vascularization and resistance pathways (HGF, ANG, and VEGF) and blocks tumor invasion and metastasis. Altiratinib exhibits properties amenable to oral administration and exhibits substantial blood-brain barrier penetration, an attribute of significance for eventual treatment of brain cancers and brain metastases. Mol Cancer Ther; 14(9); 2023-34. ©2015 AACR.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(altiratinib inhibited tumor growth, invasion, angiogenesis, and micro environment mediated drug resistance through balanced inhibition of MET, TIE2, and VEGFR2 in human cancer cell lines and mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



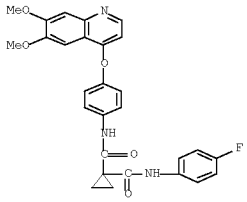
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 82 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1392691 CAPLUS Full-text
DOCUMENT NUMBER: 163:345656
TITLE: Use of ibrutinib to treat EGFR mutant cancer
INVENTOR(S): Fang, Bingliang; Roth, Jack A.; Wang, Michael; Wang, Li; Wu, Shuhong; Heymach, John V.; Swisher, Stephen G.; Hofstetter, Wayne L.
PATENT ASSIGNEE(S): The University of Texas System, USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015127234	A1	20150827	WO 2015-US16859	20150220

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61942255 P 20140220
AB Provided herein are methods of using irreversible BTK inhibitors, such as, for example, ibrutinib (PCI-32765), to treat EGFR mutant cancers, HER2 amplified cancers, and/or HER2 overexpressing cancers. In certain aspects, the method further comprises administering at least a second anticancer therapy to the subject.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of ibrutinib to treat EGFR mutant cancer and combination with other therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 83 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1362724 CAPLUS Full-text
DOCUMENT NUMBER: 163:299275
TITLE: Preparation of crystalline solid forms of cabozantinib
INVENTOR(S): Aftab, Dana T.; Guz, Nathan; Lau, Stephen; Hamill, Noel; Walker, Tracy; Galbraith, Jana; Yau, Simon; Shah, Khalid
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

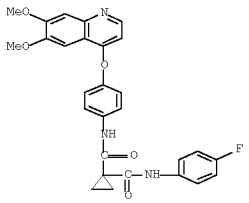
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015123639	A1	20150820	WO 2015-US16052	20150216

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61939985 P 20140214
AB The invention relates to novel cryst. solid forms of cabozantinib., and solvates thereof, including hydrates, that are useful for the treatment of cancer. Also disclosed are pharmaceutical compns. comprising the crystalline solid forms and processes for making the crystalline solid forms, as well as methods of using them for the treatment of cancer, particularly thyroid cancer, prostate cancer, hepatocellular cancer, renal cancer, and non-small cell lung carcinoma. The crystalline solid forms can be used to make the L-malate salt of cabozantinib.
IT 1140909-48-3P, Cabozantinib S-malate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystalline solid forms of cabozantinib)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

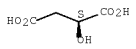
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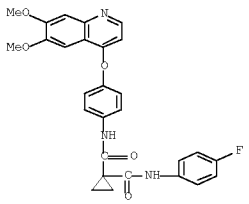
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

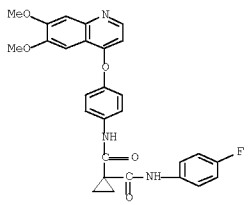


IT 849217-68-1
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of crystalline solid forms of cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 84 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1349511 CAPLUS Full-text
DOCUMENT NUMBER: 163:449411
TITLE: Identification of triazolo[4,5-b]pyrazine derivatives as hepatocyte growth factor receptor inhibitors through structure-activity relationships and molecular docking simulations
AUTHOR(S): Dong, Minghui; Ren, Yujie; Gao, Xiaodong
CORPORATE SOURCE: School of Chemical and Environmental Engineering, Shanghai Institute of Technology, Shanghai, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2015), 25(19), 4118-4126
CODEN: BMCLE8; ISSN: 0960-894X
DIGITAL OBJECT ID: 10.1016/j.bmcl.2015.08.025
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB C-MET is a receptor tyrosine kinase and potential oncol. target for cancer therapy. The activities of 1,2,3-triazolo[4,5-b]pyrazine series of c-MET inhibitors were analyzed according to the three-dimensional quant. structure-activity relationship and mol. docking methods. The results indicated that the hydrophobic and electrostatic fields play key roles in activity and QSAR model was reliable enough for activity prediction. Moreover, the docking results do validate the predicted 3D-QSAR scores, vital residues Asp1222, Asp1231, Met1160, Tyr1259 and Tyr1230 found in binding site. Four new c-MET inhibitor analogs designed in this Letter which are being currently synthesized by our labs.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triazolo-pyrazine derivs. identification as HGFR inhibitors through SAR and mol. docking simulation)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

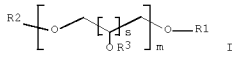
L4 ANSWER 85 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1315537 CAPLUS Full-text
DOCUMENT NUMBER: 163:323284
TITLE: Composition for vectorizing an anti-cancer agent
INVENTOR(S): Robic, Caroline; Mayer, Jean-Francois
PATENT ASSIGNEE(S): Guerbet, Fr.
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015118113	A1	20150813	WO 2015-EP52527	20150206

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

FR 3017295	A1	20150814	FR 2014-50972	20140207

PRIORITY APPLN. INFO.: FR 2014-50972 A 20140207
GI



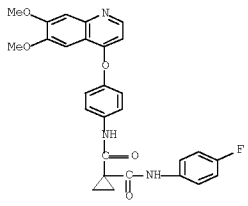
AB The invention relates to a stable water-in-oil emulsion compn. contg.: 20% to 40% (volume/volume) aqueous phase in the form of droplets and containing an anti-cancer agent; and 60% to 80% (volume/volume) lipid phase containing an iodized oil and at least one surfactant, having formula I, in a proportion, of surfactant mass relative to the total volume of the composition, of 0.3% to 5%, formula II for said surfactant being the following in which: s has a value of 0 or 1; m is a whole number from 2 to 30; R1 is a formula I grouping wherein n is a whole number from 4 to 10, o is a whole number from 1 to 4,

p is a whole number from 3 to 7; q is a whole number from 2 to 10, and r has a value of 0 or 1; R2 is a hydrogen atom or is identical to R1; and each R3 is, sep., a hydrogen atom or is identical to R1. The invention also relates to an emulsion obtained from said composition, to the preparing method thereof, and to the use thereof for treating cancer and the metastases thereof. An emulsion containing 50 mg doxorubicin, 1% PGPR in Lipidol, and 2.5 mL Xenetix 250 was prepared

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition for vectorizing anti-cancer agent)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 86 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1289334 CAPLUS Full-text

DOCUMENT NUMBER: 163:438199

TITLE: Response to MET Inhibitors in Patients with Stage IV Lung Adenocarcinomas Harboring MET Mutations Causing Exon 14 Skipping

AUTHOR(S): Paik, Paul K.; Drilon, Alexander; Fan, Pang-Dian; Yu, Helena; Rekhtman, Natasha; Ginsberg, Michelle S.; Borsu, Laetitia; Schultz, Nikolaus; Berger, Michael F.; Rudin, Charles M.; Ladanyi, Marc

CORPORATE SOURCE: Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

SOURCE: Cancer Discovery (2015), 5(8), 842-849
CODEN: CDAIB2; ISSN: 2159-8274

DIGITAL OBJECT ID: 10.1158/2159-8290.CD-14-1467

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

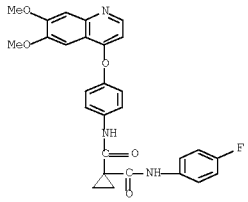
LANGUAGE: English

AB Mutations in the MET exon 14 RNA splice acceptor and donor sites, which lead to exon skipping, deletion of the juxtamembrane domain containing the CBL E3-ubiquitin ligase-binding site, and decreased turnover of the resultant aberrant MET protein, were previously reported to be oncogenic in preclin. models. We now report responses to the MET inhibitors crizotinib and cabozantinib in four patients with stage IV lung adenocarcinomas harboring mutations leading to MET exon 14 skipping, highlighting a new therapeutic strategy for the 4% of lung adenocarcinoma patients whose tumors harbor this previously underappreciated genetic alteration. Significance: Oncogenic mutations in the MET exon 14 splice sites that cause exon 14 skipping occur in 4% of lung adenocarcinomas. We report responses to the MET inhibitors crizotinib and cabozantinib in patients with lung adenocarcinomas harboring MET exon 14 splice site mutations, identifying a new potential therapeutic target in this disease. Cancer Discov; 5(8); 842-9. ©2015 AACR. See related commentary by Ma, p. 802. See related article by Frampton et al., p. 850. This article is highlighted in the In This Issue feature, p. 783.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response to MET inhibitors in patients with stage IV lung adenocarcinomas harboring MET mutations causing exon 14 skipping)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 87 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1265280 CAPLUS Full-text

TITLE: Pharmacokinetic (PK) drug interaction studies of cabozantinib: Effect of CYP3A inducer rifampin and inhibitor ketoconazole on cabozantinib plasma PK and effect of cabozantinib on CYP2C8 probe substrate rosiglitazone plasma PK

AUTHOR(S): Nguyen, Linh; Holland, Jaymes; Miles, Dale; Engel, Caroline; Benrimoh, Natacha; O'Reilly, Terry; Lacy, Steven

CORPORATE SOURCE: Exelixis, Inc., So. San Francisco, CA, USA

SOURCE: Journal of Clinical Pharmacology (2015), 55(9), 1012-1023
CODEN: JCPCBR; ISSN: 0091-2700

DIGITAL OBJECT ID: 10.1002/jcph.510

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

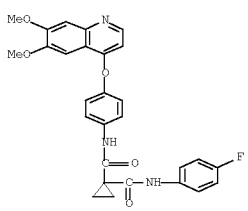
AB Cabozantinib is a small-mol. tyrosine kinase inhibitor that has been approved for the treatment of patients with progressive, metastatic medullary thyroid cancer. In vitro data indicate that (1) cytochrome P 450 (CYP) 3A4 is the primary CYP isoenzyme involved in the metabolism of cabozantinib, and (2) CYP2C8 is the CYP isoenzyme most potently inhibited by cabozantinib with potential for in vivo inhibition at clin. relevant plasma exposures. Pharmacokinetic (PK) drug-drug interactions (DDIs) were evaluated clin. between cabozantinib and (1) a CYP3A inducer (rifampin) in healthy volunteers, (2) a CYP3A inhibitor (ketoconazole) in healthy volunteers, and (3) a CYP2C8 substrate (rosiglitazone) in patients with solid tumors. Compared with cabozantinib given alone, coadministration with rifampin resulted in a 4.3-fold higher plasma clearance (CL/F) of cabozantinib and a 77% decrease in cabozantinib plasma AUC0-inf, whereas coadministration with ketoconazole decreased cabozantinib CL/F by 29% and increased cabozantinib AUC0-inf by 38%. Chronic coadministration with cabozantinib resulted in no significant effect on rosiglitazone plasma Cmax, AUC0-24, or AUC0-inf. In summary, chronic use of strong CYP3A inducers and inhibitors should be avoided when cabozantinib is administered, and cabozantinib at clin. relevant exposures is not anticipated to markedly affect the PK of concomitant medications via CYP enzyme inhibition.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetic drug interaction studies of cabozantinib, effect of CYP3A inducer rifampin and inhibitor ketoconazole on cabozantinib plasma PK and effect of cabozantinib on CYP2C8 probe substrate rosiglitazone plasma pharmacokinetics)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 88 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1258933 CAPLUS Full-text

DOCUMENT NUMBER: 164:142494

TITLE: Small-molecule kinase inhibitors: an analysis of FDA-approved drugs

AUTHOR(S): Wu, Peng; Nielsen, Thomas E.; Clausen, Mads H.

CORPORATE SOURCE: Department of Chemistry, Technical University of Denmark, Kgs. Lyngby, DK-2800, Den.

SOURCE: Drug Discovery Today (2016), 21(1), 5-10
CODEN: DDTOFS; ISSN: 1359-6446

DIGITAL OBJECT ID: 10.1016/j.drudis.2015.07.008

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; (online computer file)

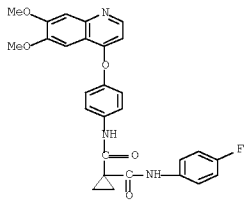
LANGUAGE: English

AB Small-mol. kinase inhibitors (SMKIs), 28 of which are approved by the US Food and Drug Administration (FDA), have been actively pursued as promising targeted therapeutics. Here, we assess the key structural and physicochem. properties, target selectivity and mechanism of function, and therapeutic indications of these approved inhibitors. Our anal. showed that >30% of approved SMKIs have a mol. weight (MW) exceeding 500 and all have a total ring count of between three and five. The assumption that type II inhibitors tend to be more selective than type I inhibitors has been proved to be unreliable. Although previous SMKI research was concentrated on tyrosine kinase inhibitors for cancer treatment, recent progress indicates diversification of SMKI research in terms of new targets, mechanistic types, and therapeutic indications.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural and physicochem. properties, target selectivity and mechanism of function therapeutic indications of FDA approved small-mol. kinase inhibitor)

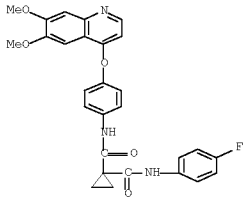
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 89 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1256269 CAPLUS Full-text
TITLE: 2ME2 inhibits the activated hypoxia-inducible pathways by cabozantinib and enhances its efficacy against medullary thyroid carcinoma
AUTHOR(S): Lin, Han; Jiang, Xian; Zhu, Huaqiang; Jiang, Wenjing; Dong, Xuesong; Qiao, Haiquan; Sun, Xueying; Jiang, Hongchi
CORPORATE SOURCE: Key Laboratory of Hepatosplenic Surgery, Department of General Surgery, The First Affiliated Hospital of Harbin Medical University, Harbin, 150001, Peop. Rep. China
SOURCE: Tumor Biology (2016), 37(1), 381-391
CODEN: TUMBEA; ISSN: 1010-4283
DIGITAL OBJECT ID: 10.1007/s13277-015-3816-1
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is a multi-targeted tyrosine kinase inhibitor targeting vascular endothelial growth factor (VEGF) receptor (VEGFR)-2, MET (c-Met, also called hepatocyte growth factor (HGF) receptor), and other receptor tyrosine kinases. Cabozantinib has recently been approved for treating advanced medullary thyroid carcinoma (MTC), but its long-term benefit remains uncertain and dose-dependent adverse events are very common. The present study has demonstrated that 2-methoxyestradiol (2ME2), an inhibitor of hypoxia-inducible factors (HIFs) and a promising anticancer agent under investigation in clin. trials, strengthens anticancer activities of cabozantinib against MTC cells in vitro and in vivo. The activated hypoxia-inducible pathways, which are mainly regulated by HIF-1, contribute to the resistance of hypoxic MTC cells to cabozantinib. Cabozantinib upregulated HIF-1α expression at translational levels and increased the expression of the downstream factors including VEGF, lactate dehydrogenase A (LDHA), HGF, and MET. 2ME2 corrected the activated pathways by cabozantinib through downregulating HIF-1α expression and inhibiting its nuclear translocation in hypoxic MTC cells. Administration of 2ME2 enhanced the efficacy of cabozantinib in suppressing the growth of MTC cell line xenografts and patient-derived xenografts established in mice. Given that 2ME2 targets insensitive hypoxic cancer cells to cabozantinib and can inhibit the activated pathways by cabozantinib, the present results warrant further investigation of 2ME2, particularly in combination with cabozantinib, for the treatment of MTC.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2ME2 inhibits activated hypoxia-inducible pathways by cabozantinib and enhances its efficacy against medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

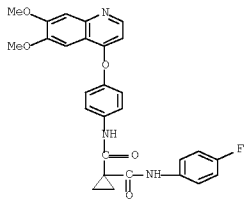


REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 90 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1243654 CAPLUS Full-text
DOCUMENT NUMBER: 163:316612
TITLE: Biomarker TTF1 for predicting effect of c-met inhibitor
INVENTOR(S): Kim, Bo Gyou; Lee, Eunjin; Kim, Kyung Ah; Ahn, Tae Jin
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 92pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150212077	A1	20150730	US 2015-14604361	20150123
KR 2015088433	A	20150803	KR 2014-8733	20140124
PRIORITY APPLN. INFO.:			KR 2014-8733 A	20140124

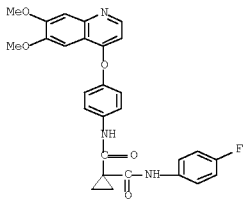
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method of predicting an effect of a c-Met inhibitor and/or selecting a subject for application of a c-Met inhibitor using trefoil factor 1 (TFF1), a method of monitoring an effect of a c-Met inhibitor using TFF1, and a method of treating and/or preventing cancer including administering a c-Met inhibitor to the selected subject. Herein, the effect of a c-Met inhibitor may refer to the prevention, improvement, alleviation, and/or treatment of a c-Met related disease such as cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biomarker TTF1 for predicting effect of c-met inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 91 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1226166 CAPLUS Full-text
TITLE: The study on synthetic technology of cabozantinib (S)-malate
AUTHOR(S): Qi, Baohui; He, Huan
CORPORATE SOURCE: Department of Bioengineering, Zhuhai Campus, Zunyi Medical College, Zhuhai, 519041, Peop. Rep. China
SOURCE: Guangdong Huagong (2014), 41(19), 22-23
CODEN: GHUAFI; ISSN: 1007-1865
PUBLISHER: Guangdong Huagong Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The cabozantinib(S)-malate, which was used for the treatment of locally advanced or metastatic progressive medullary thyroid cancer, was prepared from 3, 4-dimethoxyacetophenone by nitration, condensation, cyclization, chlorination and substitution, etc. In this synthetic route, raw materials were com. available, and reactive conditions were mild, and the operation was easy, and the yield was higher.
IT INDEXING IN PROGRESS
IT 1140909-48-3P, Cabozantinib (S)-malate
RL: SPN (Synthetic preparation); PREP (Preparation)
(study on synthetic technol. of cabozantinib S-malate)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

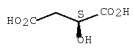
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

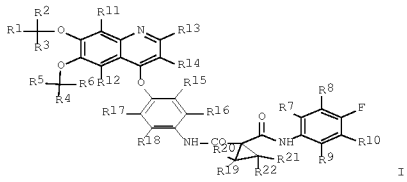
Absolute stereochemistry. Rotation (-).



L4 ANSWER 92 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1213912 CAPLUS Full-text
DOCUMENT NUMBER: 163:271103
TITLE: Preparation of deuterated cabozantinib derivatives and their application as anticancer agents
INVENTOR(S): Chen, Xinghai; Peng, Wei; Parker, Omar; Zheng, Feiming; Fu, Yong
PATENT ASSIGNEE(S): Shanghai Shenqkao Pharmaceutical Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 35pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104788372	A	20150722	CN 2014-10361351	20140725
PRIORITY APPLN. INFO.:			CN 2014-10361351	20140725

OTHER SOURCE(S): MARPAT 163:271103
GI

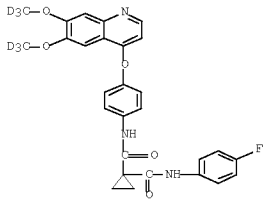


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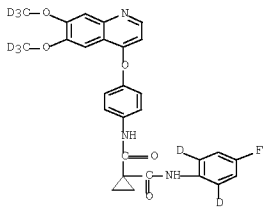
AB The invention is related to the prepn. of deuterated cabozantinib derivs. I and their application as anticancer agents. The invention compound I, wherein R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, and R22 are H or D independently and contain at least one D and their pharmaceutically acceptable salts, crystalline hydrates, solvates, prodrugs, single crystal or polymorph are claimed. Compound I was prepared by multi-step procedure (procedure given). The deuterated cabozantinib derivs. have slow decomposition in vivo, thereby reducing adverse metabolism of drugs. The invention compds. were evaluated for their anticancer activity.

IT 1802168-46-2P 1802168-48-4P 1802168-49-5P
1802168-50-8P 1802168-52-0P 1802168-53-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of deuterated cabozantinib derivs. and their application as anticancer agents)

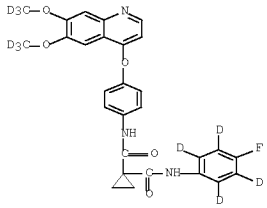
RN 1802168-46-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 1802168-48-4 CAPLUS

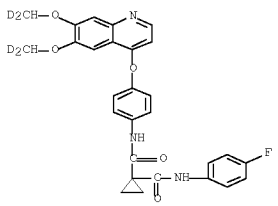


RN 1802168-51-9 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)- (CA INDEX NAME)

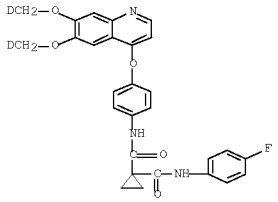


RN 1802168-52-0 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)- (CA INDEX NAME)

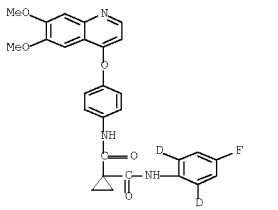
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d2)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



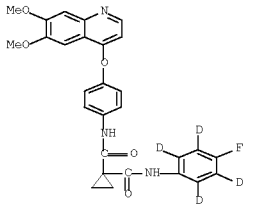
RN 1802168-49-5 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 1802168-50-8 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)- (CA INDEX NAME)



RN 1802168-53-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)- (CA INDEX NAME)



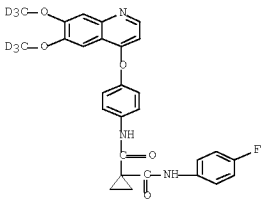
IT 1802168-54-2P 1802168-55-3P 1802168-56-4P
1802168-57-5P 1802168-58-6P 1802168-59-7P
1802168-60-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of deuterated cabozantinib derivs. and their application as anticancer agents)

RN 1802168-54-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

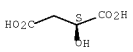
CRN 1802168-46-2
CMF C28 H18 D6 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

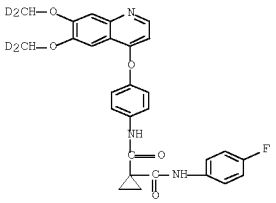


RN 1802168-55-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[[6,7-di(methoxy-d2)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

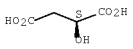
CRN 1802168-48-4
CMF C28 H20 D4 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

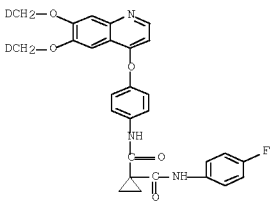


RN 1802168-56-4 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[[6,7-di(methoxy-d)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

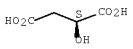
CRN 1802168-49-5
CMF C28 H22 D2 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

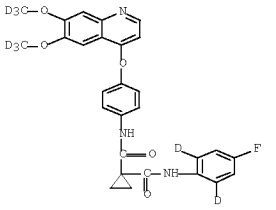


RN 1802168-57-5 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

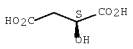
CRN 1802168-50-8
CMF C28 H16 D8 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

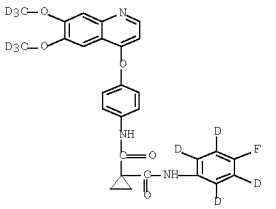
Absolute stereochemistry. Rotation (-).



RN 1802168-58-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

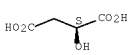
CRN 1802168-51-9
CMF C28 H14 D10 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

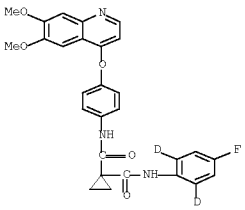


RN 1802168-59-7 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

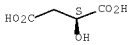
CRN 1802168-52-0
CMF C28 H22 D2 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

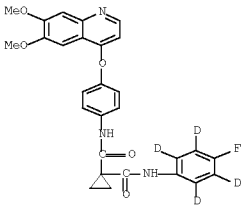


RN 1802168-60-0 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

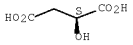
CRN 1802168-53-1
CMF C28 H20 D4 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

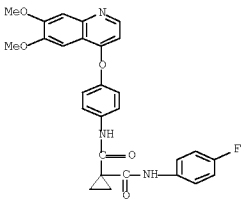


L4 ANSWER 93 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1181814 CAPLUS Full-text
TITLE: Population Pharmacokinetic Model of Cabozantinib in Patients with Medullary Thyroid Carcinoma and Its Application to an Exposure-Response Analysis

AUTHOR(S): Miles, Dale; Jumbe, Nelson L.; Lacy, Steven; Nguyen, Linh
CORPORATE SOURCE: Genentech (A member of the Roche Group), South San Francisco, CA, USA
SOURCE: Clinical Pharmacokinetics (2016), 55(1), 93-105
CODEN: CPKNDH; ISSN: 0312-5963
DIGITAL OBJECT ID: 10.1007/s40262-015-0295-x
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background and Objectives: Cabozantinib is a tyrosine kinase inhibitor approved in the USA and EU for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC). The indicated cabozantinib dose is 140 mg/day, with dose modifications allowed for patients who develop adverse events (AEs). The anal. objective was to develop a population pharmacokinetic (PopPK) model in MTC patients and to use the model for exposure-response (ER) anal. of dose modifications. Methods: A PopPK model for cabozantinib was developed using data from three clin. trials (2079 evaluations from 289 patients), including a randomized, double-blind, placebo-controlled phase III study of patients with progressive, metastatic MTC. The PopPK model predictions [model-predicted steady-state area under the plasma concentration-time curve (AUCss,pred)] were used for an ER anal. of the time to first dose modification. Results: The final PopPK model was a one-compartment model with first-order absorption and first-order elimination. Estimated cabozantinib apparent oral clearance (CL/F) and apparent volume of distribution (Vc/F) were 106 L/day [±2.98 % relative standard error (RSE)] (males) and 349 L (±2.73 % RSE), resp. CL/F was reduced by 22 % (to 83 L/day) in females. Sex and body mass index (BMI) were significant covariates that combined contributed 15 % to the variability in cabozantinib CL/F, but did not warrant dose adjustment. Higher cabozantinib AUCss,pred was correlated to an increased risk of early dose modification and a lower average dose through to Day 85. Early cabozantinib dose modification was not associated with a reduction in progression-free survival (PFS). Conclusion: A PopPK model was developed for cabozantinib pharmacokinetics in MTC patients. Higher cabozantinib exposure was associated with earlier first dose modification and a lower average administered dose through to Day 85. Early first dose modification did not appear to impact PFS.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(population pharmacokinetic model of cabozantinib in patients with medullary thyroid carcinoma and its application to exposure)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 94 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1173698 CAPLUS Full-text
DOCUMENT NUMBER: 163:302461
TITLE: Compositions and methods for the treatment of intraocular neovascularization and/or leakage using tyrosine kinase inhibitors
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 12pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150196649	A1	20150716	US 2015-14593704	20150109
WO 2015108787	A2	20150723	WO 2015-US10867	20150109
WO 2015108787	A3	20151112		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

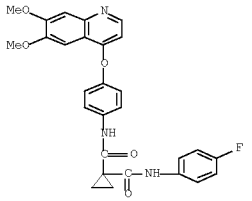
PRIORITY APPLN. INFO.: US 2014-61928061 P 20140116
US 2014-61969861 P 20140325
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides compns. and methods for the treatment of intraocular neovascularization and/or leakage including wet age-related macular degeneration. The compns. preferably use tyrosine kinase inhibitors with an IC50 for VEGFR2 of 20 nanomolar or less and an IC50 for c-MET of 20 nanomolar or less.

IT 849217-68-1, Cabozantinib 1235470-36-6
1642298-56-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treatment of intraocular neovascularization and/or leakage using tyrosine kinase inhibitors of VEGFR2 and c-MET)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

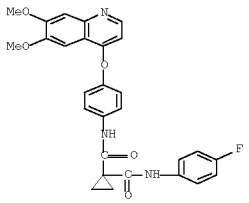


RN 1235470-36-6 CAPLUS

CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

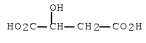
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 6915-15-7
CMF C4 H6 O5

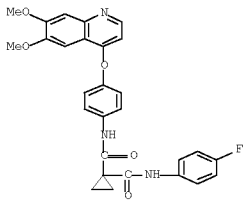


RN 1642298-56-3 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 75-75-2
CMF C H4 O3 S



L4 ANSWER 95 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1169349 CAPLUS Full-text

DOCUMENT NUMBER: 163:218113

TITLE: Preparation of heterocyclic modulators of lipid synthesis for use against cancer and viral infections

INVENTOR(S): Wagman, Allan S.; Johnson, Russell J.; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.; Duke, Greg; Ohol, Yamini; Heuer, Timothy; O'Farrell, Marie

PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA

SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015105860	A1	20150716	WO 2015-US10459	20150107
WO 2015105860	A9	20160204		

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61924520 P 20140107

OTHER SOURCE(S): CASREACT 163:218113; MARPAT 163:218113

GI

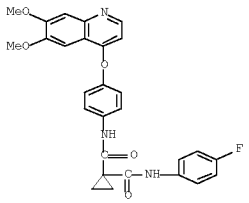
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [LAr = II-IV; Ar = V; R1 = H, CN, halo, etc.; R2 = H, halo, alkyl; R3 = H or F; R21 = H, halo, alkyl, etc.; R22 = H, halo, alkyl; R24 = alkoxy, O(alkylene)alkoxy, cycloalkoxy, etc.; R25 = H, halo, alkyl, etc.; with the provisos], useful for treating conditions characterized by dysregulation of a fatty acid synthase pathway, were prepared E.g., a multi-step synthesis of VI, starting from Me propanoate and Me formate, was described. Exemplified compds. I were evaluated for their FASN inhibition (data given for representative compds. I). Pharmaceutical composition comprising I was disclosed.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of heterocyclic modulators of lipid synthesis for use
against cancer and viral infections)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 96 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1169171 CAPLUS Full-text

DOCUMENT NUMBER: 163:217976

TITLE: Preparation of tertiary amines and amine oxides as LXR agonists

INVENTOR(S): Martinez, Eduardo J.; Kaiser, Bernd; Tavazoie, Sohail F.; Kurth, Isabel; Gonsalves, Foster Casimir; Darst, David M., Jr.; Tavazoie, Masoud Fakhr

PATENT ASSIGNEE(S): Rgenix, Inc., USA

SOURCE: PCT Int. Appl., 163pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

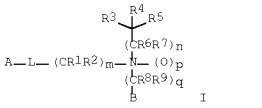
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

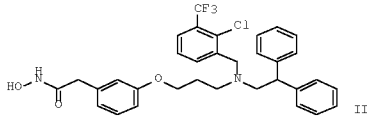
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015106164	A1	20150716	WO 2015-US10909	20150109

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2014-61926150 P 20140110
OTHER SOURCE(S): CASREACT 163:217976; MARPAT 163:217976
GI



I

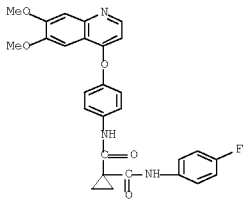


II

AB This invention features compds. of formula I that modulate the activity of liver X receptors, pharmaceutical compns. including the compds. of the invention, and methods of utilizing those compns. for modulating the activity of liver X receptors in the treatment of cancer. Compds. of formula I wherein A is substituted Ph, (un)substituted azacyclyl, and (un)substituted oxobenzopyranyl; L is absent, O, S, amino and CR4R5; m is 2, 3, 4, 5, 6, 7 and 8;, n, p and q are independently 0 and 1; R1, R2, R6, R7, R8 and R9 are independently H, OH, halo, amino, thio, etc.; R3 is H, OH, amino, (un)substituted C1-6 alkyl, etc.; R4 and R6 are independently H, OH, halo, amino, thio, etc.; and pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by reductive amination of 2-chloro-3-trifluoromethylbenzaldehyde with 2,2-diphenethylamine followed by alkylation with 1,3-dibromopropane; the resulting (3-bromopropyl)({[2-chloro-3-(trifluoromethyl)phenyl]methyl})(2,2-diphenylethyl)amine underwent etherification with Me 3-hydroxyphenylacetate to give Me 2-{3-[3-({[2-chloro-3-(trifluoromethyl)phenyl]methyl}-(2,2-diphenylethyl)- amino)-propoxy]phenyl}acetate, which underwent amidation with hydroxylamine hydrochloride to give compound II. The invention compds. were evaluated for their LXR agonistic activity. From the assay it was determine that compound exhibited ApoE induction . 80% at 1 μM and > 40 % at 10 μM, and EC50 value of 1.0 μM.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of tertiary amines and amine oxides as LXR agonists)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



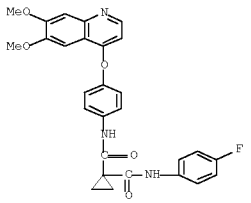
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 97 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1144766 CAPLUS Full-text
DOCUMENT NUMBER: 164:320926
TITLE: Salvage systemic therapy for advanced urothelial carcinoma: on the cusp of a sea change?
AUTHOR(S): Sonpavde, Guru; Bellmunt, Joaquim
CORPORATE SOURCE: University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, AL, USA
SOURCE: Oncologist (2015), 20(5), 461-463
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2015-0077
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This paper studies about the salvage systemic therapy for advanced urothelial carcinoma.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on salvage systemic therapy for advanced urothelial carcinoma)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



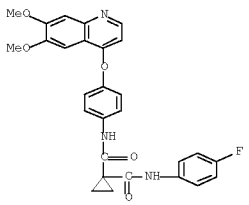
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 98 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1144752 CAPLUS Full-text
DOCUMENT NUMBER: 163:384755
TITLE: Prospective comprehensive genomic profiling of advanced gastric carcinoma cases reveals frequent clinically relevant genomic alterations and new routes for targeted therapies
AUTHOR(S): Ali, Siraj M.; Sanford, Eric M.; Klempner, Samuel J.; Rubinson, Douglas A.; Wang, Kai; Palma, Norma A.; Chmielecki, Juliann; Yelensky, Roman; Palmer, Gary A.; Morosini, Deborah; Lipson, Doron; Catenacci, Daniel V.; Braiteh, Fadi; Erlich, Rachel; Stephens, Philip J.; Ross, Jeffrey S.; Ou, Sai-Hong Ignatius; Miller, Vincent A.
CORPORATE SOURCE: Foundation Medicine Inc., Cambridge, MA, USA
SOURCE: Oncologist (2015), 20(5), 499-507
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2014-0378
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Gastric cancer (GC) is a major global cancer burden and the second most common cause of global cancer-related deaths. The addition of anti-ERBB2 (HER2) targeted therapy to chemotherapy improves survival for ERBB2-amplified advanced GC patients; however, the majority of GC patients do not harbor this alteration and thus cannot benefit from targeted therapy under current practice paradigms. Materials and Methods: Prospective comprehensive genomic profiling of 116 predominantly locally advanced or metastatic (90.0%) gastric cancer cases was performed to identify genomic alterations (GAs) associated with a potential response to targeted therapies approved by the U.S. Food and Drug Administration or targeted therapy-based clin. trials. Results: Overall, 78% of GC cases harbored one clin. relevant GA or more, with the most frequent alterations being found in TP53 (50%), ARID1A (24%), KRAS (16%), CDH1 (15%), CDKN2A (14%), CCND1 (9.5%), ERBB2 (8.5%), PIK3CA (8.6%), MLL2 (6.9%), FGFR2 (6.0%), and MET (6.0%). Receptor tyrosine kinase genomic alterations were detected in 20.6% of cases, primarily ERBB2, FGFR2, and MET amplification, with ERBB2 alterations evenly split between amplifications and base substitutions. Rare BRAF mutations (2.6%) were also observed One MET-amplified GC patient responded for 5 mo to crizotinib, a multitargeted ALK/ROS1/MET inhibitor. Conclusion: Comprehensive genomic profiling of GC identifies clin. relevant GAs that suggest benefit from targeted therapy including MET-amplified GC and ERBB2 base substitutions.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prospective comprehensive genomic profiling of advanced gastric carcinoma cases reveals frequent clin. relevant genomic alterations and new routes for targeted therapies)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 99 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1128572 CAPLUS Full-text
TITLE: Metabolism and disposition of cabozantinib in healthy male volunteers and pharmacologic characterization of its major metabolites
AUTHOR(S): Lacy, Steven; Hsu, Bih; Miles, Dale; Aftab, Dana; Wang, Ronghua; Nguyen, Linh
CORPORATE SOURCE: Department of Non-Clinical Development, Exelixis, Inc., South San Francisco, CA, USA
SOURCE: Drug Metabolism & Disposition (2015), 43(8), 1190-1207
CODEN: DMDSAI; ISSN: 1521-009X
DIGITAL OBJECT ID: 10.1124/dmd.115.063610
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

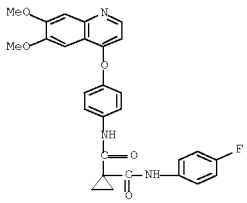
AB Metab. and excretion of cabozantinib, an oral inhibitor of receptor tyrosine kinases, was studied in 8 healthy male volunteers after a single oral dose of 175 mg cabozantinib l-malate containing 14C-cabozantinib (100 μCi/subject). Total mean radioactivity recovery within 48 days was 81.09%; radioactivity was eliminated in feces (53.79%) and urine (27.29%). Cabozantinib was extensively metabolized with 17 individual metabolites identified by liquid chromatog.-tandem mass spectrometry (LC-MS/MS) in plasma, urine, and feces. Relative plasma radioactivity exposures (analyte AUC0-t/total AUC0-t for cabozantinib + major metabolites) were 27.2, 25.2, 32.3, 7, and 6% for cabozantinib and major metabolites monohydroxy sulfate (EXEL-1646), 6-desmethyl amide cleavage product sulfate (EXEL-1644), N-oxide (EXEL-5162), and amide cleavage product (EXEL-5366), resp. Comparable relative plasma exposures determined by LC-MS/MS anal. were 32.4, 13.8, 45.9, 4.9, and 3.1%, resp. These major metabolites each possess in vitro inhibition potencies ≤1/10th of parent cabozantinib against the targeted kinases MET, RET, and VEGFR2/KDR. In an in vitro cytochrome P 450 (CYP) panel, cabozantinib and EXEL-1644 both inhibited most potently CYP2C8 (Kiapp = 4.6 and 1.1 μM, resp.). In an in vitro drug transporter panel, cabozantinib inhibited most potently MATE1 and MATE2-K (IC50 = 5.94 and 3.12 μM, resp.) and was a MRP2 substrate; EXEL-1644 inhibited most potently OAT1, OAT3, OATP1B1, MATE1, and OATP1B3 (IC50 = 4.3, 4.3, 6.1, 16.7, and 20.6 μM, resp.) and was a substrate of MRP2, OAT3, OATP1B1, OATP1B3, and possibly P-gp. Therefore, cabozantinib appears to be the primary pharmacol. active circulating analyte, whereas both cabozantinib and EXEL-1644 may represent potential for drug-drug interactions.

IT INDEXING IN PROGRESS

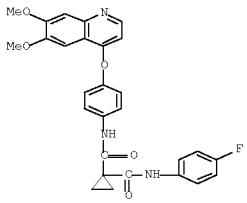
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolism, disposition and pharmacokinetics of cabozantinib and its biotransformation products in healthy male volunteers and pharmacol. characterization of its major metabolites)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 101 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1124138 CAPLUS Full-text

DOCUMENT NUMBER: 163:187706

TITLE: Biomarker for predicting or monitoring efficacy of c-Met inhibitor

INVENTOR(S): Jung, Soo Yeon; Shim, Seon Hui; Song, Yun Jeong; Yoo, Hyeon-Seok

PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea

SOURCE: Eur. Pat. Appl., 147pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2891884	A2	20150708	EP 2015-150360	20150107
EP 2891884	A3	20151014		
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015082121	A	20150715	KR 2015-956	20150106
CN 104762371	A	20150708	CN 2015-10008065	20150107
US 20150192588	A1	20150709	US 2015-14591787	20150107
JP 2015129755	A	20150716	JP 2015-1880	20150107
PRIORITY APPLN. INFO.:			KR 2014-1799 A	20140107
			KR 2015-956 A	20150106

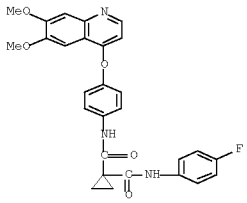
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A biomarker for predicting and/or monitoring the efficacy of a c-Met inhibitor; a composition for predicting and/or monitoring the efficacy of a c-Met inhibitor, comprising a material detecting the biomarker; a composition for selecting a subject suitable for the application of a c-Met inhibitor, comprising a material detecting the biomarker is presented. In addition a method for predicting and/or monitoring the efficacy of a c-Met inhibitor using the biomarker; a method for selecting a subject suitable for the application of a c-Met inhibitor using the biomarker; and a method for preventing and/or treating cancer comprising administering a c-Met inhibitor to the selected subject is given. One embodiment provides a biomarker for use in predicting and/or monitoring the therapeutic effect of a c-Met inhibitor or selecting a subject suitable for the application of a c-Met inhibitor, wherein the biomarker includes at least one selected from the group consisting of IL-8, BIGH3, or MIF and nucleic acids encoding the proteins. Another embodiment provides a c-Met inhibitor or a pharmaceutical composition including a c-Met inhibitor, for use in inhibiting c-Met and/or treating a cancer in a subject, wherein the subject has a high level of IL-8 or a nucleic acid encoding IL-8 compared to a reference sample in which a c-Met inhibitor is not effective; shows a decreased level of IL-8, BIGH3, MIF, and/or nucleic acids encoding them after administering a c-Met inhibitor; and/or has a mutation of KRAS, BRAF, and/or nucleic acids encoding them. A specific example shows the IL-8 levels in cancer cell-implanted mouse models showing relationship between IL-8 level and responsiveness to an anti-c-Met antibody.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biomarker for predicting or monitoring efficacy of c-Met inhibitor)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

L4 ANSWER 102 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1079985 CAPLUS Full-text

DOCUMENT NUMBER: 163:231592

TITLE: Heteroaromatic compound and its application in medicine for treating proliferative diseases

INVENTOR(S): Liu, Bing; Liu, Jinlei; Zhang, Yingjun; Zhang, Jiancun

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 189pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

L4 ANSWER 100 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1127378 CAPLUS Full-text

DOCUMENT NUMBER: 164:142135

TITLE: MET inhibitors for treatment of advanced hepatocellular carcinoma: a review

AUTHOR(S): Qi, Xing-Shun; Guo, Xiao-Zhong; Han, Guo-Hong; Li, Hong-Yu; Chen, Jiang

CORPORATE SOURCE: Department of Gastroenterology, General Hospital of Shenyang Military Area, Shenyang, Liaoning Province, 100840, Peop. Rep. China

SOURCE: World Journal of Gastroenterology (2015), 21(18), 5445-5453
CODEN: WJGAF2; ISSN: 2219-2840

DIGITAL OBJECT ID: 10.3748/wjg.v21.i18.5445

PUBLISHER: Baishideng Publishing Group Inc.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB The current std. treatment option for advanced hepatocellular carcinoma (HCC) is sorafenib, but its clin. benefit is modest. In spite of many attempts, few drugs can provide any significant improvement of survival as the first- or second-line therapy of choice in phase III randomized controlled trials. Recently, the subgroup anal. of a phase II randomized controlled trial has shown that tivantinib, a selective MET inhibitor, can significantly improve the overall survival in patients with MET-pos. advanced HCC after the failure or intolerance of a prior systemic therapy. These findings enlighten the role of MET inhibitors in the treatment of advanced HCC. In this paper, we review all ongoing and completed clin. trials regarding this topic. As for the first-line therapy of advanced HCC, INC280 and foretinib are being evaluated in 2 phase II single-arm trials; and MSC2156119J and golvatinib plus sorafenib are being compared with sorafenib alone in 2 phase II randomized controlled trials. As for the second-line therapy of advanced HCC, tivantinib and cabozantinib are being compared with placebo in 2 phase II randomized controlled trials.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase II and III clin. trials regarding MET inhibitors used for treatment of human advanced hepatocellular carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CN 104744446	A	20150701	CN 2014-10835175		20141229
PRIORITY APPLN. INFO.:			CN 2013-10746766	A	20131230
			CN 2014-10108590	A	20140322

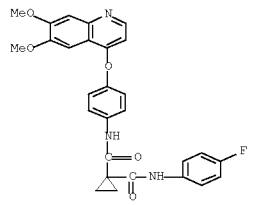
OTHER SOURCE(S): MARPAT 163:231592

AB The invention provides a class of heteroarom. compd. or stereisomer, geometrical isomer, tautomer, racemate, oxynitride, hydrate, solvate, metabolite, metabolic precursor and pharmaceutically acceptable salt, or prodrug thereof, used for the treatment of proliferative disease. The invention also discloses the pharmaceutical composition containing such compound and application of the compound of this invention or its pharmaceutical composition in the preparation of medicine for the treatment of proliferative disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heteroarom. compound and its application in medicine for treating proliferative diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



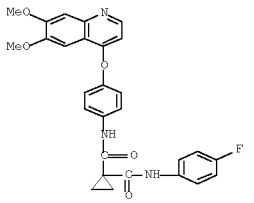
L4 ANSWER 103 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1073487 CAPLUS Full-text
DOCUMENT NUMBER: 163:480792
TITLE: Response and toxicity of small-molecule tyrosine kinase inhibitors in patients with thyroid carcinoma: a systematic review and meta-analysis
AUTHOR(S): N. Klein Hesselink, E.; Steenvoorden, D.; Kapiteijn, E.; Corssmit, E. P.; van der Horst-Schrivers, A. N. A.; Lefrandt, J. D.; Links, T. P.; Dekkers, O. M.
CORPORATE SOURCE: Department of Endocrinology, Department of Internal Medicine, Division of Vascular Medicine, University Medical Center Groningen, University of Groningen, Groningen, Neth.
SOURCE: European Journal of Endocrinology (2015), 172(5), R215-R225
CODEN: EJOEEP; ISSN: 0804-4643
DIGITAL OBJECT ID: 10.1530/EJE-14-0788
PUBLISHER: BioScientifica Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Context: Many tyrosine kinase inhibitors (TKIs) have been studied in patients with thyroid carcinoma (TC). However, the effect and toxicity of various TKIs in differentiated TC (DTC) and medullary TC (MTC) patients have not been directly compared. The aim of the present systematic review and meta-anal. was to systematically summarize response and toxicity of TKIs in TC patients. Methods: All major databases were systematically searched for publications on TKIs in TC. Primary endpoint was objective response; secondary endpoints were clin. benefit, percentage TKI dose reduction/discontinuation, hand-foot syndrome, diarrhea, and nausea/vomiting. Meta-anal. was performed using an exact likelihood approach and a logistic regression. Pooled percentages and 95% CIs were reported. Results: In total, 22 publications were included. For DTC patients, gefitinib induced no objective responses. Pooled percentage was highest for pazopanib, 49 (95% CI 33-64)%, and was 17 (95% CI 12-24)% for sorafenib. For MTC, gefitinib and imatinib induced no objective responses, whereas sunitinib induced objective response in 43 (95% CI 14-77)%. For vandetanib and cabozantinib, these nos. were 40 (95% CI 34-46)% and 27 (95% CI 22-32)% resp. Clin. benefit was found in 53 (95% CI 48-59)% of DTC patients on sorafenib, and in 84 (95% CI 79-88)% and 55 (95% CI 49-61)% of MTC patients on vandetanib and cabozantinib resp. All TKIs were associated with considerable toxicity. Conclusion: The currently studied TKIs show a modest response, while side effects are not negligible. Therefore, we suggest to solely consider TKIs in TC patients with rapid progressive disease, for whom the benefits of treatment outweigh toxicity.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response and toxicity of small-mol. tyrosine kinase inhibitors in patients with thyroid carcinoma: systematic review and meta-anal.)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 104 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1053832 CAPLUS Full-text
DOCUMENT NUMBER: 163:145772
TITLE: Preparation of heterocyclic modulators of lipid synthesis
INVENTOR(S): Heuer, Timothy Sean; Oslob, Johan D.; Mcdowell, Robert S.; Johnson, Russell; Yang, Hanbiao; Evanchik, Marc; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.
PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 488pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015095767	A1	20150625	WO 2014-US71617	20141219
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2013-61919235	P 20131220

OTHER SOURCE(S): CASREACT 163:145772; MARPAT 163:145772
GI

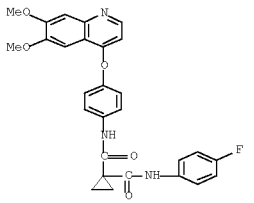
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This invention relates to heterocyclic modulators of lipid synthesis as well as pharmaceutically acceptable salts thereof; to pharmaceutical compns. comprising such compds.; and to methods of treating conditions characterized by dysregulation of a fatty acid synthase pathway by the administration of such compds. and combinations of such compds. and other therapeutic agents. Method of treating a condition characterized by dysregulation of a fatty acid synthase pathway in a subject by administering to the subject a therapeutically effective amount of compound I [LAr = II-IV; Ar = V-IX (wherein Het = 5-6 membered heteroaryl; R1 = H, CN, halo, etc.; R2 = H, halo, alkyl; R3 = H or F; R11 = H or Me); R21 = H, halo, alkyl, etc.; R22 = H, halo, alkyl; R24 = H, CN, alkyl, etc.; R25 = halo, CN, alkyl, etc.], in combination with other therapeutic agent, was claimed. Over three-hundred-eighty compds. I and their heterocyclic analogs were prepared E.g., a multi-step synthesis of X, starting from tert-Bu 4-iodopiperidine-1-carboxylate and 4-bromobenzonitrile, was described. The antiviral activities of the exemplified compds. I were assessed using the HCV1b replicon system (data given).

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of heterocyclic modulators of lipid synthesis useful for treating conditions characterized by dysregulation of a fatty acid synthase pathway)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 105 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:999711 CAPLUS Full-text
DOCUMENT NUMBER: 164:270620
TITLE: Iodide- and glucose-handling gene expression regulated by sorafenib or cabozantinib in papillary thyroid cancer
AUTHOR(S): Ruan, Maomei; Liu, Min; Dong, Qianggang; Chen, Libo
CORPORATE SOURCE: Department of Nuclear Medicine, Sixth People's Hospital, Shanghai Jiao Tong University, Shanghai, 200233, Peop. Rep. China
SOURCE: Journal of Clinical Endocrinology and Metabolism (2015), 100(5), 1771-1779
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2014-3023
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

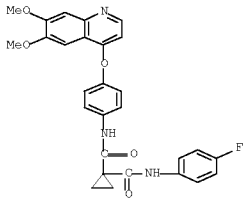
AB Context: The aberrant silencing of iodide-handling genes accompanied by up-regulation of glucose metabolism presents a major challenge for

radioiodine treatment of papillary thyroid cancer (PTC). Objective: This study aimed to evaluate the effect of tyrosine kinase inhibitors on iodide-handling and glucose-handling gene expression in BHP 2-7 cells harboring RET/PTC1 rearrangement. Main Outcome Measures: In this in vitro study, the effects of sorafenib or cabozantinib on cell growth, cycles, and apoptosis were investigated by cell proliferation assay, cell cycle anal., and Annexin V-FITC apoptosis assay, resp. The effect of both agents on signal transduction pathways was evaluated using the Western blot. Quant. real-time PCR, Western blot, immunofluorescence, and radioisotope uptake assays were used to assess iodide-handling and glucose-handling gene expression. Results: Both compds. inhibited cell proliferation in a time-dependent and dose-dependent manner and caused cell cycle arrest in the G0/G1 phase. Sorafenib blocked RET, AKT, and ERK1/2 phosphorylation, whereas cabozantinib blocked RET and AKT phosphorylation. The restoration of iodide-handling gene expression and inhibition of glucose transporter 1 and 3 expression could be induced by either drug. The robust expression of sodium/iodide symporter induced by either agent was confirmed, and 125I uptake was correspondingly enhanced. 18F-fluorodeoxyglucose accumulation was significantly decreased after treatment by either sorafenib or cabozantinib. Conclusions: Sorafenib and cabozantinib had marked effects on cell proliferation, cell cycle arrest, and signal transduction pathways in PTC cells harboring RET/PTC1 rearrangement. Both agents could be potentially used to enhance the expression of iodide-handling genes and inhibit the expression of glucose transporter genes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of tyrosine kinase inhibitors including sorafenib and cabozantinib effect iodide- and glucose-handling gene expression in human papillary thyroid cancer HP 2-7 cells)

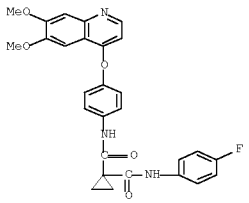
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 107 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:960349 CAPLUS Full-text

DOCUMENT NUMBER: 164:270197

TITLE: Cabozantinib as a new drug for treating metastatic medullary thyroid cancer

AUTHOR(S): Chen, Hui-ling; Zhang, Zhi-ye; Yang, Yan-biao

CORPORATE SOURCE: Department of Pharmacy, Lanzhou City First People's Hospital, Lanzhou, 730050, Peop. Rep. China

SOURCE: Zhongguo Yaofang (2014), 25(29), 2766-2769
CODEN: ZYHAA4; ISSN: 1001-0408

DIGITAL OBJECT ID: 10.6039/j.issn.1001-0408.2014.29.27

PUBLISHER: Zhongguo Yaofang Zazhishe

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Chinese

AB A review with 12 refs. is given on the cabozantinib as a new drug for treating metastatic medullary thyroid cancer. The topic discussed include:: (1) clin. pharmacol. research of cabozantinib(action mechanism and pharmacol. effects), (2) clin. research of cabozantinib, (3) adaptation disease and dosage and administration of cabozantinib, (4) drug interactions with cytochrome P 450 and p-glycoprotein, (5) attention and safety evaluation of cabozantinib, (6) administration for special population.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as a new drug for treating metastatic medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

L4 ANSWER 106 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:981422 CAPLUS Full-text

DOCUMENT NUMBER: 163:88178

TITLE: Methods of selecting treatment regimens of cancer with chemotherapy plus VEGF signaling inhibitors using the predictive potential of serum protein and tumor gene expression

INVENTOR(S): Barry, Simon T.; Critchlow, Susan E.; Pommier, Aurelien J.C.

PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited

SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015082880	A1	20150611	WO 2014-GB53485	20141125

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

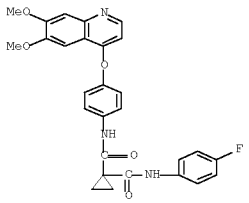
PRIORITY APPLN. INFO.: US 2013-61910652 P 20131202

AB The present invention is directed to, inter alia, the predictive potential of serum protein and tumor gene expression in patients with metastatic colorectal cancer (mCRC) receiving either chemotherapy plus placebo or chemotherapy plus the VEGF signaling inhibitor cediranib, sunitinib, sorafenib, pazopanib, tivozanib, vandetanib, soraninib, axitinib, cabozantinib, bevacizumab, aflibercept or ramucirumab. The present invention, in addition, provides for patient selection methods, as well as kits, that may be used in determining suitable cancer treatment regimens in subjects with cancer, with particular reference to whether the subject will gain benefit from treatment with VEGF signaling inhibitors.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of selecting treatment regimens of cancer with chemotherapy plus VEGF signaling inhibitors using the predictive potential of serum protein and tumor gene expression)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 108 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:948166 CAPLUS Full-text

DOCUMENT NUMBER: 164:367374

TITLE: Update on Cardiovascular Safety of Tyrosine Kinase Inhibitors: With a Special Focus on QT Interval, Left Ventricular Dysfunction and Overall Risk/Benefit

AUTHOR(S): Shah, Rashmi R.; Morganroth, Joel

CORPORATE SOURCE: Rashmi Shah Consultancy Ltd, Buckinghamshire, SL9 7JA, UK

SOURCE: Drug Safety (2015), 38(8), 693-710
CODEN: DRSAEA; ISSN: 0114-5916

DIGITAL OBJECT ID: 10.1007/s40264-015-0300-1

PUBLISHER: Springer International Publishing AG

DOCUMENT TYPE: Journal; General Review; (online computer file)

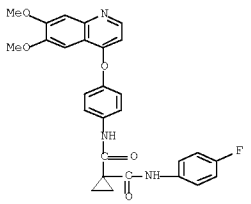
LANGUAGE: English

AB We previously reviewed the cardiovascular safety of 16 tyrosine kinase inhibitors (TKIs), approved for use in oncol. as of 30 Sept. 2012. Since then, the indications for some of them have been widened and an addnl. nine TKIs have also been approved as of 30 Apr. 2015. Eight of these nine are indicated for use in oncol. and one (nintedanib) for idiopathic pulmonary fibrosis. This report is an update on the cardiovascular safety of those 16 TKIs, including the post-marketing data concerning their pro-arrhythmic effects, and reviews the cardiovascular safety of the nine new TKIs approved since (afatinib, cabozantinib, ceritinib, dabrafenib, ibrutinib, lenvatinib, nintedanib, ponatinib, and trametinib). As before, we focus on specific aspects of cardiovascular safety, namely their potential to induce QT interval prolongation, left ventricular (LV) dysfunction and hypertension but now also summarise the risks of arterial thromboembolic events (ATEs) associated with these agents. Of the newer TKIs, cabozantinib and ceritinib have been shown to induce a mild to moderate degree of QTc interval prolongation while cardiac dysfunction has been reported with the use of afatinib, dabrafenib, lenvatinib, ponatinib and trametinib. The label for axitinib was revised to include a new association with cardiac dysfunction. Hypertension is associated with cabozantinib, lenvatinib, nintedanib, ponatinib and trametinib. Ponatinib, within 10 mo of its approval in Dec. 2012, required voluntary (temporary) suspension of its marketing until significant safety revisions (restricted indication, addnl. warnings and precautions about the risk of arterial occlusion and thromboembolic events and amended dose) were made to its label. Compared with the previous 16 TKIs,

more of the recently introduced TKIs are associated with the risk of LV dysfunction, and fewer with QT prolongation. Available data on morbidity and mortality associated with TKIs, together with post-marketing experience with lapatinib and ponatinib, emphasize the need for effective pharmacovigilance and ongoing re-assessment of their risk/benefit after approval of these novel agents. If not adequately managed, these cardiovascular effects significantly decrease the quality of life and increase the morbidity and mortality in a population already at high risk. Evidence accumulated over the last decade suggests that their clin. benefit, although worthwhile, is modest and extends only to progression-free survival and complete response without any effect on overall survival. During uncontrolled use in routine clin. practice, their risk/benefit is likely to be inferior to that perceived from highly controlled clin. trials.

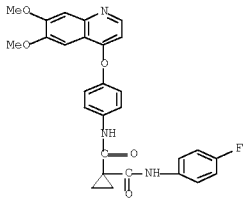
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(update on cardiovascular safety of tyrosine kinase inhibitors with special focus on QT interval, left ventricular dysfunction and overall risk/benefit)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

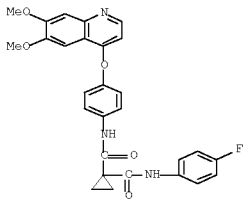
L4 ANSWER 109 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:920388 CAPLUS Full-text
DOCUMENT NUMBER: 164:271039
TITLE: SnapShot: Kinase Inhibitors II
AUTHOR(S): Wang, Jinhua; Gray, Nathanael S.
CORPORATE SOURCE: Department of Cancer Biology, Dana-Farber Cancer Institute, Boston, MA, 02215, USA
SOURCE: Molecular Cell (2015), 58(4), 710-710.e1
CODEN: MOCEFL; ISSN: 1097-2765
DIGITAL OBJECT ID: 10.1016/j.molcel.2015.05.002
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Selective small-mol. inhibitors of protein kinases can serve as powerful tools to elucidate biol. function. Efforts to develop potential drug candidates have yielded a wealth of kinase inhibitors. However, selecting the optimal kinase inhibitor for a particular application can be challenging. While the optimal inhibitor will be application specific, we have attempted to summarize some of the best reported inhibitors for various kinases.
IT 849217-68-1 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discussion on small-mol. of kinases inhibitors II)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

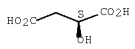
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

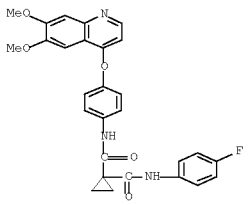


L4 ANSWER 110 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:894377 CAPLUS Full-text
DOCUMENT NUMBER: 163:1020
TITLE: Compositions and methods for diagnosing, evaluating and treating cancer by means of the DNA methylation status
INVENTOR(S): Clement, Kendell; Getz, Gad; Landau, Dan-Avi; Meissner, Alexander; Wu, Catherine Ju-Ying
PATENT ASSIGNEE(S): The Broad Institute Inc., USA; Dana-Farber Cancer Institute, Inc.; The General Hospital Corporation; President and Fellows of Harvard College
SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015077717	A1	20150528	WO 2014-US67146	20141124

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61908316 P 20131125
AB The present invention relates to methods of detg. a cancer treatment prognosis for a subject in need thereof by evaluating epigenetic and genetic changes within a tumor sample from the subject. The present invention further provides methods of treating cancer in a subject by evaluating epigenetic and genetic changes within a tumor sample from the subject, in addition, the present invention provides methods of screening test agents to identify agents that decrease tumor cell plasticity.
IT 849217-68-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for diagnosing, evaluating and treating cancer by means of the DNA methylation status)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 111 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:893490 CAPLUS Full-text
DOCUMENT NUMBER: 163:51687
TITLE: Process for the preparation of cabozantinib salt and its crystal form
INVENTOR(S): Shen, Anxiong; Tang, Dongjun; Kou, Jingping
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 19pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104649969	A	20150527	CN 2014-10676653	20141121

PRIORITY APPLN. INFO.: CN 2013-10596247 A 20131122

AB The invention relates to the cabozantinib L-malate crystal form A2, which has absorption peaks at 9.33°, 11.75°, 13.44°, 15.16°, 19.72°, 23.14°, and 25.92° determined by X-ray powder diffraction at 2θ. The invention also relates to cabozantinib hydrobromide crystal form I, which has absorption peaks at 8.68°, 13.01°, 7.45°, 19.52°, 20.05°, 21.71°, 23.29°, and 26.28° determined by X-ray powder diffraction at 2θ.

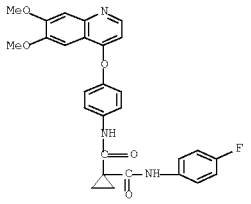
IT 1140909-48-3P 1788329-76-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of cabozantinib salt and its crystal form)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

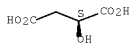
CRN 849217-68-1
CMF C28 H24 F N3 O5



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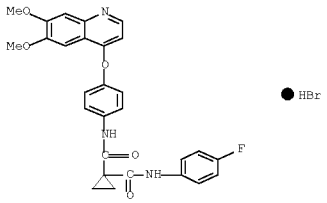
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CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



RN 1786398-76-2 CAPLUS

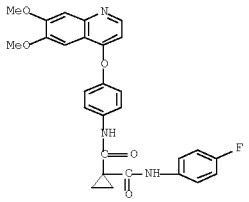
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrobromide (1:1) (CA INDEX NAME)



IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of cabozantinib salt and its crystal form)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

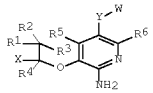


L4 ANSWER 112 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:893241 CAPLUS Full-text
DOCUMENT NUMBER: 163:66113
TITLE: Aminopyridine compounds as protein kinase receptor inhibitors and their preparation, pharmaceutical compositions and use in the treatment of proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Liang; Wang, Tingjin
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 109pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104650049	A	20150527	CN 2014-10429046	20140827

PRIORITY APPLN. INFO.: CN 2013-10383121 A 20130828
CN 2014-10144178 A 20140410

OTHER SOURCE(S): MARPAT 163:66113
GI



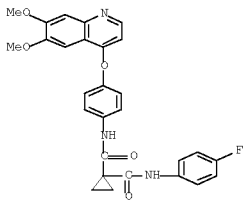
I

AB The invention relates to aminopyridine compds. of formula I, their pharmaceutically acceptable salts, and pharmaceutical formulations, which is used for regulating protein kinase activity, and adjusting signal response within cells or between cells. The invention also relates to compds. I and their stereoisomer, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts or prodrugs which are used in treating mammal, particularly to human hyperproliferative disorders. The pharmaceutical compns. includes the title compds., pharmaceutically acceptable carriers, excipients, diluents, adjuvants, and/or mediums, and other treating agents. The pharmaceutical compns. are used in preparing medicines for preventing, handling, treating or relieving proliferative disorders such as metastatic cancer, colon cancer, gastric adenocarcinoma, bladder cancer, breast cancer, kidney cancer, liver cancer, lung cancer, thyroid cancer, head and neck cancer, prostate cancer, pancreatic cancer, central nervous system cancer, spongioblastoma, bone marrow hyperplasia, atherosclerosis or pulmonary fibrosis. Compds. of formula I wherein R1- R6 are independently H, D or F; X, Y are independently (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl; W is C3-8 cycloalkyl, -(C1-4 alkylene)-(C3-8 cycloalkyl), C3-7 heterocyclyl or -(C1-4 alkylene)-(C3-7 heterocyclyl), etc.; and their stereoisomer, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts or prodrugs as protein kinase receptor inhibitors useful in the treatment of proliferative disorders thereof, are claimed. Compds. of formula I were prepared by using condensation, reduction, and cross-coupling as the key steps. All the invention compds. were evaluated for their protein kinase inhibitory activity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of aminopyridine compds. as protein kinase receptor inhibitors useful in the treatment of proliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

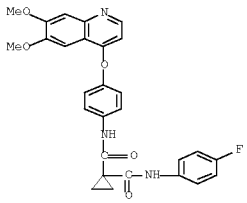
L4 ANSWER 113 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:884680 CAPLUS Full-text
TITLE: Comprehensive transcriptomic analysis of molecularly targeted drugs in cancer for target pathway evaluation
AUTHOR(S): Mashima, Tetsuo; Ushijima, Masaru; Matsuura, Masaaki; Tsukahara, Satomi; Kunimasa, Kazuhiro; Furuno, Aki; Saito, Sakae; Kitamura, Masami; Soma-Nagae, Taeko; Seimiya, Hiroyuki; Dan, Shingo; Yamori, Takao; Tomida, Akihiro
CORPORATE SOURCE: Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo, Japan
SOURCE: Cancer Science (2015), 106(7), 909-920
CODEN: CSACCM; ISSN: 1349-7006
DIGITAL OBJECT ID: 10.1111/cas.12682
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Targeted therapy is a rational and promising strategy for the treatment of advanced cancer. For the development of clin. agents targeting oncogenic signaling pathways, it is important to define the specificity of compds. to the target mol. pathway. Genome-wide transcriptomic anal. is an unbiased approach to evaluate the compound mode of action, but it is still unknown whether the anal. could be widely applicable to classify molecularly targeted anticancer agents. We comprehensively obtained and analyzed 129 transcriptomic datasets of cancer cells treated with 83 anticancer drugs or related agents, covering most clin. used, molecularly targeted drugs alongside promising inhibitors of mol. cancer targets. Hierarchical clustering and principal component anal. revealed that compds. targeting

similar target mols. or pathways were clustered together. These results confirmed that the gene signatures of these drugs reflected their modes of action. Of note, inhibitors of oncogenic kinase pathways formed a large unique cluster, showing that these agents affect a shared mol. pathway distinct from classical antitumor agents and other classes of agents. The gene signature anal. further classified kinome-targeting agents depending on their target signaling pathways, and we identified target pathway-selective signature gene sets. The gene expression anal. was also valuable in uncovering unexpected target pathways of some anticancer agents. These results indicate that comprehensive transcriptomic anal. with our database (http://scads.jfcr.or.jp/db/cs/) is a powerful strategy to validate and re-evaluate the target pathways of anticancer compds.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comprehensive transcriptomic anal. of molecularly targeted drugs in cancer for target pathway evaluation)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 114 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:866343 CAPLUS Full-text
DOCUMENT NUMBER: 163:1013
TITLE: mTOR protein kinase inhibitors for enhancing the immune response for treatment of diseases such as cancer
INVENTOR(S): Mannick, Joan; Glass, David Jonathan; Murphy, Leon
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 149pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015073644	A1	20150521	WO 2014-US65408	20141113
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150140036	A1	20150521	US 2014-14540867	20141113

PRIORITY APPLN. INFO.:

US 2013-61903636	P	20131113
US 2014-62027121	P	20140721
US 2014-62052629	P	20140919
US 2014-62076142	P	20141106

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

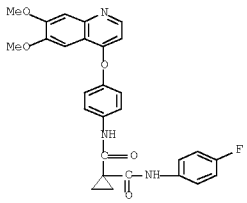
AB The present invention relates, in part, to compns. and methods for enhancement of an immune response by partial mTOR inhibition, e.g., with low, immune enhancing, doses of an mTOR inhibitor, such as RAD001 or rapamycin. In an embodiment, the subject has cancer and the method comprises promoting the subject's immune response to treat cancer.

IT 1140909-48-3, Cabozantinib-S-Malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mTOR protein kinase inhibitors for enhancing the immune response for treatment of diseases such as cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

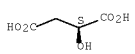
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



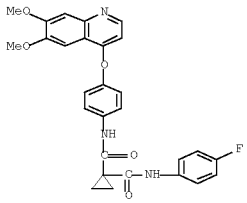
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 115 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:847958 CAPLUS Full-text
DOCUMENT NUMBER: 164:260451
TITLE: Cabozantinib: A MET, RET, and VEGFR2 Tyrosine Kinase Inhibitor
AUTHOR(S): Gruellich, Carsten
CORPORATE SOURCE: Department of Medical Oncology, National Center for Tumor Diseases, Heidelberg University Medical Center, Heidelberg, 69120, Germany
SOURCE: Recent Results in Cancer Research (2014), 201(Small Molecules in Oncology), 207-214
CODEN: RRCRBU; ISSN: 2197-6767
DIGITAL OBJECT ID: 10.1007/978-3-642-54490-3_12
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib is a receptor tyrosine kinase inhibitor with activity against MET, VEGFR2, FLT3, c-KIT, and RET. Activity of cabozantinib toward a broad range of tumor models could be detected in several preclin. studies. Of note, cabozantinib decreases metastasis potential and tumor invasiveness when compared with placebo or agents that target VEGFR and have no activity against MET. Clin. phase I and II studies with cabozantinib have been conducted in various malignancies including medullary thyroid cancer (MTC), NSCLC, breast, ovarian, pancreatic, and prostate cancer. In MTC, gain of function mutations of RET are central for tumorigenesis. Hereditary forms of MTC (MEN II) are caused by germline mutations of RET, in sporadic MTC in up to 50 % of cases RET mutations occur. Addnl., activating mol. changes in VEGFR and MET pathways have also been implicated in MTC progression. Clin. responses with cabozantinib in MTC could be observed in early clin. trials, and following confirmation of clin. benefit in a randomized phase III trial, cabozantinib gained FDA approval for first-line treatment of advanced MTC in 2012. In prostate cancer models, MET expression increases with androgen ablation and clin. progression of bone and lymph node metastasis. A phase II trial with cabozantinib also showed very promising response rates in patients with metastatic prostate cancer. Therefore, randomized phase III studies are currently ongoing to validate the efficacy of cabozantinib in heavily pretreated prostate cancer patients.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as MET, RET, and VEGFR2 tyrosine kinase inhibitor)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

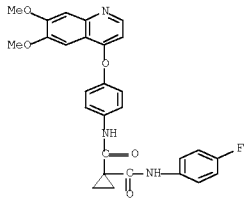


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 116 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:827243 CAPLUS Full-text
DOCUMENT NUMBER: 162:650141
TITLE: Methods using TIE2 kinase inhibitors for the treatment of cancer
INVENTOR(S): Flynn, Daniel L.; Kaufman, Michael D.; Smith, Bryan; Rudoltz, Marc S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 121pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

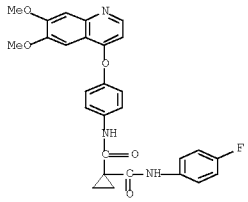
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015069266	A1	20150514	WO 2013-US69005	20131107
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,				

SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: WO 2013-US69005 20131107
AB The present invention relates to methods using TIE2 kinase inhibitors for the treatment of tumor growth, invasiveness, intravasation, dissemination, metastasis, and immunosuppression. Specifically, the invention relates to methods of using 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea and salts thereof.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods using TIE2 kinase inhibitors for the treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 117 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:821056 CAPLUS Full-text
DOCUMENT NUMBER: 164:219602
TITLE: Pharmacological Inhibition of KIT Activates MET Signaling in Gastrointestinal Stromal Tumors
AUTHOR(S): Cohen, Noah A.; Zeng, Shan; Seifert, Adrian M.; Kim, Teresa S.; Sorenson, Eric C.; Greer, Jonathan B.; Beckman, Michael J.; Santamaria-Barria, Juan A.; Crawley, Megan H.; Green, Benjamin L.; Rossi, Ferdinand; Besmer, Peter; Antonescu, Cristina R.; DeMatteo, Ronald P.
CORPORATE SOURCE: Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Cancer Research (2015), 75(10), 2061-2070
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-14-2564
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB These findings offer a preclin. rationale to immediately reposition the MET kinase inhibitor cabozantinib for clin. evaluation in treatment of gastrointestinal stromal tumors that are either sensitive or resistant to imatinib, the kinase inhibitor used to treat this type of sarcoma. Gastrointestinal stromal tumors (GIST) are the most common adult sarcomas and the oncogenic driver is usually a KIT or PDGFRA mutation. Although GISTs are often initially sensitive to imatinib or other tyrosine kinase inhibitors, resistance generally develops, necessitating backup strategies for therapy. In this study, we determined that a subset of human GIST specimens that acquired imatinib resistance acquired expression of activated forms of the MET oncogene. MET activation also developed after imatinib therapy in a mouse model of GIST (KitV558del/+ mice), where it was associated with increased tumor hypoxia. MET activation also occurred in imatinib-sensitive human GIST cell lines after imatinib treatment in vitro. MET inhibition by crizotinib or RNA interference was cytotoxic to an imatinib-resistant human GIST cell population. Moreover, combining crizotinib and imatinib was more effective than imatinib alone in imatinib-sensitive GIST models. Finally, cabozantinib, a dual MET and KIT small-mol. inhibitor, was markedly more effective than imatinib in multiple preclin. models of imatinib-sensitive and imatinib-resistant GIST. Collectively, our findings showed that activation of compensatory MET signaling by KIT inhibition may contribute to tumor resistance. Furthermore, our work offered a preclin. proof of concept for MET inhibition by cabozantinib as an effective strategy for GIST treatment. Cancer Res; 75(10); 2061-70. ©2015 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. inhibition of KIT activates MET signaling in gastrointestinal stromal tumors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

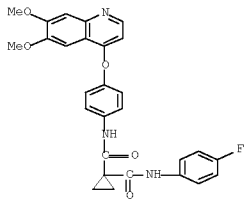


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 118 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:739043 CAPLUS Full-text
DOCUMENT NUMBER: 162:567725
TITLE: Solid particulate formulations of tyrosine derivatives
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: PCT Int. Appl., 20pp.; Chemical Indexing Equivalent to 162:567667 (US)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015061288	A1	20150430	WO 2014-US61527	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150112116	A1	20150423	US 2013-14062194	20131024
PRIORITY APPLN. INFO.:			US 2013-61894279 P	20131022
			US 2013-14062194 A	20131024

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Provided are methods comprising providing a tyrosine deriv. such as α-methyltyrosine, and a solid particulate material (and, optionally, melanin) and applying force to said tyrosine derivative and said solid particulate material for a time and under conditions effective to impregnate at least one of said tyrosine derivative and said solid particulate material with the other of said tyrosine derivative and said solid particulate material.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid particulate formulations of tyrosine derivs.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 119 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:734279 CAPLUS Full-text
DOCUMENT NUMBER: 162:594407
TITLE: High-speed centrifugal mixing devices for uses in pharmaceuticals
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015061256	A1	20150430	WO 2014-US61481	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150110735	A1	20150423	US 2013-14059837	20131022
PRIORITY APPLN. INFO.:			US 2013-14059837 A	20131022

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A centrifugal mixing device can include a shaft assembly that is operably coupled to a motor such that the motor rotates the shaft assembly about a first axis. The devices can further include a turret that is rotatably coupled to the shaft assembly such that the turret rotates about the first axis relative to the shaft assembly. The turret can include a first support,

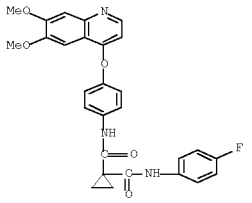
a first canister rotatably coupled to the first support such that the first canister rotates about a second axis, and a second canister rotatably coupled to the first support such that the second canister rotates about a third axis. The turret is configured to rotate about the first axis in a first rotational direction and each of the first and second canisters is configured to rotate about the second and third axes, resp., in a second rotational direction that is opposite the first rotational direction. The centrifugal mixing device consists of the canisters comprising at least 2 different particulate materials. The particulate materials comprises an active pharmaceutical ingredient.

IT 849217-68-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-speed centrifugal mixing devices for uses in pharmaceuticals)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 120 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:694096 CAPLUS Full-text

DOCUMENT NUMBER: 163:240819

TITLE: New therapies for dedifferentiated papillary thyroid cancer

AUTHOR(S): Fallahi, Poupak; Mazzi, Valeria; Vita, Roberto; Ferrari, Silvia Martina; Materazzi, Gabriele; Galleri, David; Benvenga, Salvatore; Miccoli, Paolo; Antonelli, Alessandro

CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56126, Italy

SOURCE: International Journal of Molecular Sciences (2015), 16(3), 6153-6182
CODEN: IJMCFK; ISSN: 1422-0067

DIGITAL OBJECT ID: 10.3390/ijms16036153

PUBLISHER: MDPI AG

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

SOURCE: U.S. Pat. Appl. Publ., 15pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150110735	A1	20150423	US 2013-14059837	20131022
WO 2015061256	A1	20150430	WO 2014-US61481	20141021

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-14059837 A 20131022

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A centrifugal mixing device can include a shaft assembly that is operably coupled to a motor such that the motor rotates the shaft assembly about a first axis. The devices can further include a turret that is rotatably coupled to the shaft assembly such that the turret rotates about the first axis relative to the shaft assembly. The turret can include a first support, a first canister rotatably coupled to the first support such that the first canister rotates about a second axis, and a second canister rotatably coupled to the first support such that the second canister rotates about a third axis. The turret is configured to rotate about the first axis in a first rotational direction and each of the first and second canisters is configured to rotate about the second and third axes, resp., in a second rotational direction that is opposite the first rotational direction. The centrifugal mixing device consists of the canisters comprising at least 2 different particulate materials. The particulate materials comprises an active pharmaceutical ingredient.

IT 849217-68-1, Cabozantinib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-speed centrifugal mixing devices for uses in pharmaceuticals)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

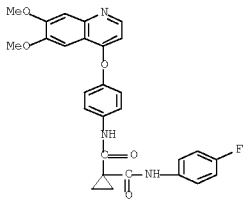
AB The no. of thyroid cancers is increasing. Std. treatment usually includes primary surgery, TSH suppressive therapy, and ablation of the thyroid remnant with radioactive iodine (RAI). Despite the generally good prognosis of thyroid carcinoma, about 5% of patients will develop metastatic disease, which fails to respond to RAI, exhibiting a more aggressive behavior. The lack of specific, effective and well-tolerated drugs, the scarcity of data about the association of multi-targeting drugs, and the limited role of radioiodine for dedifferentiated thyroid cancer, call for further efforts in the field of new drugs development. Rearranged during transfection (RET)/papillary thyroid carcinoma gene rearrangements, BRAF (B-RAF proto-oncogene, serine/threonine kinase) gene mutations, RAS (rat sarcoma) mutations, and vascular endothelial growth factor receptor 2 angiogenesis pathways are some of the known pathways playing a crucial role in the development of thyroid cancer. Targeted novel compds. have been demonstrated to induce clin. responses and stabilization of disease. Sorafenib has been approved for differentiated thyroid cancer refractory to RAI.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discussion on new therapies for dedifferentiated papillary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 178 THERE ARE 178 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 121 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

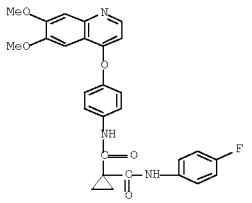
ACCESSION NUMBER: 2015:691735 CAPLUS Full-text

DOCUMENT NUMBER: 162:567753

TITLE: High-speed centrifugal mixing devices for uses in pharmaceuticals

INVENTOR(S): Hoffman, Steven

PATENT ASSIGNEE(S): Tyme, Inc., USA



L4 ANSWER 122 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:691420 CAPLUS Full-text

DOCUMENT NUMBER: 162:567667

TITLE: Solid particulate formulations of tyrosine derivatives

INVENTOR(S): Hoffman, Steven

PATENT ASSIGNEE(S): Tyme, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 6pp.; Chemical Indexing Equivalent to 162:567725 (WO)
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150112116	A1	20150423	US 2013-14062194	20131024
WO 2015061288	A1	20150430	WO 2014-US61527	20141021

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

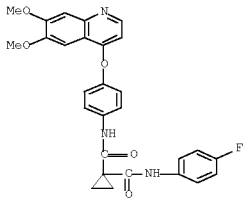
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61894279 P 20131022
US 2013-14062194 A 20131024

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided are methods comprising providing a tyrosine deriv. such as α-methyltyrosine, and a solid particulate material (and, optionally, melanin) and applying force to said tyrosine derivative and said solid particulate material for a time and under conditions effective to impregnate at least one of said tyrosine derivative and said solid particulate material

with the other of said tyrosine derivative and said solid particulate material.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid particulate formulations of tyrosine derivs.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



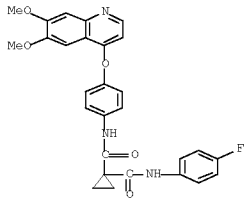
L4 ANSWER 123 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:656704 CAPLUS Full-text
DOCUMENT NUMBER: 162:487306
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Institut de Recerca Biomedica (IRB Barcelona), Spain; Institucio Catalana de Recerca i Estudis Avancats
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015052583	A2	20150416	WO 2014-IB2675	20141007
WO 2015052583	A3	20150723		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2926894 A1 20150416 CA 2014-2926894 20141007
PRIORITY APPLN. INFO.: US 2013-61888984 P 20131009
WO 2014-IB2675 W 20141007

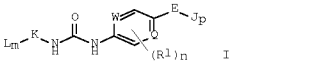
AB The present invention relates to a method for the prognosis of bone metastasis in HER2+ breast cancer, which comprises determining if the MAF gene is amplified in a primary tumor sample. Likewise, the present invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the MAF gene expression level, amplification or translocation. The present invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The present invention also relates to a c-Maf inhibitor as therapeutic agent for use in the treatment of HER2+ breast cancer metastasis. The present invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the present invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for determining prognosis of bone metastasis in HER2+ breast cancer
and use of c-Maf inhibitor as therapeutic agent)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



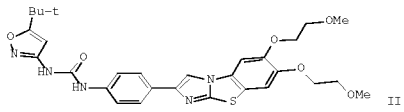
L4 ANSWER 124 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:639512 CAPLUS Full-text
DOCUMENT NUMBER: 162:590248
TITLE: Preparation of substituted urea derivatives for treating FLT3 kinase mediated or induced diseases
INVENTOR(S): Zheng, Changchun; Liu, Bing; Zhang, Weihong; Zhang, Yingjun; Long, Bohua
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 69pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104513257	A	20150415	CN 2014-10498232	20140925
CN 104513258	A	20150415	CN 2014-10498181	20140925

PRIORITY APPLN. INFO.: CN 2013-10445435 A 20130926
CN 2014-10108087 A 20140322
OTHER SOURCE(S): CASREACT 162:590248; MARPAT 162:590248
GI

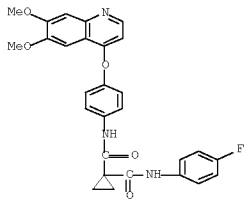


I



II

AB This invention provides substituted urea derivs. I [wherein K = 5- or 6-membered heteroaryl; Q and W = independently CH or N; L = independently NH2, NO2, alkylthio, alkyl, etc.; R1 = independently H, F, Cl, Br, I, etc.; E = bicyclic or tricyclic heteroaryl; J = G-(CH2)q-R; G = independently O, S, SO, SO2, CO, etc.; R = independently H, alkoxy, alkyl, alkenyl, etc.; m = 1-4; n = 0-4; p = 2-4; q = 1-4], stereoisomers, geometrical isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, esters, pharmaceutically acceptable salts, or prodrugs for treating FLT3 kinase mediated or induced diseases, such as autoimmune diseases, inflammatory diseases and proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 6.0 nM against FLT3 kinase.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. for treating FLT3 kinase mediated or induced diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



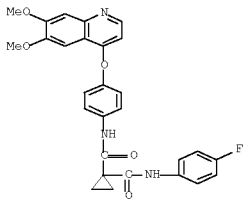
L4 ANSWER 125 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:613471 CAPLUS Full-text
DOCUMENT NUMBER: 162:532738
TITLE: High drug loading system to co-deliver anticancer drugs and nucleic acids for cancer therapy
INVENTOR(S): Cheng, Gang; Tang, Qiong; Cao, Bin
PATENT ASSIGNEE(S): The University of Akron, USA
SOURCE: U.S. Pat. Appl. Publ., 10pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150099005	A1	20150409	US 2014-14510442	20141009

PRIORITY APPLN. INFO.: US 2013-61888709 P 20131009
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A high drug loading system is described comprising of at least one anticancer drug; at least one peptide; and at least one nucleic acid.
IT 1140909-48-3, Cabozantinib-S-malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high drug loading system to co-deliver anticancer drugs and nucleic acids for cancer therapy)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

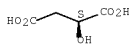
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



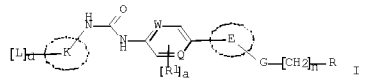
L4 ANSWER 126 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:560353 CAPLUS Full-text
DOCUMENT NUMBER: 162:488682
TITLE: Preparation of substituted urea derivatives for modulating the FLT3 kinase activity and inhibiting FLT3-ITD
INVENTOR(S): Cheng, Changchung; Liu, Bing; Zhang, Yingjun; Long, Bohua; Zhang, Weihong
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015043492	A1	20150402	WO 2014-CN87469	20140925

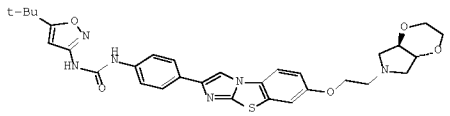
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CN 104513259	A	20150415	CN 2014-10498216	20140925
CN 104513252	A	20150415	CN 2014-10499464	20140925

PRIORITY APPLN. INFO.: CN 2013-10445605 A 20130926
CN 2014-10107854 A 20140322
OTHER SOURCE(S): CASREACT 162:488682; MARPAT 162:488682
GI

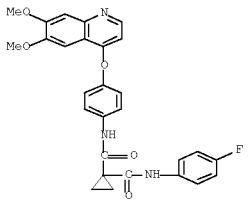


I



II

AB The title compds. I [each of Q and W = (independently) CH or N; G = O, S, C(O), etc.; R = alkoxy, alkyl, (un)substituted amino, etc.; ring K = 5-6 membered heteroaryl group, of which at least two ring members are heteroatoms independently selected from O, S, NR4 and N; each L = (independently) amino, nitro, alkylthio, etc.; ring E = bicyclic or tricyclic heteroarylene; R1 = H, halo, haloalkyl, etc.; R4 = H, alkyl, cycloalkyl, etc.; a = 0-4; d, n = 1-4; with the provisos] which are useful in modulating the FLT3 kinase activity, inhibiting FLT3-ITD, and treating the diseases mediated by FLT3 kinase or caused by FLT3-ITD, were prepared and claimed. E.g., a multi-step synthesis of II, starting from (4aS,7aS)-hexahydro-2H-[1,4]dioxino[2,3-c]pyrrole and 2-chloroethanol, was described. Exemplified compds. I were tested for FLT3 kinase inhibition (data given for representative compds. I). Pharmaceutical compns. comprising compound I, alone or in combination with other therapeutic agents, were disclosed.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. for modulating the FLT3 kinase activity and inhibiting FLT3-ITD)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

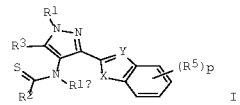


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

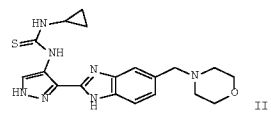
L4 ANSWER 127 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:527604 CAPLUS Full-text
DOCUMENT NUMBER: 162:475187
TITLE: Preparation of pyrazole derivatives as protein kinase over expression inhibitors
INVENTOR(S): Zhang, Jiancun; Liu, Bing; Zhang, Yingjun; Nie, Linlin; Yang, Xueqi
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 80pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104447701	A	20150325	CN 2014-10471458	20140916

PRIORITY APPLN. INFO.: CN 2013-10426478 A 20130917
CN 2014-10109414 A 20140321
OTHER SOURCE(S): MARPAT 162:475187
GI

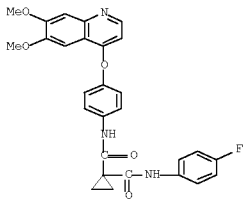


I

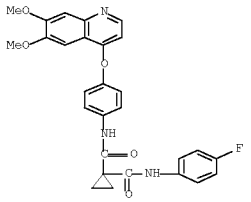


II

AB The title compds. with general formula I [wherein R1 and R1a are independently H or C1-4 alkyl; R2 is alkyl amino, aryl, heteroaryl, etc.; X is CR4aR4 or NR6; Y is CR4a or N; R3 is H, F, Cl, etc.; R3 is H, F, Cl, Br, etc.; R5 is H, alkyl, alkenyl, alkynyl, etc.; p = 1 -4] or isomers, N-oxide, hydrates, solvates, metabolites, esters, prodrugs, or pharmaceutically acceptable salts there of were prepared as protein kinase over expression inhibitors. For example, compound II was prepared in a multi-step synthesis. The title substituted pyrazole derivative for inhibiting protein kinase over expression, or stereoisomer, geometric isomer, tautomer, oxynitride, solvate, hydrate, metabolite, ester, pharmaceutically acceptable salt or prodrug thereof, pharmaceutical compns. containing these compds. as active ingredients, and the application of these compds. or pharmaceutical compns. in preparing the drugs for preventing, treating of reducing cell growth disorders. (assay data given).
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of pyrazolylaminopyrimidine derivs. as aurora kinase
inhibitor useful in the treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 128 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:494404 CAPLUS Full-text
DOCUMENT NUMBER: 162:570128
TITLE: Dermatologic adverse events in pediatric patients receiving targeted anticancer therapies: A pooled analysis
AUTHOR(S): Belum, Viswanath Reddy; Washington, Courtney; Pratilas, Christine A.; Sibaud, Vincent; Boralevi, Franck; Lacouture, Mario E.
CORPORATE SOURCE: Department of Dermatology, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Pediatric Blood & Cancer (2015), 62(5), 798-806
CODEN: PBCEAQ; ISSN: 1545-5017
DIGITAL OBJECT ID: 10.1002/pbc.25429
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background : The dermatol. adverse events (AEs) of various molecularly targeted therapies are well-described in adult cancer patients. Little has been reported on the incidence and clin. presentation of such AEs in pediatric patients with cancer. To address this gap, we analyzed the dermatol. AEs reported across clin. trials of targeted anticancer therapies in pediatric patients. Procedures : We conducted an electronic literature search (PubMed, American Society of Clin. Oncol. annual meetings' abstrs., , NCI's Pediatric Oncol. Branch webpage) to identify clin. trials involving targeted anticancer therapies that reported dermatol. AEs in their safety data. Studies were limited to the pediatric population, monotherapy trials (oncol.), and English language publications. Results : Pooled data from 19 clin. studies investigating 11 targeted anticancer agents (alemtuzumab, rituximab, imatinib, dasatinib, erlotinib, vandetanib, sorafenib, cabozantinib, pazopanib, everolimus, and temsirolimus) were analyzed. The most frequently encountered dermatol. AEs were rash (127/660; 19%), xerosis (18/100; 18%), mucositis (68/402; 17%), and pruritus (12/169; 7%). Other AEs included pigmentary abnormalities of the skin/hair (13%), hair disorders (trichomegaly, hypertrichosis, alopecia, and madarosis; 14%), urticaria (7%), palmoplantar erythrodysesthesia (7%), erythema, acne, purpura, skin fissures, other 'unknown skin changes', exanthem, infection, flushing, telangiectasia, and photosensitivity. Conclusion : This study describes the dermatol. manifestations of targeted anticancer therapy-related AEs in the pediatric population. Since these AEs are often associated with significant morbidity, it is imperative that pediatric oncologists be familiar with their recognition and management, to avoid unnecessary dose modifications and/or termination, and to prevent impairments in patients' quality of life. Pediatr Blood Cancer 2015;62:798-806. © 2015 Wiley Periodicals, Inc.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dermatol. adverse events in pediatric patients receiving targeted anticancer therapies)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

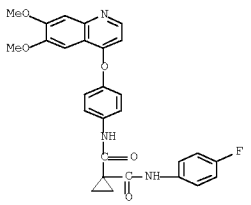


REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 129 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:460229 CAPLUS full-text
DOCUMENT NUMBER: 162:398722
TITLE: Anti-human angiopoietin 2 antibody for enhancing efficacy of antitumor agent and for combination cancer therapy
INVENTOR(S): Kim, Kyung Eun; Han, Sang Yeul; Koh, Gou Young; Lee, Hyo Seon; Kim, Chan
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd, S. Korea; Korea Advanced Institute of Science and Technology
SOURCE: Eur. Pat. Appl., 66pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2848631	A1	20150318	EP 2014-178842	20140729
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015032075	A	20150325	KR 2013-112089	20130917
US 20150079112	A1	20150319	US 2014-14446199	20140729
PRIORITY APPLN. INFO.:			KR 2013-112089 A	20130917

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method of preventing or treating cancer using an anti-Ang2 antibody or an antigen-binding fragment thereof that specifically binds to an angiogenesis-inducing factor Angiopoietin-2 (Ang2) and complexes to a Tie2 receptor while bound with Ang2.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human angiopoietin 2 antibody for enhancing efficacy of antitumor agent and for combination cancer therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

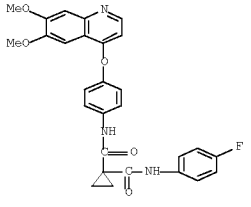


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 130 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:458209 CAPLUS full-text
DOCUMENT NUMBER: 162:447668
TITLE: Anti-human VSTM5 antibodies, fragments and conjugates for therapy and diagnosis of cancer, infection and immune disease
INVENTOR(S): Levine, Zurit; Rotman, Galit; Dassa, Liat; Levy, Ofer; Cojocaru, Gad S.; Toporik, Amir; Kliger, Yossef; Pow, Andrew; Liang, Spencer
PATENT ASSIGNEE(S): Compugen Ltd., Israel
SOURCE: PCT Int. Appl., 490pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015037005	A1	20150319	WO 2014-IL50814	20140911
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2922805	A1	20150319	CA 2014-2922805	20140911
AU 2014319921	A1	20160317	AU 2014-319921	20140911
PRIORITY APPLN. INFO.:			US 2013-61876324 P	20130911
			WO 2014-IL50814 W	20140911

AB The present invention relates to VSTM5-specific antibodies, antibody fragments, and VSTM5 polypeptides, conjugates and compns. comprising same, for modulating (antagonizing or agonizing) one or more of the effects of VSTM5 expression on immunity. More specifically, the present invention relates to VSTM5-specific antibodies, antibody fragments, and VSTM5 polypeptides, conjugates and compns. comprising same for treating and aiding in the diagnosis of cancer, infectious diseases and immune related diseases, e.g., those associated with aberrant (higher or lower than normal) VSTM5 expression by diseased and/or immune cells and/or aberrant (increased or reduced) VSTM5-mediated effects on immunity.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human VSTM5 antibodies, fragments and conjugates for therapy and diagnosis of cancer, infection and immune disease)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



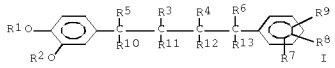
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

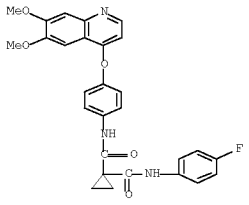
L4 ANSWER 131 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:423197 CAPLUS Full-text
DOCUMENT NUMBER: 162:419539
TITLE: Cancer therapy using dual kinase inhibitors such as catecholic butanes
INVENTOR(S): White, Thomas F.; Hoth, Daniel
PATENT ASSIGNEE(S): Triact Therapeutic, Inc., USA
SOURCE: PCT Int. Appl., 76pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015035410	A1	20150312	WO 2014-US54832	20140909
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2923667	A1	20150312	CA 2014-2923667	20140909
US 20150071919	A1	20150312	US 2014-14481837	20140909

PRIORITY APPLN. INFO.: US 2013-61875502 P 20130909
WO 2014-US54832 W 20140909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 162:419539
GI



AB The application relates to methods for treating a proliferative disorder by administering to a subject a pharmaceutical composition of a dual kinase inhibitor e.g. catecholic butanes of formula I [R1, R2 = independently H, lower alkyl, lower acyl; R3 - R6, R10 - R13 = independently H, lower alkyl; R7 - R9 = independently H, OH, lower alkoxy, lower acyloxy]. Patients to be treated include those that have been treated with Tarceva or other therapeutic compds. and relapsed or are resistant to treatment. The compds. described herein may exhibit a synergistic effect when administered with another agent.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer therapy using a dual kinase inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

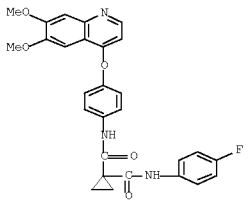


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 132 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:422447 CAPLUS Full-text
DOCUMENT NUMBER: 162:371151
TITLE: Combination therapy for the treatment of cancer using c-met inhibitor and c-myc inhibitor
INVENTOR(S): Lee, Ji Min; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 83pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150071932	A1	20150312	US 2014-14481509	20140909
KR 2015029175	A	20150318	KR 2013-107995	20130909

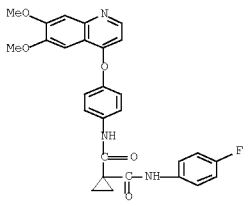
PRIORITY APPLN. INFO.: KR 2013-107995 A 20130909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 162:371151
AB The invention relates to a method of preventing and/or treating a cancer including co-administering a c-Met inhibitor and a c-Myc Inhibitor to a subject in need thereof. The invention relates to a pharmaceutical composition comprising a c-Met inhibitor and a c-Myc inhibitor. The inhibitor comprises at least one selected from the group consisting of an antibody, an antigen-binding fragment thereof, aptamers, siRNA, shRNA, microRNA, or a small mol. The invention relates to a kit comprising a pharmaceutically effective amount of a c-Met inhibitor as an active ingredient, and a second pharmaceutical composition comprising a pharmaceutically effective amount of a c-Myc inhibitor as an active ingredient, packaged together.
IT 849217-68-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for the treatment of cancer using c-met inhibitor and c-myc inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 133 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:422412 CAPLUS Full-text
DOCUMENT NUMBER: 162:423721
TITLE: Combination cancer therapy using c-met inhibitor and β-catenin inhibitor
INVENTOR(S): Lee, Ji Min; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 98pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150071930	A1	20150312	US 2014-14480174	20140908
KR 2015028652	A	20150316	KR 2013-107568	20130906

PRIORITY APPLN. INFO.: KR 2013-107568 A 20130906
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose a method of preventing and/or treating cancer. The method comprises the administration of a c-Met inhibitor and a β-catenin inhibitor. In several examples, an anti-MET receptor antibody in combination with a β-catenin inhibitor are shown to be effective in inhibiting the proliferation of breast, colon, and renal cancer cells.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy using MET inhibitor and β-catenin inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



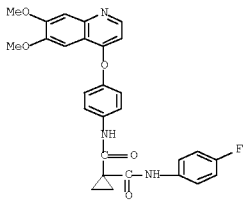
L4 ANSWER 134 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:414572 CAPLUS Full-text
DOCUMENT NUMBER: 162:425170
TITLE: Preparation of substituted pyridine compounds as tyrosine kinase inhibitors for treating proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Liang; Wang, Tingjin
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 142pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

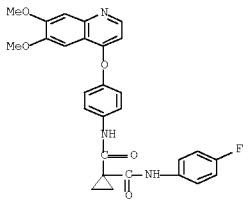
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015034729	A1	20150312	WO 2014-US53017	20140827
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS,				

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PRIORITY APPLN. INFO.: US 2013-61873963 P 20130905
OTHER SOURCE(S): CASREACT 162:425170; MARPAT 162:425170
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

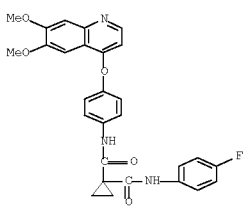
AB The present invention provides novel substituted pyridine compds. of general formula I (wherein each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; each of X and Y is independently C6-10aryl or 5-10 membered heteroaryl, both optionally substituted; W is C3-8cycloalkyl, -(C1-4-alkylene)(C3-8cycloalkyl), C3-7heterocyclyl or -(C1-4-alkylene)-C3-7heterocyclyl, each optionally substituted), pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 4-step synthesis that involved reaction of intermediate tert-Bu 4-(5-bromopyridin-2-yl)piperazine-1-carboxylate with III, and deprotecting the intermediate formed. The stability of the example compds. in human and rat liver microsomes, their pharmacokinetic profile in rats, and their ALK kinase and c-met kinase inhibitory activities were measured.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyridine compds. as tyrosine kinase inhibitors for treating proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 136 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:359181 CAPLUS Full-text
DOCUMENT NUMBER: 163:714261
TITLE: Patient-Derived Xenografts from Non-Small Cell Lung Cancer Brain Metastases Are Valuable Translational Platforms for the Development of Personalized Targeted Therapy
AUTHOR(S): Lee, Hye Won; Lee, Jung-il; Lee, Se Jeong; Cho, Hyun Jung; Song, Hye Jin; Jeong, Da Eun; Seo, Yun Jee; Shin, Sang; Joung, Je-Gun; Kwon, Yong-Jun; Choi, Yoon-La; Park, Woong-Yang; Lee, Hyun Moo; Seol, Ho Jun; Shim, Young Mog; Joo, Kyeung Min; Nam, Do-Hyun
CORPORATE SOURCE: Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, S. Korea
SOURCE: Clinical Cancer Research (2015), 21(5), 1172-1182
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-14-1589
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: The increasing prevalence of distant metastases from non-small cell lung cancer (NSCLC) indicates an urgent need for novel therapeutic modalities. Brain metastasis is particularly common in NSCLC, with severe adverse effects on clin. prognosis. Although the mol. heterogeneity of NSCLC and availability of various targeted agents suggest personalized therapeutic approaches for such brain metastases, further development of appropriate preclin. models is needed to validate the strategies. Exptl. Design: We established patient-derived xenografts (PDX) using NSCLC brain metastasis surgical samples and elucidated their possible preclin. and clin. implications for personalized treatment. Results: NSCLC brain metastases (n = 34) showed a significantly higher successful PDX establishment rate than primary specimens (n = 64; 74% vs. 23%). PDXs derived from NSCLC brain metastases recapitulated the pathol., genetic, and functional properties of corresponding parental tumors. Furthermore, tumor spheres established in vitro from the xenografts under serum-free conditions maintained their in vivo brain metastatic potential. Differential phenotypic and mol. responses to 20 targeted agents could subsequently be screened in vitro using these NSCLC PDXs derived from brain metastases. Although PDX establishment from primary NSCLCs was significantly influenced by histol. subtype, clin. aggressiveness, and genetic alteration status, the brain metastases exhibited consistently adequate in vivo tumor take rate and in vitro tumor sphere formation capacity, regardless of clin. and mol. conditions. Conclusions: Therefore, PDXs from NSCLC brain metastases may better represent the heterogeneous advanced NSCLC population and could be utilized as preclin. models to meet unmet clin. needs such as drug screening for personalized treatments. Clin Cancer Res; 21(5); 1172-82. ©2014 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(patient-derived xenografts from non-small cell lung cancer brain metastases are valuable translational platforms for the development of personalized targeted therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 137 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:316867 CAPLUS Full-text
DOCUMENT NUMBER: 162:399931
TITLE: Novel crystal form of quinoline compound and preparation method thereof
INVENTOR(S): Tang, Dongjun; Liu, Yanping; Kou, Jingping
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104370811	A	20150225	CN 2014-10399795	20140814

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 135 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:383707 CAPLUS Full-text
DOCUMENT NUMBER: 162:337080
TITLE: Gene expression signatures predictive of subject response to a multi-kinase inhibitor and methods of using the same
INVENTOR(S): Guo, Sheng; Chen, Dawei; Zhang, Juan; Cai, Jie; Li, Henry Qixiang
PATENT ASSIGNEE(S): Crown Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015031604	A1	20150305	WO 2014-US53142	20140828
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: WO 2013-CN82487 A 20130828
AB Gene expression signature predictive of cancer patient response to multi-kinase inhibitor is disclosed. Also disclosed are methods predicting the efficacy of the multi-kinase inhibitor for treating cancer in a patient. Also disclosed are methods for distinguishing responders from non-responders to a multi-kinase inhibitor in treating cancer. Also disclosed are methods for treating a cancer patient with a multi-kinase inhibitor.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene expression signature predictive of subject response to a multi-kinase inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

PRIORITY APPLN. INFO.: CN 2013-10356174 A 20130815

AB The present invention relates to a novel crystal form of quinoline compd. N-(4-{[6,7-dimethoxyquinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarbonamide and preparation method thereof, and belongs to medicinal chemical field. The crystal form is basically pure crystal form I or crystal form II. In the X-ray powder diffraction pattern of crystal form I, there are peaks at 2θ angles of about 11.9, 12.9, 14.4, 16.0, 22.1 and 26.0 degrees. In the X-ray powder diffraction pattern of crystal form II, there are peaks at 2θ angles of about 11.6, 14.1, 18.5, 21.1, 22.2, 23.2, 24.1 and 29.0 degrees. The novel crystal form possesses good stability and mobility, which is conducive to operate in storage, transfer and production, and the novel crystal form can be used for preparing pharmaceutically acceptable salt thereof for application in pharmaceutics.

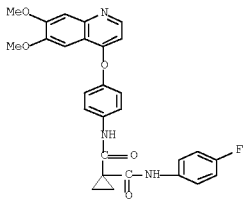
IT 849217-68-1 1669412-61-6 1669412-63-8

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crystal forms of quinoline compound by using three-component coupling and/or condensation as the key steps)

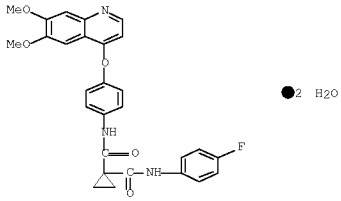
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



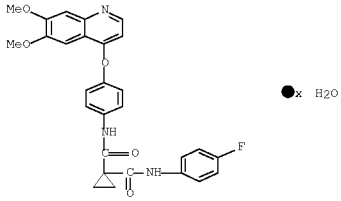
RN 1669412-61-6 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrate (1:2) (CA INDEX NAME)



RN 1669412-63-8 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrate (1:?) (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 138 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:312826 CAPLUS Full-text

DOCUMENT NUMBER: 163:407215

TITLE: Treating medullary thyroid cancer in the age of targeted therapy

AUTHOR(S): Cabanillas, Maria E.; Hu, Mimi I.; Jimenez, Camilo; Grubbs, Elizabeth G.; Cote, Gilbert J.

CORPORATE SOURCE: Department of Endocrine Neoplasia & Hormonal Disorders, Unit 1461, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX, 77030, USA

SOURCE: International Journal of Endocrine Oncology (2014), 1(2), 203-216
CODEN: IJEOBC; ISSN: 2045-0869

DIGITAL OBJECT ID: 10.2217/ije.14.26

PUBLISHER: Future Medicine Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor deriving from the thyroid parafollicular cell. Thyroidectomy continues to serve as the primary initial treatment for this cancer. Because standard cytotoxic chemotherapy has proven ineffective, reoperation and external beam radiation therapy had been the only tools to treat recurrences or distant disease. The discovery that aberrant activation of RET, a receptor tyrosine kinase, is a primary driver of MTC tumorigenesis led to clin. trials using RET-targeting tyrosine kinase inhibitors. The successes of those trials led to the approval of vandetanib and cabozantinib for treating patients with progressive or symptomatic MTC. The availability of these drugs, along with addnl. targeted therapies in development, requires a thoughtful reconsideration of the approach to treating patients with unresectable locally advanced and/or metastatic progressive MTC.

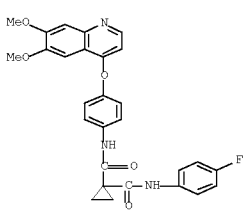
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treating medullary thyroid cancer in age of targeted therapy)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 139 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:312823 CAPLUS Full-text

DOCUMENT NUMBER: 163:437839

TITLE: Protein kinase inhibitor therapy in advanced thyroid cancer: ethical challenges and potential solutions

AUTHOR(S): Bible, Keith C.; Ain, Kenneth B.; Rosenthal, M. Sara

CORPORATE SOURCE: Mayo Clinic, Division of Medical Oncology, Rochester, MN, USA

SOURCE: International Journal of Endocrine Oncology (2014), 1(2), 145-151
CODEN: IJEOBC; ISSN: 2045-0869

DIGITAL OBJECT ID: 10.2217/ije.14.24

PUBLISHER: Future Medicine Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB Protein kinase inhibitors (PKIs) have emerged as highly promising therapies in progressive metastatic radioiodine-refractory differentiated thyroid cancer and in medullary thyroid cancer; two were recently approved in the USA for use in medullary thyroid cancer (vandetanib, cabozantinib), and another for use in progressive metastatic radioiodine-refractory differentiated thyroid cancer (sorafenib). Although more than 90% of thyroid cancer patients fare well in response to conventional treatment, PKI therapy has the potential to provide benefit. Nonetheless, PKIs produce numerous side effects, may worsen quality of life, may hasten mortality (by 1-2%), require discerning clin. acumen, are not yet proven to improve thyroid cancer survival and are very costly. This raises questions about who should prescribe PKIs, and about whether their use in thyroid cancer is truly beneficent and ethically justified. Restraint should be exercised in their use in thyroid cancer, with potential risks and benefits carefully weighed and solns. devised to help ameliorate many of the problems associated with their use.

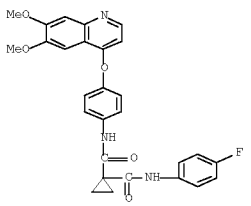
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(protein kinase inhibitor therapy in advanced thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 140 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:293134 CAPLUS full-text

DOCUMENT NUMBER: 162:337073

TITLE: 1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy

INVENTOR(S): Jefford, Charles William; Hoessli, Daniel

PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 69pp.; Chemical Indexing Equivalent to 162:337069 (GB)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

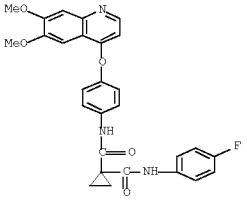
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015022497	A1	20150219	WO 2014-GB52392	20140805
GB 2517199	A	20150218	GB 2013-14639	20130815

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW

PRIORITY APPLN. INFO.: GB 2013-14639 A 20130815
OTHER SOURCE(S): MARPAT 162:337073

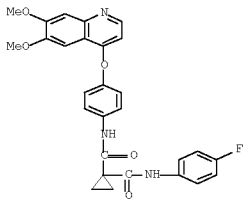
AB The invention provides 1,2,4-trioxane compds. or pharmaceutically acceptable salts, esters, solvates, tautomers, stereoisomers thereof, for use as adjuvants for tyrosine kinase inhibitors in the treatment of cancer. Preferably the tyrosine kinase inhibitor is selected from imatinib, gefitinib, erlotinib, lapatinib, canertinib, vatalanib, sorafenib or genistein. The cancer may be selected from lymphoma, breast cancer, leukemia, gastrointestinal tumors, nonsmall cell lung cancer, melanoma, renal carcinoma, multiple myeloma, kidney cancer, colon cancer, pancreatic cancer, lung cancer, ovarian cancer and prostate cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 142 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:283246 CAPLUS Full-text
DOCUMENT NUMBER: 163:418637
TITLE: Cabozantinib reverses multidrug resistance of human hepatoma HepG2/adr cells by modulating the function of P-glycoprotein
AUTHOR(S): Xiang, Qing-feng; Zhang, Dong-mei; Wang, Jing-nan; Zhang, Hong-wu; Zheng, Zhe-yu; Yu, Da-cheng; Li, Ying-jie; Xu, Jun; Chen, Ya-jin; Shang, Chang-zhen
CORPORATE SOURCE: Department of Hepatopancreatobiliary Surgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Peop. Rep. China
SOURCE: Liver International (2015), 35(3), 1010-1023
CODEN: LIINCM; ISSN: 1478-3223
DIGITAL OBJECT ID: 10.1111/liv.12524
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 141 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:283370 CAPLUS Full-text
DOCUMENT NUMBER: 163:438161
TITLE: Is there an antiandrogen withdrawal syndrome with enzalutamide?
AUTHOR(S): Rodriguez-Vida, Alejo; Bianchini, Diletta; Van Hemelrijck, Mieke; Hughes, Simon; Malik, Zafar; Powles, Thomas; Bahl, Amit; Rudman, Sarah; Payne, Heather; de Bono, Johann; Chowdhury, Simon
CORPORATE SOURCE: Great Maze Pond, Guy's and St Thomas' NHS Foundation Trust, London, UK
SOURCE: BJU International (2015), 115(3), 373-380
CODEN: BJINFO; ISSN: 1464-410X
DIGITAL OBJECT ID: 10.1111/bju.12826
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

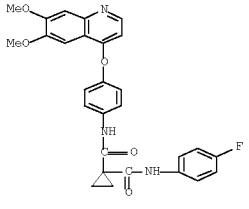
AB Objective : To examine prostate-specific antigen (PSA) levels after enzalutamide discontinuation to assess whether an antiandrogen withdrawal syndrome (AAWS) exists with enzalutamide. Methods : We retrospectively identified 30 consecutive patients with metastatic prostate cancer who were treated with enzalutamide after docetaxel. Post-discontinuation PSA results were available for all patients and were determined at 2-weekly intervals until starting further anticancer systemic therapy. PSA withdrawal response was defined as a PSA decline by ≥50% from the last on-treatment PSA, with a confirmed decrease ≥3 wk later. Patient characteristics were evaluated in relation to the AAWS using univariate logistic regression anal. Results : The median (range) patient age was 70.5 (56-86) years and the median (range) follow-up was 9.0 (0.5-16) months. The most common metastatic sites were the bone (86.7%) and lymph nodes (66.7%). Most patients (70%) had previously received abiraterone and 12 patients (40%) had also received cabazitaxel. The median (range) treatment duration with enzalutamide was 3.68 (1.12-21.39) months. PSA levels after enzalutamide withdrawal were monitored for a median (range) time of 35 (10-120) days. Only one patient (3.3%) had a confirmed PSA response ≥50% after enzalutamide discontinuation. One patient (3.3%) had a confirmed PSA response of between 30 and 50% and another patient (3.3%) had an unconfirmed PSA response of between 30 and 50%. The median overall survival was 15.5 mo (95% CI 8.1-24.7). None of the factors analyzed in the univariate anal. were significant predictors of PSA decline after enzalutamide discontinuation. Conclusions : This retrospective study provides the first evidence that enzalutamide may have an AAWS in a minority of patients with metastatic castration-resistant prostate cancer. Further studies are needed to confirm the existence of an enzalutamide AAWS and to assess its relevance in prostate cancer management.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiandrogen withdrawal syndrome with enzalutamide)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

LANGUAGE: English

AB Background & Aims : Cabozantinib, a small-mol. multitargeted tyrosine kinase inhibitor, has entered into a phase III clin. trial for the treatment of hepatocellular carcinoma (HCC). This study assessed the mechanistic effect of cabozantinib on the reversal of P-glycoprotein (P-gp)-mediated multidrug resistance (MDR). Methods : CCK-8 assays and tumor xenografts were used to investigate the reversal of MDR in vitro and in vivo resp. Substrate retention assays were evaluated by fluorescence microscope and flow cytometry. Western blotting was used to detect protein expression levels. mRNA expression was determined by qPCR. The ATPase activity of P-gp was investigated using Pgp-Glo® assay systems. The binding mechanism of cabozantinib to P-gp at the mol. level was evaluated using docking anal. Results : Cabozantinib enhanced the cytotoxicity of P-gp substrate drugs in HepG2/adr and HEK293-MDR1 cells but had no effect on non-P-gp substrates. In addition, cabozantinib increased the accumulation of P-gp substrates in HepG2/adr cells but had no effect in HepG2 cells. Furthermore, cabozantinib did not alter the expression of P-gp mRNA or protein but did stimulate the activity of P-gp ATPase. The docking study indicated that cabozantinib and verapamil may partially share a binding site on P-gp. The reversal concns. of cabozantinib did not affect the expression of MET, AKT and ERK1/2. Significantly, cabozantinib increased the inhibitory efficacy of doxorubicin in P-gp-overexpressing HepG2/adr cell xenografts in nude mice. Conclusion : Cabozantinib reverses P-gp-mediated MDR by directly inhibiting the efflux function of P-gp, indicating that cabozantinib may help to reverse P-gp-mediated MDR in HCC and other cancer chemotherapy.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on cabozantinib reverses multidrug resistance of human hepatoma HepG2/adr cells by modulating function of P-glycoprotein)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



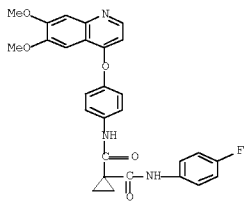
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 143 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:281739 CAPLUS Full-text
DOCUMENT NUMBER: 162:337069
TITLE: 1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy
INVENTOR(S): Jefford, Charles William; Hoessli, Daniel Christian
PATENT ASSIGNEE(S): Switz.
SOURCE: Brit. UK Pat. Appl., 66pp.; Chemical Indexing Equivalent to 162:337073 (WO)
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2517199	A	20150218	GB 2013-14639	20130815
WO 2015022497	A1	20150219	WO 2014-GB52392	20140805

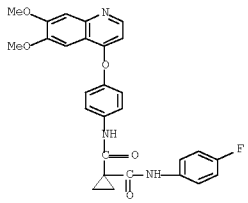
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2013-14639 A 20130815
AB The invention provides 1,2,4-trioxane compds. or pharmaceutically acceptable salts, esters, solvates, tautomers, stereoisomers thereof, for use as adjuvants for tyrosine kinase inhibitors in the treatment of cancer. Preferably the tyrosine kinase inhibitor is selected from imatinib, gefitinib, erlotinib, lapatinib, canertinib, vatalanib, sorafenib or genistein. The cancer may be selected from lymphoma, breast cancer, leukemia, gastrointestinal tumors, nonsmall cell lung cancer, melanoma, renal carcinoma, multiple myeloma, kidney cancer, colon cancer, pancreatic cancer, lung cancer, ovarian cancer and prostate cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



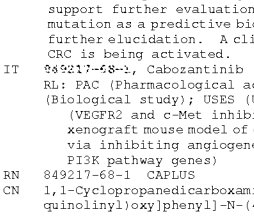
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 145 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:232900 CAPLUS Full-text
DOCUMENT NUMBER: 163:340057
TITLE: Potent antitumor activity of cabozantinib, a c-MET and VEGFR2 inhibitor, in a colorectal cancer patient-derived tumor explant model
AUTHOR(S): Song, Eun-Kee; Tai, W. M.; Messersmith, Wells A.; Bagby, Stacey; Purkey, Alicia; Quackenbush, Kevin S.; Pitts, Todd M.; Wang, Guoliang; Blatchford, Patrick; Yahn, Rachel; Kaplan, Jeffrey; Tan, Aik Choon; Atreya, Chloe E.; Eckhardt, Gail; Kelley, Robin K.; Venook, Alan; Kwak, Eunice L.; Ryan, David; Arcaroli, John J.
CORPORATE SOURCE: Division of Medical Oncology, University of Colorado Denver and University of Colorado Cancer Center, Aurora, CO, USA
SOURCE: International Journal of Cancer (2015), 136(8), 1967-1975
CODEN: IJCNAW; ISSN: 0020-7136
DIGITAL OBJECT ID: 10.1002/ijc.29225
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Antiangiogenic therapy is commonly used for the treatment of colorectal cancer (CRC). Although patients derive some clin. benefit, treatment resistance inevitably occurs. The MET signaling pathway has been proposed to be a major contributor of resistance to antiangiogenic therapy. MET is upregulated in response to vascular endothelial growth factor pathway inhibition and plays an essential role in tumorigenesis and progression of tumors. In this study, we set out to determine the efficacy of cabozantinib in a preclin. CRC patient-derived tumor xenograft model. We demonstrate potent inhibitory effects on tumor growth in 80% of tumors treated. The greatest antitumor effects were observed in tumors that possess a mutation in the PIK3CA gene. The underlying antitumor mechanisms of cabozantinib consisted of inhibition of angiogenesis and Akt activation and significantly decreased expression of genes involved in the PI3K pathway. These findings support further evaluation of cabozantinib in patients with CRC. PIK3CA mutation as a predictive biomarker of sensitivity is intriguing and warrants further elucidation. A clin. trial of cabozantinib in refractory metastatic CRC is being activated.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VEGFR2 and c-Met inhibitor, cabozantinib show antitumor activity in xenograft mouse model of colorectal cancer especially with PIK3CA mutation via inhibiting angiogenesis, Akt activation and lowering expression of PI3K pathway genes)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 144 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:258957 CAPLUS Full-text
DOCUMENT NUMBER: 162:370540
TITLE: Design and Optimization of a Series of 1-Sulfonylpyrazolo[4,3-b]pyridines as Selective c-Met Inhibitors
AUTHOR(S): Ma, Yuchi; Sun, Guangqiang; Chen, Danqi; Peng, Xia; Chen, Yue-Lei; Su, Yi; Ji, Yinchun; Liang, Jin; Wang, Xin; Chen, Lin; Ding, Jian; Xiong, Bing; Ai, Jing; Geng, Meiyu; Shen, Jingkang
CORPORATE SOURCE: Department of Medicinal Chemistry, State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 201203, Peop. Rep. China
SOURCE: Journal of Medicinal Chemistry (2015), 58(5), 2513-2529
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/jm502018y
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 162:370540
AB C-Met has emerged as an attractive target for targeted cancer therapy because of its abnormal activation in many cancer cells. To identify high potent and selective c-Met inhibitors, we started with profiling the potency and in vitro metabolic stability of a reported hit 7. By rational design, a novel sulfonylpyrazolo[4,3-b]pyridine 9 with improved DMPK properties was discovered. Further elaboration of π-π stacking interactions and solvent accessible polar moieties led to a series of highly potent and selective type I c-Met inhibitors. On the basis of in vitro and in vivo pharmacol. and pharmacokinetics studies, compound 46 was selected as a preclin. candidate for further anticancer drug development.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design and optimization of a series of 1-sulfonylpyrazolo[4,3-b]pyridines as selective c-Met inhibitors)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

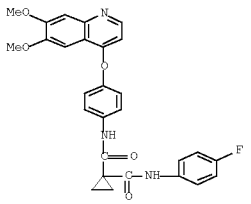
L4 ANSWER 146 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:226654 CAPLUS Full-text
DOCUMENT NUMBER: 163:214328
TITLE: Dual effects of a targeted small-molecule inhibitor (cabozantinib) on immune-mediated killing of tumor cells and immune tumor microenvironment permissiveness when combined with a cancer vaccine
AUTHOR(S): Kwilas, Anna R.; Ardiani, Andressa; Donahue, Renee N.; Aftab, Dana T.; Hodge, James W.
CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Translational Medicine (2014), 12, 294/1-294/15, 15 pp.

CODEN: JTMOBV; ISSN: 1479-5876
DIGITAL OBJECT ID: 10.1186/s12967-014-0294-y
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background: Growing awareness of the complexity of carcinogenesis has made multimodal therapies for cancer increasingly compelling and relevant. In recent years, immunotherapy has gained acceptance as an active therapeutic approach to cancer treatment, even though cancer is widely considered an immunosuppressive disease. Combining immunotherapy with targeted agents that have immunomodulatory capabilities could significantly improve its efficacy. Methods: We evaluated the ability of cabozantinib, a receptor tyrosine kinase inhibitor, to modulate the immune system in vivo as well as alter the phenotype of tumor cells in vitro in order to determine if this inhibitor could act synergistically with a cancer vaccine. Results: Our studies indicated that cabozantinib altered the phenotype of MC38-CEA murine tumor cells, rendering them more sensitive to immune-mediated killing. Cabozantinib also altered the frequency of immune sub-populations in the periphery as well as in the tumor microenvironment, which generated a more permissive immune environment. When cabozantinib was combined with a poxviral-based cancer vaccine targeting a self-antigen, the combination significantly reduced the function of regulatory T cells and increased cytokine production from effector T cells in response to the antigen. These alterations to the immune landscape, along with direct modification of tumor cells, led to markedly improved antitumor efficacy. Conclusions: These studies support the clin. combination of cabozantinib with immunotherapy for the treatment of cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual role of targeted small mol. inhibitor cabozantinib combined with cancer vaccine on immune mediated killing of tumor cells and immune tumor microenvironment permissiveness)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

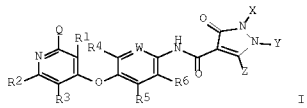


REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

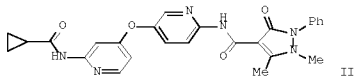
L4 ANSWER 147 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:213358 CAPLUS Full-text
DOCUMENT NUMBER: 162:245319
TITLE: Preparation of pyrazolone compounds that are protein tyrosine kinase activity modulators useful in treatment of proliferative and other diseases
INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20150037280	A1	20150205	US 2013-13945924		20130719
US 8975282	B2	20150310			
US 20150050239	A1	20150219	US 2013-13945925		20130719
US 8969388	B2	20150303			
US 20150141463	A1	20150521	US 2015-14601207		20150120
PRIORITY APPLN. INFO.:			US 2012-61676944	P	20120728
			US 2012-61679416	P	20120803
			US 2013-13945924	A3	20130719

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 162:245319; MARPAT 162:245319
GI



I

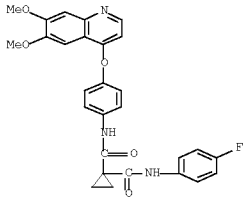


II

AB The invention provides novel substituted pyrazolone compds. of formula I [each of R1-R7 is independently H, F, Cl, (C1-C6)alkyl, (C1-C6)haloalkyl, etc.; each of X, Y and Z is independently H, (C1-C6)alkyl, (C6-C10)aryl, etc.; W is CR7 or N; Q as defined in the disclosure], pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The example compound II was prepared in two-step synthesis (procedure shown) was tested in multiple bioassay for activity in modulation of protein tyrosine kinase, pharmacokinetics and metabolic stability, as well as for antiproliferative activity. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyrazolone compds. that are protein tyrosine kinase activity modulators useful in treatment of proliferative and other diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 148 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:210763 CAPLUS Full-text
DOCUMENT NUMBER: 162:283487
TITLE: Dielectrophoresis methods for determining a property of a plurality of cancer cells to determine drug efficacy and/or resistance
INVENTOR(S): Schmelz, Eva M.; Elvington, Elizabeth S.; Salmanzadeh, Alireza; Sano, Mike; Roberts, Paul C.; Davalos, Rafael V.
PATENT ASSIGNEE(S): Virginia Tech Intellectual Properties, Inc., USA
SOURCE: PCT Int. Appl., 82pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2015017729	A1	20150205	WO 2014-US49296		20140731
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20100224493	A1	20100909	US 2010-720406		20100309
US 8968542	B2	20150303			
US 20120085649	A1	20120412	US 2011-13269286		20111007
PRIORITY APPLN. INFO.:			US 2010-720406	A2	20100309
			US 2011-13269286	A2	20111007
			US 2013-61860309	P	20130731
			US 2009-61158553	P	20090309
			US 2009-61252942	P	20091019
			US 2010-61390748	P	20101007

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

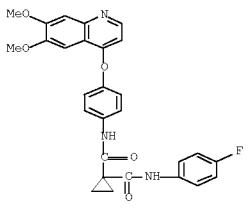
AB Provided are dielectrophoresis (DEP) devices and methods that allow cell sorting to identify, isolate, and/or sep. cells of interest based on elec. and phys. properties of the cells. Particularly, provided are systems and methods for manipulating particles suspended in a fluid, e.g., cells, micro- or nano-particles, using their elec. signatures. Such methods can be performed using DEP, iDEP, and/or cDEP (contactless dielectrophoresis, where direct contact between the electrodes and the sample is avoided). Typically, an elec. field is induced in a sample comprising the target particles and/or cells, such as cancer cells, and the spatial distribution of cells is measured to identify one or more characteristics or properties of the cancer cells. The identified characteristics of the sorted cells can be used to determine drug efficacy and/or resistance with respect to the cells.

IT 1140909-48-3, Cabozantinib-S-Malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dielectrophoresis methods for determining a property of a plurality of cancer cells to determine drug efficacy and/or resistance)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

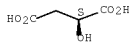
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 149 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:203193 CAPLUS Full-text
DOCUMENT NUMBER: 162:294277
TITLE: Methods of treating a cancer through targeted disruption of alpha connexin 43-zonula occludens-1 (zo-1) interaction
INVENTOR(S): Gourdie, Robert G.; Sheng, Zhi
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 152pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015017034	A1	20150205	WO 2014-US42528	20140616

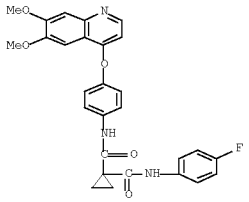
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2013-61861686 P 20130802
zTJ3BmW_X2bkC4P5BgQ1mm8VtAmNAHH4J2TXXTJDe5Bxw@@f6vPex9fJQJ117h5ui7MPAUPwJ2CUC

e targeted disruption of alpha connexin 43-zonula occludens-1 (ZO-1) interaction. The methods may include administering to a subject an effective amount of a composition comprising a peptide with a contiguous sequence of amino acids representing a portion of the C-terminus of an alpha connexin protein or conservative variant thereof, wherein said C-terminus includes the sequence up to the transmembrane domain, optionally in combination with administration of a chemotherapeutic agent. In embodiments, the cancer is glioma and the chemotherapeutic agent is temozolomide. The methods may also include administration of vectors encoding the peptide or host cells comprising the vectors. Also described are compns. for treating a cancer comprising one or more peptides, nucleic acids, vectors, and/or host cells, optionally in combination with a chemotherapeutic agent such as temozolomide.

IT 1140909-48-3, Cabozantinib-s-malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of treating cancer through targeted disruption of alpha connexin 43-zonula occludens-1 interaction)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

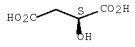
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

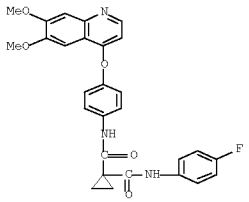


OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 150 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:173876 CAPLUS Full-text
DOCUMENT NUMBER: 162:320090
TITLE: An LC-MS/MS method for the quantitation of cabozantinib in rat plasma: Application to a pharmacokinetic study
AUTHOR(S): Su, Qinghong; Li, Jian; Ji, Xiwei; Li, Jingyun; Zhou, Tianyan; Lu, Wei; Li, Liang
CORPORATE SOURCE: Department of Pharmaceutics, School of Pharmaceutical Sciences, Peking University Health Science Center, Beijing, 100191, Peop. Rep. China
SOURCE: Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences (2015), 985, 119-123
CODEN: JCBAAI; ISSN: 1570-0232
DIGITAL OBJECT ID: 10.1016/j.jchromb.2015.01.024
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB A simple, rapid and sensitive high-performance liq. chromatog. tandem mass-spectrometric method (LC-MS/MS) for the novel multiple tyrosine kinase inhibitor (TKI) cabozantinib was developed and validated using erlotinib as internal standard (IS). Plasma samples were pre-treated by liquid-liquid extraction with Et acetate. Separation was achieved on a reversed phase C18 column (50 × 2 mm, 5 μm) at ambient temperature using isocratic elution with acetonitrile-water (45:55, volume/volume) containing 5 mM ammonium formate buffer (finally adjusted to apparent pH* = 5.0 with formic acid) at a flow rate of 0.4 mL/min. The analytes were monitored by a triple quadrupole tandem mass spectrometer with electrospray ionization source in the pos. ion mode. Calibration curve was linear (r > 0.99) in a concentration range of 0.5-1000 ng/mL with the lower limit of quantification (LLOQ) of 0.5 ng/mL. Intra- and inter-day accuracy and precision were validated by relative error values (RE) and relative standard deviation values (RSD), resp., which were both lower than the limit of 15%. This method was successfully applied to a pharmacokinetic study of cabozantinib in rats.

IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(LC-MS/MS method for the quantitation of cabozantinib in rat plasma with application to a pharmacokinetic study)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

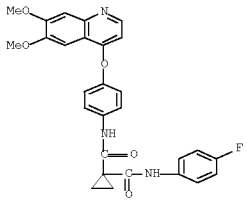


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 151 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:159139 CAPLUS Full-text
DOCUMENT NUMBER: 162:560084
TITLE: Progress in Discovery of KIF5B-RET Kinase Inhibitors for the Treatment of Non-Small-Cell Lung Cancer
AUTHOR(S): Song, Minsoo
CORPORATE SOURCE: New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Taegu, 701 310, S. Korea
SOURCE: Journal of Medicinal Chemistry (2015), 58(9), 3672-3681
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/jm501464c
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

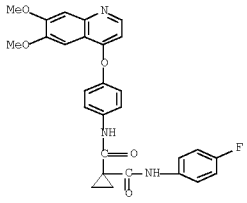
AB A review. A new chimeric fusion transcript of KIF5B (the kinesin family 5B gene) and the RET (Rearranged during Transcription) oncogene, KIF5B-RET, was found in 1-2% of lung adenocarcinomas (LADCs) in late 2011. Several related clin. trials for non-small-cell lung cancer (NSCLC) with KIF5B-RET rearrangements using existing RET inhibitors, such as lenvatinib, vandetanib, sunitinib, ponatinib, cabozantinib, and AUY922, have been swiftly initiated by the discovery of the KIF5B-RET fusion gene. Anti-RET activity and the status of clin. development of these known RET tyrosine kinase inhibitors (TKIs) for KIF5B-RET fusion-pos. NSCLC are discussed. A kinase inhibitor that can target a driver mutation specifically may lead to a superior clin. benefit compared with broad-spectrum kinase inhibitors. In this regard, an anal. of the structure of RET kinase and its complex with known RET inhibitors are also briefly discussed.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progress in discovery of KIF5B-RET kinase inhibitors for the treatment of nonsmall cell lung cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



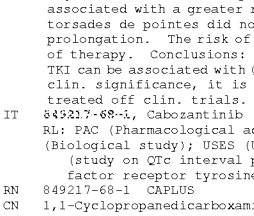
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 152 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:152289 CAPLUS Full-text
DOCUMENT NUMBER: 162:320143
TITLE: Pharmacokinetics and tissue distribution model of cabozantinib in rat determined by UPLC-MS/MS
AUTHOR(S): Wang, Xiangin; Wang, Shuanghu; Lin, Feiyan; Zhang, Qingwei; Chen, HuiLing; Wang, Xianchuan; Wen, Congcong; Ma, Jianshe; Hu, Lufeng
CORPORATE SOURCE: Analytical and Testing Center, Wenzhou Medical University, Wenzhou, 325035, Peop. Rep. China
SOURCE: Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences (2015), 983-984, 125-131
CODEN: JCBAAI; ISSN: 1570-0232
DIGITAL OBJECT ID: 10.1016/j.jchromb.2015.01.020
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib (XL184) is a novel small mol. inhibitor of receptor tyrosine kinases (RTKs) targeted at mesenchymal-epithelial transition factor (MET). To study the pharmacokinetics and tissue distribution in rat, a specific ultra-performance liquid chromatog.-tandem mass spectrometry (UPLC-MS/MS) method was developed with midazolam as internal standard The calibration curves in plasma and tissues were linear in the range of 5-5000 ng/mL (R2 > 0.99). The recoveries were better than 80.4% and matrix effects ranged from 96.9% to 105.1%. Then, the developed UPLC-MS/MS method was applied to determine the concentration of XL184 in blood and tissues. The pharmacokinetics of four different dosages (iv 5, 10 mg/kg and ig 15, 30 mg/kg) revealed that XL184 was eliminated slowly, the t1/2 was longer than 10 h and the absolute bioavailability was 25.6±8.3%. The concentration distribution of XL184 in tissues was liver > lung > kidney > spleen > heart. Based on the concentration-time of XL184 in tissues, a BP-ANN distribution model was developed with good performance, and can be used to predict the concentration of XL184 in tissues.
IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); PKT (Pharmacokinetics); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(XL184; pharmacokinetics and tissue distribution model of cabozantinib in rat determined by UPLC-MS/MS)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



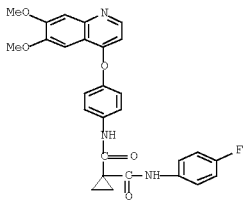
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 153 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:142298 CAPLUS Full-text
DOCUMENT NUMBER: 163:360237
TITLE: QTc interval prolongation with vascular endothelial growth factor receptor tyrosine kinase inhibitors
AUTHOR(S): Ghatalia, P.; Je, Y.; Kaymakcalan, M. D.; Sonpavde, G.; Choueiri, T. K.
CORPORATE SOURCE: Department of Internal Medicine, University of Alabama at Birmingham (UAB), Birmingham, AL, USA
SOURCE: British Journal of Cancer (2015), 112(2), 296-305
CODEN: BJCAAI; ISSN: 0007-0920
DIGITAL OBJECT ID: 10.1038/bjc.2014.564
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Multi-targeted vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) are known to cause cardiac toxicity, but the relative risk (RR) of QTc interval prolongation and serious arrhythmias associated with them are not reported. Methods: We conducted a trial-level meta-anal. of randomized phase II and III trials comparing arms with and without a US Food and Drug Administration-approved VEGFR TKI (sunitinib, sorafenib, pazopanib, axitinib, vandetanib, cabozantinib, ponatinib and regorafenib). A total of 6548 patients from 18 trials were selected. Statistical analyses were conducted to calculate the summary incidence, RR and 95% CIs. Results: The RR for all-grade and high-grade QTc prolongation for the TKI vs no TKI arms was 8.66 (95% CI 4.92-15.2, P<0.001) and 2.69 (95% CI 1.33-5.44, P=0.006), resp., with most of the events being asymptomatic QTc prolongation. Resp., 4.4% and 0.83% of patients exposed to VEGFR TKI had all-grade and high-grade QTc prolongation. On subgroup anal., only sunitinib and vandetanib were associated with a statistically significant risk of QTc prolongation, with higher doses of vandetanib associated with a greater risk. The rate of serious arrhythmias including torsades de pointes did not seem to be higher with high-grade QTc prolongation. The risk of QTc prolongation was independent of the duration of therapy. Conclusions: In the largest study to date, we show that VEGFR TKI can be associated with QTc prolongation. Although most cases were of low clin. significance, it is unclear whether the same applies to patients treated off clin. trials.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on QTc interval prolongation with vascular endothelial growth factor receptor tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

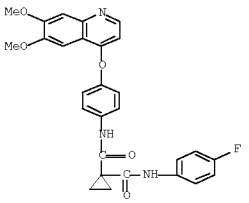
L4 ANSWER 154 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:138904 CAPLUS Full-text
DOCUMENT NUMBER: 163:511501
TITLE: Current role of cabozantinib in metastatic castration-resistant prostate cancer
AUTHOR(S): Fay, Andre P.; Albiges, Laurence; Bellmunt, Joaquim
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02215, USA
SOURCE: Expert Review of Anticancer Therapy (2015), 15(2), 151-156
CODEN: ERATBJ; ISSN: 1473-7140
DIGITAL OBJECT ID: 10.1586/14737140.2015.1003047
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Over 80% of men with castration-resistant prostate cancer have bone metastases. This condition can dramatically impact quality of life and is associated with short-term survival. Consequently, the development of bone-targeted therapies is a relevant topic on prostate cancer management. Hepatocyte growth factor receptor and vascular endothelial growth factor signaling pathways have been identified to play a role in prostate cancer progression and bone metastasis and are potential targets for therapeutic intervention. Early-phase studies have shown encouraging responses in bone metastases and pain control with cabozantinib, a multi-tyrosine kinase inhibitor targeting hepatocyte growth factor receptor and vascular endothelial growth factor receptor. Despite striking responses seen in some patients, preliminary results from a pivotal Phase III study have failed to produce survival benefit. This review encompasses preclin. and clin. data of cabozantinib in metastatic castration-resistant prostate cancer highlighting future research options for this agent.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(current role of cabozantinib in metastatic castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

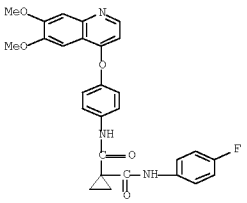
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 155 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:104550 CAPLUS Full-text
DOCUMENT NUMBER: 162:265265
TITLE: Thyroid carcinoma, version 2.2014: featured updates to the NCCN guidelines
AUTHOR(S): Tutele, R. Michael; Haddad, Robert I.; Ball, Douglas W.; Byrd, David; Dickson, Paxton; Duh, Quan-Yang; Ehya, Hormoz; Haymart, Megan; Hoh, Carl; Hunt, Jason P.; Iagaru, Andrei; Kandeel, Fouad; Kopp, Peter; Lamonica, Dominick M.; Lydiatt, William M.; McCaffrey, Judith; Moley, Jeffrey F.; Parks, Lee; Raeburn, Christopher D.; Ridge, John A.; Ringel, Matthew D.; Scheri, Randall P.; Shah, Jatin P.; Sherman, Steven I.; Sturgeon, Cord; Waguespack, Steven G.; Wang, Thomas N.; Wirth, Lori J.; Hoffmann, Karin G.; Hughes, Miranda
CORPORATE SOURCE: Memorial Sloan Kettering Cancer Center, USA
SOURCE: Journal of the National Comprehensive Cancer Network (2014), 12(12), 1671-1680
CODEN: JNCCA4; ISSN: 1540-1405
PUBLISHER: Harborside Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. These NCCN Guidelines Insights focus on some of the major updates to the 2014 NCCN Guidelines for Thyroid Carcinoma. Kinase inhibitor therapy may be used to treat thyroid carcinoma that is symptomatic and/or progressive and not amenable to treatment with radioactive iodine. Sorafenib may be considered for select patients with metastatic differentiated thyroid carcinoma, whereas vandetanib or cabozantinib may be recommended for select patients with metastatic medullary thyroid carcinoma. Other kinase inhibitors may be considered for select patients with either type of thyroid carcinoma. A new section on "Principles of Kinase Inhibitor Therapy in Advanced Thyroid Cancer" was added to the NCCN Guidelines to assist with using these novel targeted agents.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(featured updates to the NCCN guidelines for thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



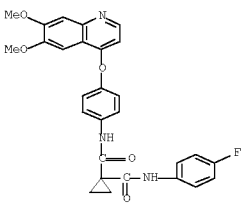
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 157 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:100878 CAPLUS Full-text
DOCUMENT NUMBER: 163:292268
TITLE: Should the Incorporation of Structural Alerts be Restricted in Drug Design? An Analysis of Structure-Toxicity Trends with Aniline-Based Drugs
AUTHOR(S): Kalgutkar, A. S.
CORPORATE SOURCE: Pharmacokinetics, Dynamics and Metabolism Department-New Chemical Entities, Pfizer Worldwide Research and Development, Cambridge, MA, 02139, USA
SOURCE: Current Medicinal Chemistry (2015), 22(4), 438-464
CODEN: CMCHE7; ISSN: 0929-8673
DIGITAL OBJECT ID: 10.2174/0929867321666141112122118
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Certain idiosyncratic adverse drug reactions (IADRs) can be triggered by electrophilic protein-reactive metabolites that are formed in the process of drug metabolism While methodologies (e.g., structural alert concept in drug design, glutathione (GSH) trapping, and protein covalent binding) for examining reactive metabolite (RM) formation are available, predicting the IADR potential applying these parameters remains a significant challenge. The present work examines toxicity trends associated with the aniline structural alert in the top 200 prescribed drugs of 2011 and recently approved (2009-2013) small mol. drugs, in relation with 30 aniline-based drugs withdrawn from com. use or associated with a black box warning for IADRs. The aniline sub-structure was found in several drugs from the toxic, mostprescribed, and recently approved category. RMs resulting from the bioactivation of the aniline alert was also noted in the three categories chosen for comparison. A major discriminator between the toxic drugs and the majority of drugs in the most-prescribed list, however, was the daily dose - drugs most frequented associated with IADRs were the ones with higher daily doses (exceeding hundreds of milligrams). A greater tolerance for IADRs was also noted with certain drugs intended to treat rare, unmet medical needs (e.g., cancer). Overall, the anal. suggests that optimization of pharmacol. potency and pharmacokinetics that would lead to a lower daily dose, and therefore, a lower body burden of parent drug/metabolites, should be taken into consideration in drug discovery.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anal. of structure-toxicity trends with aniline-based drugs)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 156 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:100945 CAPLUS Full-text
DOCUMENT NUMBER: 163:480691
TITLE: Targeting Angiogenesis in Thyroid Cancer
AUTHOR(S): Lkhoyaali, S.; Benhmida, S.; Aitelhaj, M.; Layachi, M.; Abahssain, H.; Ismaili, H. N.; Errihani, H.
CORPORATE SOURCE: Department of Medical Oncology, Mohammed VI University Hospital, Marrakech, Morocco
SOURCE: Current Angiogenesis (2014), 3(2), 107-112
CODEN: CAUNBS; ISSN: 2211-5528
DIGITAL OBJECT ID: 10.2174/2211552802666140716170521
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Thyroid cancers are characterized by a good prognosis but 10 to 15% of patients progress and become refractory to current therapies. Systemic treatment based on chemotherapy in these settings has shown limited efficacy, with response rates not exceeding 25%. At progression, differentiated thyroid cancer is characterized by a high level of expression of vascular endothelial growth factor (VEGF). This high expression of VEGF is associated with an aggressive tumor behavior and a poor clin. outcome.; We will review the recent advances in targeting angiogenesis in the treatment of recurrent and metastatic thyroid carcinoma.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting Angiogenesis in Thyroid Cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
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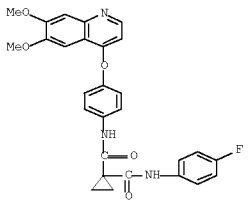
L4 ANSWER 158 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:28803 CAPLUS Full-text
DOCUMENT NUMBER: 162:393504
TITLE: Development of therapeutic drug for castration-resistant prostate cancer
AUTHOR(S): Zhou, Xiang-jun; Zhang, Jie
CORPORATE SOURCE: Department of Urology, Renmin Hospital of Wuhan University, Wuhan, 430060, Peop. Rep. China
SOURCE: Shijie Linchuang Yaowu (2014), 35(2), 74-79
CODEN: SLYHAA; ISSN: 1672-9188
PUBLISHER: Shijie Linchuang Yaowu Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 28 ref. is given on development of therapeutic drug for castration-resistant prostate cancer. The treatment of castration-resistant prostate cancer (CRPC) is still a challenge, as there are few effective therapies to lengthen life of patients. Many novel approaches with extended survival benefit currently in development yielded promising results for patients. This review describes the therapeutic drug for CRPC. The therapeutic drug comprises antiandrogen drug such as abiraterone, enzalutamide, orteronel, galeterone; cytotoxic chemotherapy such as docetaxel, cabazitaxel; immunotherapy such as sipuleucel-T,

rilimogene galvacirepvec, ipilimumab; targeting therapy including endothelin-A receptor antagonist such as atrasentan, zibotentan, tyrosine kinase inhibitor such as dasatinib and sorafenib, cabozantinib, anti-angiogenesis agent such as bevacizumab, aflibercept, tasquinimod, clusterin inhibitor such as custirsen, and radium chloride.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of therapeutic drug for castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 159 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:26950 CAPLUS Full-text

DOCUMENT NUMBER: 163:325796

TITLE: Cabozantinib Overcomes Crizotinib Resistance in ROS1 Fusion-Positive Cancer

AUTHOR(S): Katayama, Ryohei; Kobayashi, Yuka; Friboulet, Luc; Lockerman, Elizabeth L.; Koike, Sumie; Shaw, Alice T.; Engelman, Jeffrey A.; Fujita, Naoya

CORPORATE SOURCE: Division of Experimental Chemotherapy, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo, Japan

SOURCE: Clinical Cancer Research (2015), 21(1), 166-174
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-14-1385

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

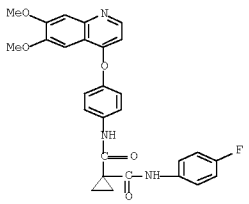
LANGUAGE: English

AB Purpose: ROS1 rearrangement leads to constitutive ROS1 activation with potent transforming activity. In an ongoing phase I trial, the ALK tyrosine kinase inhibitor (TKI) crizotinib shows remarkable initial responses in patients with non-small cell lung cancer (NSCLC) harboring ROS1 fusions; however, cancers eventually develop crizotinib resistance due to acquired mutations such as G2032R in ROS1. Thus, understanding the crizotinib-resistance mechanisms in ROS1-rearranged NSCLC and identification of therapeutic strategies to overcome the resistance are required. Exptl. Design: The sensitivity of CD74-ROS1-transformed Ba/F3 cells to multiple ALK inhibitors was examined Acquired ROS1 inhibitor-resistant mutations in CD74-ROS1 fusion were screened by N-ethyl-N-nitrosourea mutagenesis with Ba/F3 cells. To overcome the resistance mutation, we performed high-throughput drug screening with small-mol. inhibitors and anticancer drugs used in clin. practice or being currently tested in clin. trials. The effect of the identified drug was assessed in the CD74-ROS1-mutant Ba/F3 cells and crizotinib-resistant patient-derived cancer cells (MGH047) harboring G2032R-mutated CD74-ROS1. Results: We identified multiple novel crizotinib-resistance mutations in the ROS1 kinase domain, including the G2032R mutation. As the result of high-throughput drug screening, we found that the cMET/RET/VEGFR inhibitor cabozantinib (XL184) effectively inhibited the survival of CD74-ROS1 wild-type (WT) and resistant mutants harboring Ba/F3 and MGH047 cells. Furthermore, cabozantinib could overcome all the resistance by all newly identified secondary mutations. Conclusions: We developed a comprehensive model of acquired resistance to ROS1 inhibitors in NSCLC with ROS1 rearrangement and identified cabozantinib as a therapeutic strategy to overcome the resistance. Clin Cancer Res; 21(1); 166-74. cpr2014 AACR.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib overcoming crizotinib resistance in ROS1 fusion-pos. cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

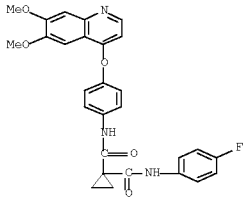


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

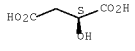
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L4 ANSWER 160 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:21816 CAPLUS Full-text

DOCUMENT NUMBER: 162:172165

TITLE: A Novel Multiple Tyrosine-kinase Targeted Agent to Explore the Future Perspectives of Anti-Angiogenic Therapy for the Treatment of Multiple Solid Tumors: Cabozantinib

AUTHOR(S): Roy, Subhajit; Narang, Bawneet K.; Rastogi, Shiva K.; Rawal, Ravindra K.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Indo-Soviet Friendship College of Pharmacy, Punjab, 142 001, India

SOURCE: Anti-Cancer Agents in Medicinal Chemistry (2015), 15(1), 37-47
CODEN: AAMCE4; ISSN: 1871-5206

DIGITAL OBJECT ID: 10.2174/1871520614666140902153840

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

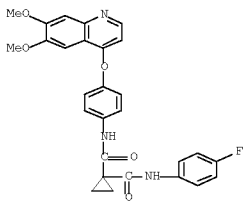
LANGUAGE: English

AB A review. The process of angiogenesis involves the formation of new blood vessels from pre-existing vasculature by the over expression of certain factors leading to the growth and development of all solid tumor types. Hepatocyte growth factor receptor abbreviated as c-Met and vascular endothelial growth factor abbreviated as VEGF are some of the factors responsible for the induction in tumor growth and development. Recently a number of analogs associated with these receptors are under study. US FDA on Nov. 29, 2012 approved a drug named cabozantinib formerly known as XL184 which is being marketed under the trade name of Cometriq for the treatment of Medullary Thyroid Cancer (MTC). Designing of the drug has been done in such a fashion that it can inhibit both VEGFR2 and c-Met simultaneously without over expressing any of the factors leading to the inhibition of angiogenesis. The drug is still under study for the evaluation of its efficacy in cases of many other solid tumor types including breast cancer, castration resistant prostate cancer (CRPC), renal cell carcinoma (RCC), hepatocellular carcinoma (HCC), gastric or gastroesophageal junction cancer, melanoma, small cell lung cancer (SCLC), ovarian cancer and primary peritoneal or fallopian tube carcinoma. This review article consists of preclin. and clin. data of cabozantinib and its efficacy and safety towards various types of solid tumors.

IT 849217-68-1, Cabozantinib 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel multiple tyrosine-kinase targeted agent, cabozantinib to explore future perspectives of anti-angiogenic therapy for treatment of human multiple solid tumors and in mouse models)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

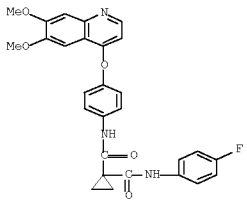


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

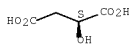
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CMF C28 H24 F N3 O5



CM 2

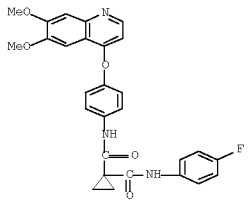
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

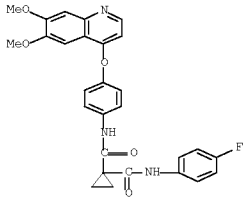


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 161 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2163755 CAPLUS Full-text
DOCUMENT NUMBER: 162:309823
TITLE: Antiangiogenic drugs for castration-resistant prostate cancer: Recent findings
AUTHOR(S): Huang, Dao-guang; Gan, Wei-dong
CORPORATE SOURCE: Department of Urology, Nanjing Drum Tower Hospital, the Affiliated Hospital, School of Medicine, Nanjing University, Nanjing, Jiangsu Province, 210008, Peop. Rep. China
SOURCE: Zhonghua Nankexue Zazhi (2014), 20(10), 932-937
CODEN: ZNZHB5
DIGITAL OBJECT ID: 10.13263/j.cnki.nja.2014.10.014
PUBLISHER: Zhonghua Nankexue Zazhi Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. In the recent years, treatment options for castration-resistant prostate cancer had evolved from conventional antiandrogens and chemotherapy to novel androgen receptor signaling inhibitors, a new generation of taxanes, and immunotherapy. Randomized clin. trials had shown that docetaxel, cabazitaxel, enzalutamide, abiraterone acetate, radium-223, and sipuleucel-T could improve the overall survival of the patients with androgen-independent prostate cancer. However, drug resistance was inevitable and androgen-independent prostate cancer remained a major clin. burden, which urgently called for novel therapeutic options for the improvement of the patients' survival and quality of life. Angiogenesis played a central role in the formation and progression of prostate cancer, and the anti angiogenic targeted therapy was shown in many clin. trials to be an effective therapeutic supplement for advanced prostate cancer beyond surgery and endocrine treatment. The recent findings of antiangiogenic mugs for castration-resistant prostate cancer was reviewed.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiangiogenic drugs for castration-resistant prostate cancer: Recent findings)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 162 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2157654 CAPLUS Full-text
DOCUMENT NUMBER: 162:99756
TITLE: New drug cabozantinib malate for medullary thyroid cancer treatment
AUTHOR(S): Lu, Juanli; Liu, Yang; Sun, Huiping
CORPORATE SOURCE: Department of Pharmacy, General Hospital of Armed Police Forces, Beijing, 100039, Peop. Rep. China
SOURCE: Zhongguo Linchuang Yaoxue Zazhi (2014), 23(1), 58-62
CODEN: ZLYZA5; ISSN: 1007-4406
PUBLISHER: Zhongguo Linchuang Yaoxue Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 21 refs. to introduce the new drug cabozantinib malate for medullary thyroid cancer treatment, including its basic properties, action mechanism, pharmacokinetic parameters, clin. trial, drug interactions, adverse reactions, and comparison on therapeutic effect with vandetanib.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new drug cabozantinib malate for medullary thyroid cancer treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

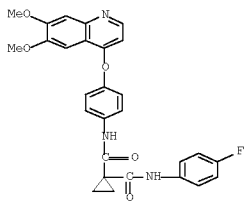


L4 ANSWER 163 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2146461 CAPLUS Full-text
DOCUMENT NUMBER: 162:114047
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 12pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
US 20140378401	A1	20141225	US 2013-14132822	20131218
WO 2014204791	A1	20141224	WO 2014-US42221	20140613

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-13924189 A2 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The ophthalmic drug delivery vehicles provide comfort and compliance; drug solubility, residence time and permeability; and reduce side effects. In addition, the delivery vehicle can be slightly modified to provide an artificial tear formulation. The ophthalmic drug delivery vehicles include 2-12% nonionic surfactant, one or more non-Newtonian high blend viscosity enhancing, non-gelling agents and 0.1-0.90% sodium chloride. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.
IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 164 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2146420 CAPLUS Full-text
DOCUMENT NUMBER: 162:144424
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 924,189.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

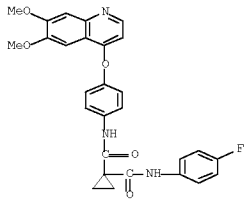
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140378401	A1	20141225	US 2013-14132822	20131218
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		

WO 2014204791 A1 20141224 WO 2014-US42221 20140613
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2013-13924189 A2 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The ophthalmic drug delivery vehicles provide comfort and compliance; drug solubility, residence time and permeability; and reduce side effects. In addition, the delivery vehicle can be slightly modified to provide an artificial tear formulation. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

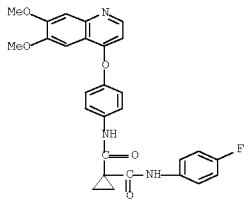


L4 ANSWER 165 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2145974 CAPLUS Full-text
DOCUMENT NUMBER: 163:58679
TITLE: Cabozantinib in chemotherapy-pretreated metastatic castration-resistant prostate cancer: results of a phase II nonrandomized expansion study
AUTHOR(S): Smith, Matthew R.; Sweeney, Christopher J.; Corn, Paul G.; Rathkopf, Dana E.; Smith, David C.; Hussain, Maha; George, Daniel J.; Higano, Celestia S.; Harzstark, Andrea L.; Sartor, A. Oliver; Vogelzang, Nicholas J.; Gordon, Michael S.; de Bono, Johann S.; Haas, Naomi B.; Logothetis, Christopher J.; Elfiky, Aymen; Scheffold, Christian; Laird, A. Douglas; Schimmoller, Frauke; Basch, Ethan M.; Scher, Howard I.
CORPORATE SOURCE: USA
SOURCE: Journal of Clinical Oncology (2014), 32(30), 3391-3399
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2013.54.5954
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose Cabozantinib (XL184), an oral inhibitor of multiple receptor tyrosine kinases such as MET and VEGFR2, was evaluated in a phase II nonrandomized expansion study in castration-resistant prostate cancer (CRPC). Patients and Methods Patients received open-label cabozantinib at daily starting doses of 100 mg or 40 mg until disease progression or unacceptable toxicity. The primary end point was bone scan response, defined as ≥ 30% reduction in bone scan lesion area. Other efficacy end points included overall survival, pain, analgesic use, and biomarkers. Results One hundred forty-four patients sequentially enrolled in either a 100-mg (n = 93) or 40-mg (n = 51) study cohort. Ninety-one patients (63%) had a bone scan response, often by week 6. Treatment resulted in clin. meaningful pain relief (57% of patients) and reduction or discontinuation of narcotic analgesics (55% of patients), as well as improvements in measurable soft tissue disease, circulating tumor cells, and bone biomarkers. Improvements in each of these outcomes were observed in both cohorts: bone scan response in 73% and 45%, resp.; redns. in measurable soft tissue disease in 80% and 79%, resp. Median overall survival was 10.8 mo for the entire population. Most common grade 3 or 4 adverse events were fatigue (22%) and hypertension (14%). Fewer dose redns. because of toxicity were required in the 40-mg group. Conclusion The evidence suggests that cabozantinib has clin. meaningful activity in CRPC. Cabozantinib resulted in improvements in bone scans, pain, analgesic use, measurable soft tissue disease, circulating tumor cells, and bone biomarkers. Taken together, these phase II observations warrant further development of cabozantinib in prostate cancer.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of cabozantinib in chemotherapy-pretreated metastatic castration-resistant prostate cancer patients in phase II nonrandomized expansion study)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 166 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2128221 CAPLUS Full-text
DOCUMENT NUMBER: 162:127174
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: PCT Int. Appl., 57pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014204791	A1	20141224	WO 2014-US42221	20140613
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
US 20140378401	A1	20141225	US 2013-14132822	20131218

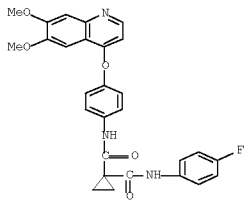
WO 2014204791 W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-13924189 A 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The ophthalmic drug delivery vehicles include 1-15% nonionic surfactant, one or more non-Newtonian high blend viscosity enhancing, non-gelling agents and 0.025-0.90% sodium chloride. Particularly, formulations that have the non-Newtonian characteristics at 37° of creating a viscosity increase in ratio of 3:1 within 1-2 s at the low shear force between blinks and drops within the fraction of a second to the high shear force of each blink, which on dilution maintain a viscosity of ≥10 cPs during each blink and which do not cause excessive stinging or discomfort, are disclosed. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.

IT 849217-68-1 1642298-56-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)

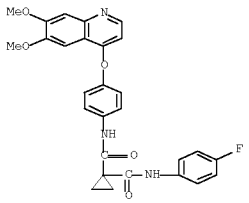
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1642298-56-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



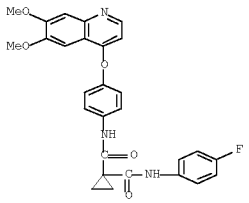
CM 2

CRN 75-75-2
CMF C H4 O3 S



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 167 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2126341 CAPLUS Full-text
DOCUMENT NUMBER: 162:148367
TITLE: Medullary thyroid cancer in the era of tyrosine kinase inhibitors: to treat or not to treat-and with which drug-those are the questions
AUTHOR(S): Cabanillas, Maria E.; Hu, Mimi I.; Jimenez, Camilo
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2014), 99(12), 4390-4396
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2014-2811
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Context: Medullary thyroid cancer (MTC) is a rare form of thyroid cancer comprising approx. 4% of all thyroid cancers. The majority of patients have a relatively good prognosis; however, a subgroup of patients will require systemic therapy. Large phase III randomized trials led to the approval of two drugs-vandetanib and cabozantinib-for progressive or symptomatic MTC. The decision regarding which drug to initiate first is not entirely clear and is a common concern amongst treating physicians. Evidence Acquisition and Synthesis: A review of the literature in English was conducted, and data were summarized and integrated into a decision matrix. Conclusions: The decision regarding which drug to initiate first for progressive MTC should be based on a careful review of the medical history, phys. examination findings, medication list, ECG, laboratory results, and tumor characteristics. It is necessary to consider the relative contraindications when choosing which drug to initiate first.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medullary thyroid cancer in era of tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

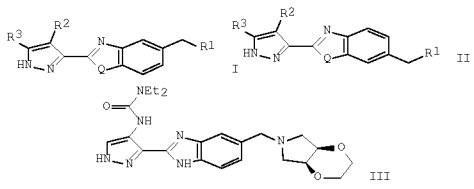


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

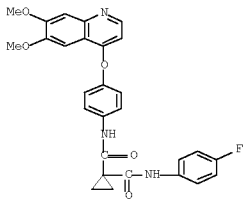
L4 ANSWER 168 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2105568 CAPLUS Full-text
DOCUMENT NUMBER: 162:137867
TITLE: Substituted pyrazole-type deriv. as aurora kinase inhibitor useful in treatment of various diseases and its preparation
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Zhang, Jiquan; Li, Yanping; Yang, Xueqi; Zhang, Jiancun; Zheng, Changchun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 96pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104211692	A	20141217	CN 2014-10245663	20140604
PRIORITY APPLN. INFO.:			CN 2013-10217864	A 20130604
			CN 2014-10109643	A 20140321

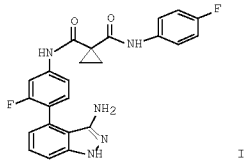
OTHER SOURCE(S): MARPAT 162:137867
GI



AB The invention relates to substituted pyrazole-type deriv. of formula I and II as aurora kinase inhibitor useful in treatment of various diseases and their preparation Compds. I and II, wherein Q is NH or O; R1 is one of morpholinyl, C5-12 bridged bicyclic group, etc.; R2 is R4R4aN-CO-NH, R5R5aCHCONH, or R6OCONH; and R3 is H or C1-6 alkyl; R4 is H, C1-6 alkyl, C3-6 cycloalkyl, etc.; R4a is C1-6 alkyl, C3-6 cycloalkyl, C6-10 aryl, etc.; R5 and R5a are independently H, C3-6 cycloalkyl, etc.; R6 is C1-6 alkyl or C6-10 aryl; their stereoisomer, geometric isomer, tautomer, nitrogen oxide, hydrate, solvate, metabolite, ester, pharmaceutically acceptable salt or prodrug are claimed. Compound III was prepared by multi-step procedure (procedure given). The invention compds. were evaluated for their aurora kinase inhibitor activity. From assay, it was determined that III exhibited the IC50 value of 2.16 nM against aurora A kinase .
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted pyrazole-type derivative as aurora kinase inhibitor
useful in treatment of various diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 169 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2087478 CAPLUS Full-text
DOCUMENT NUMBER: 162:183726
TITLE: Discovery and SAR study of c-Met kinase inhibitors bearing an 3-amino-benzo[d]isoxazole or 3-aminoindazole scaffold
AUTHOR(S): Jiang, Xiaolong; Liu, Hongyan; Song, Zilan; Peng, Xia; Ji, Yinchun; Yao, Qizheng; Geng, Meiyu; Ai, Jing; Zhang, Ao
CORPORATE SOURCE: Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry (2015), 23(3), 564-578
CODEN: BMECEP; ISSN: 0968-0896
DIGITAL OBJECT ID: 10.1016/j.bmc.2014.12.002
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 162:183726
GI



AB A series of 3-amino-benzo[d]isoxazole-/3-aminoindazole-based compds. were designed, synthesized and pharmacol. evaluated as tyrosine kinase c-Met inhibitors. The SAR study was conducted leading to identification of nine compds. with IC50s less than 10 nM against c-Met. Compound I stood out as the most potent c-Met inhibitor displaying potent inhibitory effects both at enzymic (IC50 = 1.8 nM) and cellular (IC50 = 0.18 μM on EBC-1 cells) levels. In addition, I had a relatively good selectivity compared to a panel of the inhouse 14 RTKs.

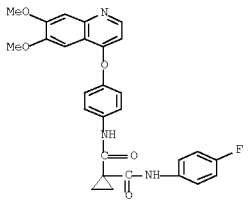
IT 849217-68-1

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(discovery and SAR study of c-Met kinase inhibitors bearing an 3-amino-benzo[d]isoxazole or 3-aminoindazole scaffold)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 170 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:2072471 CAPLUS Full-text

DOCUMENT NUMBER: 163:156450

TITLE: Adaptive Responses to Dasatinib-Treated Lung Squamous Cell Cancer Cells Harboring DDR2 Mutations

AUTHOR(S): Bai, Yun; Kim, Jae-Young; Watters, January M.; Fang, Bin; Kinose, Fumi; Song, Lanxi; Koomen, John M.; Teer, Jamie K.; Fisher, Kate; Chen, Yian Ann; Rix, Uwe; Haura, Eric B.

CORPORATE SOURCE: Department of Thoracic Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

SOURCE: Cancer Research (2014), 74(24), 7217-7228
CODEN: CNREA8; ISSN: 0008-5472

DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-14-0505

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study of cancer cell signaling perturbed by the tyrosine kinase inhibitor dasatinib suggests rational combinations to improve the efficacy of this drug in the subset of lung cancers where it is used. DDR2 mutations occur in approx. 4% of lung squamous cell cancer (SCC) where the tyrosine kinase inhibitor dasatinib has emerged as a new therapeutic option. We found that ERK and AKT phosphorylation was weakly inhibited by dasatinib in DDR2-mutant lung SCC cells, suggesting that dasatinib inhibits survival signals distinct from other oncogenic receptor tyrosine kinases (RTK) and/or compensatory signals exist that dampen dasatinib activity. To gain better insight into dasatinib's action in these cells, we assessed altered global tyrosine phosphorylation (pY) after dasatinib exposure using a mass spectrometry-based quant. phosphoproteomics approach. Overlaying protein-protein interaction relationships upon this dasatinib-regulated pY network revealed decreased phosphorylation of Src family kinases and their targets. Conversely, dasatinib enhanced tyrosine phosphorylation in a panel of RTK and their signaling adaptor complexes, including EGFR, MET/GAB1, and IGF1R/IRS2, implicating a RTK-driven adaptive response associated with dasatinib. To address the significance of this observation, these results were further integrated with results from a small-mol. chemical library screen. We found that dasatinib combined with MET and insulin-like growth factor receptor (IGF1R) inhibitors had a synergistic effect, and ligand stimulation of EGFR and MET rescued DDR2-mutant lung SCC cells from dasatinib-induced loss of cell viability. Importantly, we observed high levels of tyrosine-phosphorylated EGFR and MET in a panel of human lung SCC tissues harboring DDR2 mutations. Our results highlight potential RTK-driven adaptive-resistant mechanisms upon DDR2 targeting, and they suggest new, rationale cotargeting strategies for DDR2-mutant lung SCC. Cancer Res; 74(24); 7217-28. cpr2014 AACR.

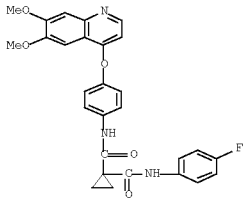
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adaptive responses to dasatinib-treated lung squamous cell cancer cells harboring DDR2 mutations)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 171 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:2068289 CAPLUS Full-text

DOCUMENT NUMBER: 162:228992

TITLE: Anti-angiogenic agents in metastatic NSCLC

AUTHOR(S): Das, Millie; Wakelee, Heather

CORPORATE SOURCE: VA Palo Alto Heath Care System, Palo Alto, CA, USA

SOURCE: Lung Cancer (4th Edition) (2014), 527-540. Editor(s): Roth, Jack A.; Hong, Waun Ki; Komaki, Ritsuko U. Wiley-Blackwell: Hoboken, N. J.
CODEN: 69THV4; ISBN: 978-1-118-46874-6

DIGITAL OBJECT ID: 10.1002/9781118468791.ch34

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB This review highlights the role of anti-angiogenic agents in metastatic non-small cell lung cancer (NSCLC). Anti-angiogenic agents being studied in NSCLC include monoclonal antibodies against VEGF, tyrosine kinase inhibitors directed at VEGF receptors, as well as vascular disrupting agents which do not involve inhibition of VEGF.

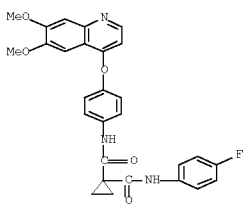
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(discussion on role of anti-angiogenic agents in metastatic non-small cell lung cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 172 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:2037552 CAPLUS Full-text

DOCUMENT NUMBER: 163:187272

TITLE: RET-Rearranged Lung Adenocarcinomas with Lymphangitic Spread, Psammoma Bodies, and Clinical Responses to Cabozantinib

AUTHOR(S): Mukhopadhyay, Sanjay; Pennell, Nathan A.; Ali, Siraj M.; Ross, Jeffrey S.; Ma, Patrick C.; Velcheti, Vamsidhar

CORPORATE SOURCE: Solid Tumor Oncology, and Translational Hematology and Oncology Research, Cleveland Clinic, Cleveland, OH, 9500, USA

SOURCE: Journal of Thoracic Oncology (2014), 9(11), 1714-1719
CODEN: JTOOB7; ISSN: 1556-0864

DIGITAL OBJECT ID: 10.1097/JTO.0000000000000323

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Oncogenic rearrangements of the RET gene have recently been described in 1% to 2% of lung adenocarcinomas. We report five cases of RET-rearranged lung adenocarcinoma with an unusual constellation of clin. and histol. features that has not previously been described in tumors with this genomic alteration. The age at diagnosis of the five patients (4F, 1M) ranged from 44 to 77 years. All were never-smokers. Radiol., four tumors showed lymphangitic spread within the lungs at presentation; three of these had multiple bilateral lung nodules. Histol. showed psammoma bodies within the tumor in four of five cases. Mol. testing for activating EGFR mutations by standard genotyping and ALK expression by immunohistochem. was neg. in all cases. Addnl. mol. anal. was prompted by the clin. profile in that all five patients were never-smokers with metastatic, relapsed, and/or refractory disease; and also by unusual histol. findings in two cases. Comprehensive genomic profiling performed by means of a clin. grade cancer gene panel next-generation sequencing assay demonstrated a KIF5B-RET fusion in three; and fluorescence in-situ hybridization documented a RET rearrangement in two. Three of the patients were treated with the RET inhibitor cabozantinib. By Response Evaluation Criteria In Solid Tumors (RECIST) criteria, two had a confirmed partial response (at 6 wk and 4 wk) and one had stable disease. Our findings suggest that the combination of lymphangitic spread and psammoma bodies may be characteristic of a subset of advanced stage RET-rearranged lung adenocarcinomas. These findings should prompt addnl. mol. testing for RET translocations, particularly in never-smokers with EGFR- and ALK-neg. lung adenocarcinoma.

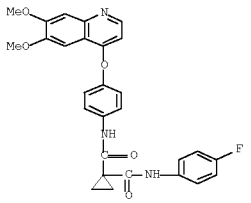
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(study on RET-rearranged lung adenocarcinomas with lymphangitic spread, psammoma bodies, and clin. responses to cabozantinib)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



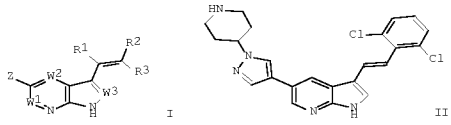
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 173 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2015786 CAPLUS Full-text
DOCUMENT NUMBER: 162:37339
TITLE: Preparation of alkenyl-pyrrolo[2,3-b]pyridine compounds as protein tyrosine kinase modulators useful for treatment of proliferative disorders
INVENTOR(S): Xi, Ning; Li, Xiaobo
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 117pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

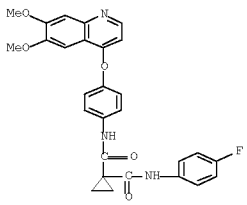
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014193647	A2	20141204	WO 2014-US37856	20140513
WO 2014193647	A3	20150129		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

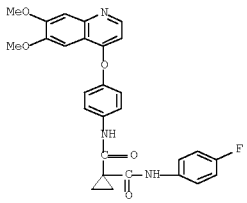
PRIORITY APPLN. INFO.: US 2013-61827599 P 20130526
OTHER SOURCE(S): CASREACT 162:37339; MARPAT 162:37339
GI



AB The invention provides substituted alkenyl pyrrolo[2,3-b]pyridine compds. of formula I, pharmaceutical acceptable salts and formulations thereof as protein tyrosine kinase modulators capable of modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion and, thus useful for the treatment of proliferative disorders. I [wherein W1, W2, and W3 are independently N or (un)substituted C; R1, R2, and R3 are independently H, CN, (hetero)aryl, etc.; Z is (un)substituted 5- to 6-membered heteroaryl] or a stereoisomer, geometric isomer, tautomer, N-oxide, hydrate, solvate, metabolite, prodrug, or pharmaceutically acceptable salt thereof is claimed. (E)-II was prepared in a multistep process (preparation given). I were evaluated for kinase inhibitor activity using radiochem. anal. and [γ33P-ATP]. From this assay it was determined that (E)-II demonstrated IC50 values of 44 nM and 8 nM for ALK kinase and c-Met kinase, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of alkenyl-pyrrolo[2,3-b]pyridine compds. as protein
tyrosine kinase modulators useful for treatment of proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 174 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1955485 CAPLUS Full-text
DOCUMENT NUMBER: 164:33863
TITLE: Novel therapies for thyroid cancer
AUTHOR(S): Krajewska, Jolanta; Jarzab, Barbara
CORPORATE SOURCE: Nuclear Medicine and Endocrine Oncology Department, Gliwice Branch, M.Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Pol.
SOURCE: Expert Opinion on Pharmacotherapy (2014), 15(18), 2641-2652
CODEN: EOPHF7; ISSN: 1465-6566
DIGITAL OBJECT ID: 10.1517/14656566.2014.969240
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Introduction: New therapeutic options for both differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC) have opened up during the past few years, as the key role of tyrosine kinases in the pathogenesis of thyroid carcinoma has been proved. Recently, two tyrosine kinase inhibitors (TKIs) targeting VEGFR vandetanib (Caprelsa) and cabozantinib (Cometriq) have been approved for advanced MTC, whereas, sorafenib (Nexavar) has been accepted to treat late-stage of DTC. Their efficacy was demonstrated in Phase III studies, compared to placebo; each of them significantly prolonged the progression-free survival. Areas covered: Common adverse reactions related to VEGFR blockade are hypertension, proteinuria, impaired wound healing, hemorrhage and thrombosis, and congestive heart failure. Fatigue, different gastrointestinal disturbances with diarrhea, appetite decrease and weight loss are observed in the majority of patients. Another frequent TKI side effect is TSH increase secondary to inhibition of MCT8-dependent T3 and T4 uptake in pituitary. Expert opinion: So far, no direct comparison of both treatment outcomes and toxicity between particular drugs has been carried out. The evidence-based medicine guidelines are necessary to precisely indicate what drug to use: more effective or less toxic and when to start the treatment.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(discussion on novel therapies for thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 175 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1943046 CAPLUS Full-text
DOCUMENT NUMBER: 161:714155
TITLE: Method for the prognosis and treatment of renal cell carcinoma metastasis
INVENTOR(S): Gomis, Roger; Lacey, David L.
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014184679	A2	20141120	WO 2014-IB1715	20140313
WO 2014184679	A3	20150319		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20160032399	A1	20160204	US 2015-14776390	20150914

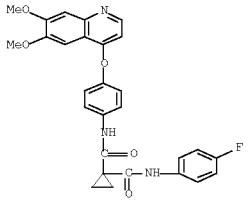
PRIORITY APPLN. INFO.:
US 2013-61801642 P 20130315
WO 2014-IB1715 W 20140313

AB The present invention relates to a method for the prognosis of bone metastasis in renal cell carcinoma which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering renal cell carcinoma. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of renal cell carcinoma metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering renal cell carcinoma and for classifying a subject from renal cell carcinoma into a cohort.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MAF gene as marker for prognosis and treatment of renal cell carcinoma metastasis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 176 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1940485 CAPLUS Full-text

DOCUMENT NUMBER: 161:765704

TITLE: Short-chain phosphatidylcholine lipids and their use in therapy

INVENTOR(S): Van Hell, Albert; Verheij, Marcel; Marrink, Siewert Jan; Koning, Gerben

PATENT ASSIGNEE(S): Stichting Het Nederlands Kanker Instituut - Antoni Van Leeuwenhoek Ziekenhuis, Neth.; Erasmus University Medical Centre; Rijksuniversiteit Groningen

SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014184726	A2	20141120	WO 2014-IB61379	20140512
WO 2014184726	A3	20150219		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2013-8753 A 20130515

OTHER SOURCE(S): MARPAT 161:765704

AB The invention pertains generally to the field of therapy and medical treatment, and more specifically to certain compds. of the following formula (for convenience, collectively referred to herein as "short-chain phosphatidylcholine lipids" and "SCPC lipids"), which, inter alia, are useful in methods of improving drug delivery, bioavailability, and efficacy. The invention also pertains to pharmaceutical formulations, and more specifically to co-formulations of known drugs (e.g., amphiphilic drugs) (e.g., anthracyclines) (e.g., doxorubicin) with these SCPC lipids, and their use in therapy, such as cancer treatment.

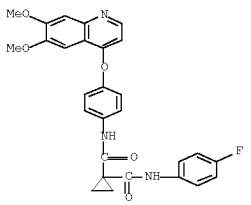
IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(short-chain phosphatidylcholine lipids co-formulations and use for treatment of diseases such as cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

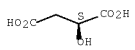
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 177 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1921290 CAPLUS Full-text

DOCUMENT NUMBER: 163:87631

TITLE: Axitinib and crizotinib combination therapy inhibits bone loss in a mouse model of castration resistant prostate cancer

AUTHOR(S): Eswaraka, Jeetendra; Giddabasappa, Anand; Han, Guangzhou; Lalwani, Kush; Eisele, Koleen; Feng, Zheng; Affolter, Timothy; Christensen, James; Li, Gang

CORPORATE SOURCE: Global Science and Technology (WCM), Pfizer Global Research and Development, San Diego, CA, 92121, USA

SOURCE: BMC Cancer (2014), 14, 742/1-742/10
CODEN: BCMACL; ISSN: 1471-2407

DIGITAL OBJECT ID: 10.1186/1471-2407-14-742

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)

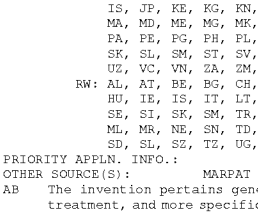
LANGUAGE: English

AB Background: Castration resistant prostate cancer (CRPC) is a leading cause of cancer-related deaths in men. The primary cause of mortality and morbidity in patients is bone metastases and remodeling resulting in osteoblastic and osteolytic lesions. Recently, cabozantinib, a multi-kinase inhibitor (VEGFR2 and c-MET inhibitor), was shown to have efficacy on bone lesions in patients. In this study we tested multi-kinase inhibitors: axitinib (VEGFR inhibitor) and crizotinib (c-MET inhibitor) in a combination trial in mice models. Methods: VCaP-Luc cells were grown as s.c. implants in intact and castrated NOD-SCID-gamma (NSG) mice to confirm the androgen dependency. For bone metastasis model two cohorts of NSG mice (castrated and intact) received orthotopic injection of VCaP-Luc cells into the bone marrow cavity of left tibia. Mice were monitored weekly for tumor growth using bioluminescence imaging. Animals were randomized into 4 groups based on the tumor bioluminescence signal: vehicle, crizotinib alone, axitinib alone, crizotinib and axitinib in combination. Animals were imaged weekly by in vivo 2-D X-ray imaging to monitor bone remodeling. At the end of the study animals were euthanized and both tibias were extracted for ex vivo high-resolution 3-D micro-computed tomog. (μCT) imaging. Results: S.c. model showed that androgen stimulation may be helpful but not essential for the growth of VCaP-Luc cells. VCaP-Luc cells grown intra-tibially in intact animals caused extensive remodeling of bone with mixed osteoblastic (bone formation) and osteolytic (bone matrix dissoln.) lesions. The osteoblastic lesions were predominant and at times extended beyond the tibial shaft into the surrounding tissue. In contrast, only osteolytic lesions were prominent throughout the study in castrated animals. Treatment with crizotinib alone reduced the osteolytic lesions in castrated animals. Axitinib alone reduced the osteoblastic lesions in the intact animals. Combination therapy with axitinib and crizotinib remarkably inhibited the tibial remodeling by VCaP-Luc cells which resulted in a significant reduction of both osteoblastic and osteolytic lesions. Conclusion: Our data show that combined inhibition of c-MET and VEGFR can be beneficial for treatment of metastatic bone disease in CRPC and that the drugs act on two different stages of the disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(axitinib and crizotinib combination therapy inhibits bone loss in mouse model of castration resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 178 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

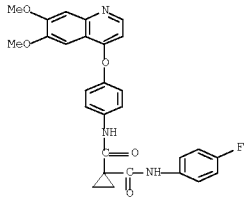
ACCESSION NUMBER: 2014:1853168 CAPLUS Full-text

DOCUMENT NUMBER: 162:33543
TITLE: Significances of RET fusion gene in non-small cell lung cancer
AUTHOR(S): Liu, Jingjing; Bi, Minghong
CORPORATE SOURCE: Department of Medical Oncology, First Affiliated Hospital of Bengbu Medical College, Bengbu, 233004, Peop. Rep. China
SOURCE: Zhongguo Feiai Zazhi (2013), 16(11), 615-620
CODEN: ZFZHAG; ISSN: 1009-3419
DIGITAL OBJECT ID: 10.3779/j.issn.1009-3419.2013.11.11
PUBLISHER: Zhongguo Feiai Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review with 33 refs. Lung cancer is the leading cause of cancer-related death worldwide, mol. target therapy has become a hot research direction of non-small cell lung cancer(NSCLC) treatment. RET fusion gene with an identifiable clin. pathol. features, is present in some subsets of lung cancer, and its treatment is effective by RET inhibitor, suggesting that RET fusion gene may be a new target for individualized treatment to the subgroup of NSCLC. This article reviews the structural characteristics of RET fusion gene and expression model in clin. samples, and treatment of NSCLC.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(significances of RET fusion gene in non-small cell lung cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 179 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1827672 CAPLUS Full-text
DOCUMENT NUMBER: 161:690410
TITLE: Pharmaceutical combinations of a protein kinase C (PKC) inhibitor and a c-MET receptor tyrosine kinase inhibitor for treatment of proliferative diseases
INVENTOR(S): Porter, Dale; Emery, Caroline; Tan, Lujian
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 180 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1821658 CAPLUS Full-text
DOCUMENT NUMBER: 161:715766
TITLE: Preparation of quinazolineamine derivatives for treating proliferative diseases
INVENTOR(S): Zhang, Yingjun; Liu, Bing; Liu, Jinlei; Zhang, Jiancun; Zheng, Changchun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 147pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104119350	A	20141029	CN 2014-10175636	20140428
WO 2014177038	A1	20141106	WO 2014-CN76377	20140428
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20160039838	A1	20160211	US 2015-14774702	20150911

PRIORITY APPLN. INFO.: CN 2013-10156470 A 20130428
CN 2014-10108773 A 20140323
WO 2014-CN76377 W 20140428
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 161:715766
GI

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

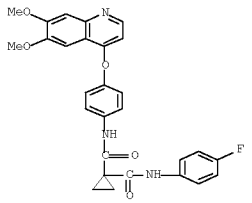
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014174478	A1	20141030	WO 2014-IB60976	20140424
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

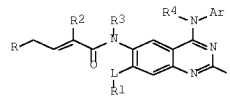
PRIORITY APPLN. INFO.: US 2013-61816266 P 20130426

AB A pharmaceutical combination comprising (a) a protein kinase C (PKC) inhibitor, or a pharmaceutically acceptable salt thereof, and (b) at least one c-MET receptor tyrosine kinase inhibitor, or a pharmaceutically acceptable salt, and optionally a pharmaceutically acceptable carrier, for simultaneous, sep. or sequential administration; the uses of such combination in the treatment of proliferative diseases; and methods of treating a subject suffering from a proliferative disease comprising administering a therapeutically effective amount of such combination.

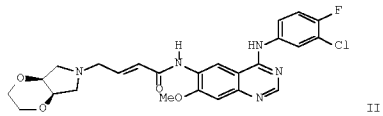
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combinations of a protein kinase C (PKC) inhibitor and a c-MET receptor tyrosine kinase inhibitor for treatment of proliferative diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





I

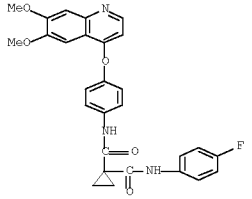


II

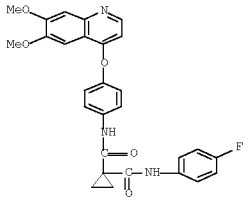
AB The present invention provides quinazolineamine derivs. I [wherein R = bicyclic heterocyclyl; R1 = H, D, F, Cl, Br, I, etc.; R2 = H, F, Cl, Br, I, NH2, etc.; R3 and R4 = independently H, D, or alkyl; R5 = H, D, F, Cl, Br, I, alkyl, etc.; Ar = (un)substituted Ph or indazole-5-yl] stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts, or prodrugs thereof for prevention, treatment, or relieving proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 3.2, 14, and 8.3 nM against EGFR, HER-2, and EGFR T790M kinases, resp. Pharmaceutical compns. comprising the title compound were also described.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of quinazolineamine derivs. for treating proliferative diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 181 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1792793 CAPLUS Full-text
DOCUMENT NUMBER: 162:498601
TITLE: Enrichment of c-Met+ tumorigenic stromal cells of giant cell tumor of bone and targeting by cabozantinib
AUTHOR(S): Liu, L.; Aleksandrowicz, E.; Fan, P.; Schoensiegel, F.; Zhang, Y.; Saehr, H.; Gladkich, J.; Mattern, J.; Depeweg, D.; Lehner, B.; Fellenberg, J.; Herr, I.
CORPORATE SOURCE: Department of Molecular OncoSurgery, General, Visceral and Transplantation Surgery, University of Heidelberg and German Cancer Research Center (DKFZ), Heidelberg, Germany
SOURCE: Cell Death & Disease (2014), 5(10), e1471
CODEN: CDDEA4; ISSN: 2041-4889
DIGITAL OBJECT ID: 10.1038/cddis.2014.440
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Giant cell tumor of bone (GCTB) is a very rare tumor entity, which is little examined owing to the lack of established cell lines and mouse models and the restriction of available primary cell lines. The stromal cells of GCTB have been made responsible for the aggressive growth and metastasis, emphasizing the presence of a cancer stem cell population. To identify and target such tumor-initiating cells, stromal cells were isolated from eight freshly resected GCTB tissues. Tumorigenic properties were examined by colony and spheroid formation, differentiation, migration, MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay, immunohistochem., antibody protein array, Alu in situ hybridization, FACS anal. and xenotransplantation into fertilized chicken eggs and mice. A sub-population of the neoplastic stromal cells formed spheroids and colonies, differentiated to osteoblasts, migrated to wounded regions and expressed the metastasis marker CXC-chemokine receptor type 4, indicating self-renewal, invasion and differentiation potential. Compared with adherent-growing cells, markers for pluripotency, stemness and cancer progression, including the CSC surface marker c-Met, were enhanced in spheroidal cells. This c-Met-enriched sub-population formed xenograft tumors in fertilized chicken eggs and mice. Cabozantinib, an inhibitor of c-Met in phase II trials, eliminated CSC features with a higher therapeutic effect than standard chemotherapy. This study identifies a c-Met+ tumorigenic sub-population within stromal GCTB cells and suggests the c-Met inhibitor cabozantinib as a new therapeutic option for targeted elimination of unresectable or recurrent GCTB.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-Met-enriched tumorigenic human stromal cells of giant cell tumor of bone formed xenograft tumors in fertilized chicken eggs and mouse where cabozantinib strongly inhibited self-renewal potential and in vivo growth of stromal cell)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



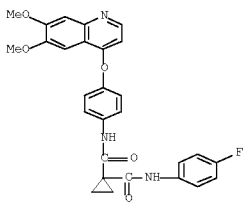
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 182 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1791911 CAPLUS Full-text
DOCUMENT NUMBER: 161:680644
TITLE: Cancer-associated chimeric genes arising from translocations and their use in diagnosis, prognosis, and therapy of cancer
INVENTOR(S): Rhodes, Daniel; Sadis, Seth; Wyngaard, Peter; Khazanov, Nikolay; Bandla, Santhoshi; Tomilo, Mark; Eddy, Sean; Bowden, Emma
PATENT ASSIGNEE(S): Life Technologies Corporation, USA
SOURCE: PCT Int. Appl., 272pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014172046	A2	20141023	WO 2014-US29592	20140314
WO 2014172046	A3	20150618		
WO 2014172046	A9	20160225		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
AU 2014254394	A1	20151203	AU 2014-254394	20140314
AU 2014254394	A9	20160317		
EP 2986736	A2	20160224	EP 2014-721666	20140314
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 105378110	A	20160302	CN 2014-80034585	20140314

PRIORITY APPLN. INFO.:
US 2013-61813182 P 20130417
US 2013-61813465 P 20130418
US 2013-61824253 P 20130516
US 2013-61860115 P 20130730
US 2013-61907939 P 20131122
US 2013-61915392 P 20131212
US 2014-61935650 P 20140204
US 2014-61940226 P 20140214
WO 2014-US29592 W 20140314

AB Chimeric genes arising from chromosomal translocations that play a role in the etiol. of cancer are identified for use in diagnosis, prognosis, and selection and monitoring of therapies. These chimeric genes were identified by a large-scale survey of 19 cancers in 4,225 patients.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selection for cancer therapy; cancer-associated chimeric genes arising from translocations and their use in diagnosis, prognosis, and therapy of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 183 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1790149 CAPLUS Full-text
DOCUMENT NUMBER: 161:686526
TITLE: Cabozantinib malate and its preparation method
INVENTOR(S): Meng, Qingyi; Zhang, Aiming; Xu, Wenwei; Zhang, Xiquan
PATENT ASSIGNEE(S): Lianyungang Runzhong Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 7pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

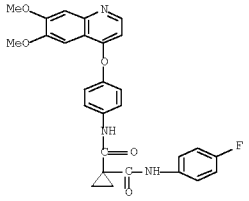
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104109128	A	20141022	CN 2013-10164410	20130419

PRIORITY APPLN. INFO.:
CN 2013-10164410 20130419

AB The present invention relates to cabozantinib malate and its prepn. method, and specifically, the present invention relates to cabozantinib·n malate, its preparation method, and a pharmaceutical composition comprising the same. The inventive cabozantinib·n malate has excellent stability, and can be used for preparing medicines for the treatment of tumors, especially in preparation of medicine for the treatment of medullary thyroid cancer. The preparation method of cabozantinib·n malate includes: (a) adding cabozantinib to an organic solvent, (b) adding malic acid n times molar amount of cabozantinib to mixture of step (a), and (c) precipitating to obtain cabozantinib·n malate, wherein, n is selected from 0.4-0.6, preferably 0.5.
IT 1140909-48-3P 1385530-43-3P 1634853-27-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cabozantinib malate and preparation method)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

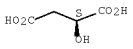
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

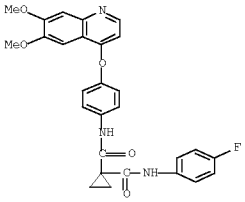
Absolute stereochemistry. Rotation (-).



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

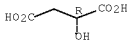
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

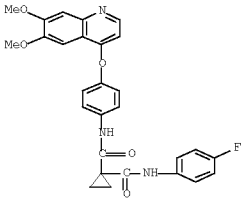
Absolute stereochemistry. Rotation (+).



RN 1634653-27-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

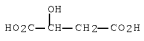
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

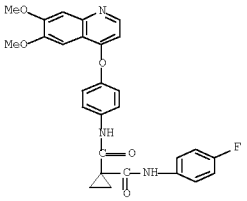


CM 2

CRN 6915-15-7
CMF C4 H6 O5



IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(cabozantinib malate and preparation method)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



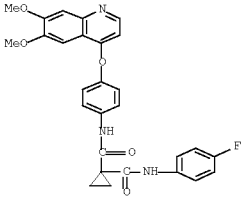
L4 ANSWER 184 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1782124 CAPLUS Full-text
DOCUMENT NUMBER: 161:705479
TITLE: Crystal of cabozantinib· 0.5 malate
INVENTOR(S): Meng, Qingyi; Zhang, Aiming; Xu, Wenwei; Zhang, Xiquan
PATENT ASSIGNEE(S): Chia Tai Tianqing Pharmaceutical Group Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104109124	A	20141022	CN 2013-10138216	20130419
PRIORITY APPLN. INFO.:			CN 2013-10138216	20130419

AB The invention relates to crystal of cabozantinib·0.5malate, a crystal composition and a pharmaceutical composition of the crystal, preparing method thereof, and application thereof in manufacture of drugs treating tumor-related diseases. In the x-ray powder diffraction spectrum of the crystal using Cu-Kα radiation, there are diffraction peaks at 2θ of 5.48°, 10.88°, 15.24°, 21.97° and 24.56°.
IT 1635373-15-7P
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(0.5 malate; crystal of cabozantinib·0.5malate)
RN 1635373-15-7 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:2) (CA INDEX NAME)

CM 1

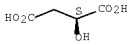
CRN 849217-68-1
CMF C28 H24 F N3 O5



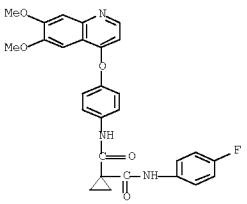
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal of cabozantinib·0.5malate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 185 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1754957 CAPLUS Full-text
DOCUMENT NUMBER: 161:635758
TITLE: Platform for targeted delivery to stem cells and tumor cells and methods thereof
INVENTOR(S): Carvalho Da Fonseca, Nuno Andre; Gomes Da Silva, Ligia Catarina; Dantas Nunes Caldeira De Moura, Vera Lucia; De Magalhaes Simoes, Sergio Paulo; Sereno De Almeida Moreira, Joao Nuno
PATENT ASSIGNEE(S): Universidade de Coimbra, Port.
SOURCE: PCT Int. Appl., 59pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2014167126	A2	20141016	WO 2014-EP57446		20140411
WO 2014167126	A3	20150108			
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM					
AU 2014253040	A1	20151105	AU 2014-253040		20140411
EP 2983720	A2	20160217	EP 2014-721226		20140411
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
US 20160058886	A1	20160303	US 2015-14784247		20151013
PRIORITY APPLN. INFO.:			WO 2014-EP57446	W	20140411

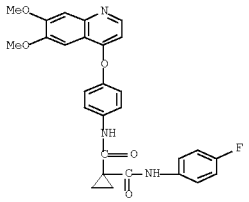
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention involves therapy and diagnostics using nanoparticles that provide targeted delivery of agents to cancer cells and stem cells, including cancer stem cells, the nanoparticles being pH sensitive and incorporating cytotoxic ceramides.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(platform for targeted delivery to stem cells and tumor cells and methods thereof)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 186 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

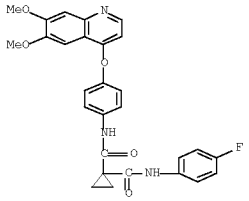
ACCESSION NUMBER: 2014:1754784 CAPLUS Full-text
DOCUMENT NUMBER: 163:225877
TITLE: Sequencing of lung cancer genomes and its translation to the therapy
AUTHOR(S): Iwakawa-Kawabata, Reika; Kohno, Takashi
CORPORATE SOURCE: Div. of Genome Biology, National Cancer Center, Japan
SOURCE: Jikken Igaku (2014), 32(12), 1865-1870
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review discussing the sequencing of lung cancer genomes and its translation to the therapy.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequencing of lung cancer genomes and its translation to the therapy)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 187 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

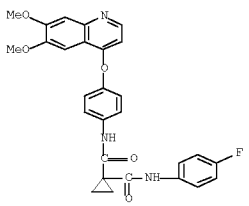
ACCESSION NUMBER: 2014:1742452 CAPLUS Full-text
DOCUMENT NUMBER: 163:438125
TITLE: A Phase I Study of Cabozantinib (XL184) in Patients with Differentiated Thyroid Cancer
AUTHOR(S): Cabanillas, Maria E.; Brose, Marcia S.; Holland, Jaymes; Ferguson, Kimberly C.; Sherman, Steven I.
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Thyroid (2014), 24(10), 1508-1514
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2014.0125
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background: Cabozantinib targets tyrosine kinases including MET, vascular endothelial growth factor (VEGF) receptor 2, and rearranged during transfection (RET). Differentiated thyroid cancer (DTC) is a tumor type that may be sensitive to cabozantinib. Therefore, we evaluated cabozantinib in a cohort of heavily pretreated patients with metastatic DTC. .Methods: This single-arm open-label phase I trial assessed the safety, tolerability, and antitumor activity of cabozantinib in DTC patients taking part in a drug-drug interaction study. Adult patients with histol. confirmed metastatic or surgically unresectable DTC (including papillary, follicular, or Huerthle cell) were enrolled. Patients received daily oral dosing of 140 mg cabozantinib. Safety was assessed by evaluation of adverse events (AEs), vital signs, electrocardiograms, laboratory tests, and concomitant medications. Tumor response by magnetic resonance imaging or computed tomog. scan was investigator assessed using Response Evaluation Criteria In Solid Tumors (RECIST) v1.0. Results: The study enrolled 15 patients who had failed standard radioactive iodine therapy. Patients had received a median of two prior systemic agents, and 11 patients (73%) had previously received at least one VEGF pathway inhibiting therapy. Common AEs included diarrhea, nausea, fatigue, and decreased appetite. Partial response was reported in eight patients (53%). Median progression-free survival and median overall survival were not reached. Conclusions: Cabozantinib demonstrates a safety profile similar to other multitargeted VEGFR inhibitors in advanced DTC patients. The antitumor activity observed in this study warrants further investigation of cabozantinib in patients with advanced DTC.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase I Study of Cabozantinib (XL184) in Patients with Differentiated Thyroid Cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

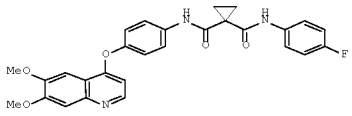


OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 188 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1716754 CAPLUS Full-text
DOCUMENT NUMBER: 161:582215
TITLE: Preparation of cabozantinib and dosage forms for treatment of cancer
INVENTOR(S): Decillis, Arthur
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165786	A1	20141009	WO 2014-US33016	20140404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2981263	A1	20160210	EP 2014-724909	20140404
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160022662	A1	20160128	US 2015-14782537	20151005
PRIORITY APPLN. INFO.:			US 2013-61808511 P	20130404
			WO 2014-US33016 W	20140404

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:582215
GI

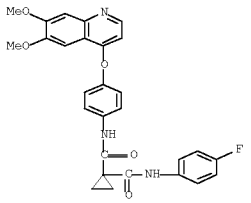


I

AB This invention relates to a dosage form of cabozantinib (I) and a method of employing the dosage form to treat cancer. I was prepared starting with 6,7-dimethoxy-4-quinolinol through a number of steps. I S-maleate was also prepared and tablets containing I were prepared

IT 849217-68-1P, Cabozantinib 1140909-48-3P, Cabozantinib S-malate 1365530-43-3P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

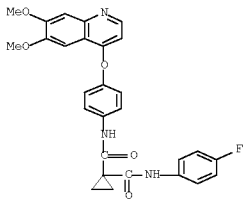
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cabozantinib and dosage forms for treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

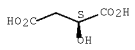
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

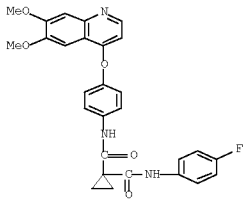
Absolute stereochemistry. Rotation (-).



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

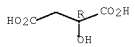
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

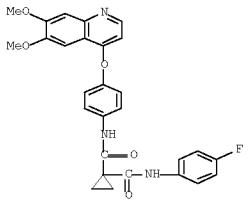


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 189 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1715795 CAPLUS Full-text
DOCUMENT NUMBER: 161:577833
TITLE: Methods and compositions for treating cancers having acquired resistance to chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): Tactical Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 23pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165412	A2	20141009	WO 2014-US32253	20140328
WO 2014165412	A3	20150129		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20140294806	A1	20141002	US 2013-13986103	20130401
US 9089570	B2	20150728		
CA 2902144	A1	20141009	CA 2014-2902144	20140328
AU 2014248377	A1	20150903	AU 2014-248377	20140328
IL 241827	A	20151130	IL 2014-241827	20140328
CN 105120663	A	20151202	CN 2014-80019712	20140328
EP 2981169	A2	20160210	EP 2014-779684	20140328
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2016026824	A	20160309	KR 2015-7022953	20140328
IN 2015DN07750	A	20160122	IN 2015-DN7750	20150828

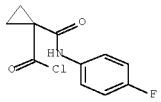
PRIORITY APPLN. INFO.: US 2013-13986103 A 20130401
WO 2014-US32253 W 20140328
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



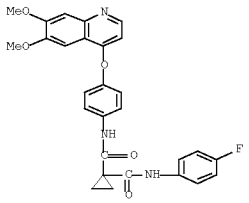
L4 ANSWER 190 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1710486 CAPLUS Full-text
DOCUMENT NUMBER: 161:577829
TITLE: Drug combinations to treat cancer
INVENTOR(S): Sweeney, Christopher J.; Kantoff, Philip W.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 78pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165779	A1	20141009	WO 2014-US33008	20140404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2908815	A1	20141009	CA 2014-2908815	20140404
AU 2014248001	A1	20151119	AU 2014-248001	20140404
IL 241868	A	20151130	IL 2014-241868	20140404
KR 2015138268	A	20151209	KR 2015-7030445	20140404

EP 2983639 A1 20160217 EP 2014-724594 20140404
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
US 20160082019 A1 20160324 US 2015-14782493 20151005
IN 2015KN03651 A 20160318 IN 2015-KN3651 20151103
PRIORITY APPLN. INFO.: US 2013-61808516 P 20130404
WO 2014-US33008 W 20140404
OTHER SOURCE(S): CASREACT 161:577829; MARPAT 161:577829
GI



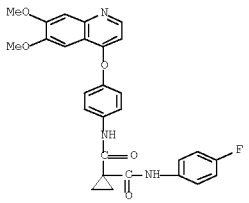
AB This invention relates to the combination of cabozantinib and abiraterone to treat cancer, particularly castration resistant prostate cancer.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug combinations to treat cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug combinations to treat cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

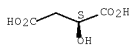
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

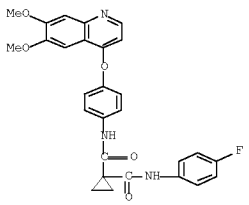
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



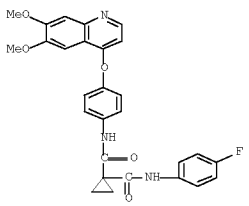
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 191 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1689164 CAPLUS Full-text
DOCUMENT NUMBER: 162:58578
TITLE: Cabozantinib inhibits growth of androgen-sensitive and castration-resistant prostate cancer and affects bone remodeling [Erratum to document cited in CA160:363229]
AUTHOR(S): Nguyen, Holly M.; Ruppender, Nazanin; Zhang, Xiaotun; Brown, Lisha G.; Gross, Ted S.; Morrissey, Colm; Gulati, Roman; Vessella, Robert L.; Schimmoller, Frauke; Aftab, Dana T.; Corey, Eva
CORPORATE SOURCE: Department of Urology, University of Washington, Seattle, WA, USA
SOURCE: PLoS One (2014), 9(8), e106797/1, 1 pp.
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0106797
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB On page 1, the funding information was incomplete; the cor. funding statement is given.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET, VEGFR2, RET expressions were found higher while cabozantinib by inhibiting these targets it safely, effectively inhibited tumor growth, improved bone remodeling in androgen-sensitive, metastatic CRPC tumor xenografted mouse (Erratum))
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



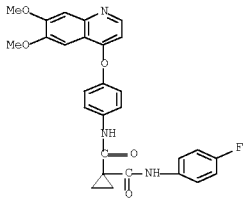
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 192 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1684883 CAPLUS Full-text
DOCUMENT NUMBER: 161:588524
TITLE: Emerging molecular targets in oncology: clinical potential of MET/hepatocyte growth-factor inhibitors
AUTHOR(S): Smyth, Elizabeth C.; Sclafani, Francesco; Cunningham, David
CORPORATE SOURCE: Department of Gastrointestinal Oncology, Royal Marsden Hospital, Sutton, UK
SOURCE: OncoTargets and Therapy (2014), 7, 1001-1014, 14 pp.
CODEN: OTNHAZ; ISSN: 1178-6930
DIGITAL OBJECT ID: 10.2147/OTT.S44941
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The MET/hepatocyte growth-factor (HGF) signaling pathway plays a key role in the processes of embryogenesis, wound healing, and organ regeneration. Aberrant activation of MET/HGF occurs through multiple mechanisms including gene amplification, mutation, protein overexpression, and abnormal gene splicing interrupting autocrine and paracrine regulatory feedback mechanisms. In many cancers including non-small-cell lung cancer, colorectal, gastric, renal, and hepatocellular cancer, dysregulation of MET may lead to a more aggressive cancer phenotype and may be a neg. prognostic indicator. Successful therapeutic targeting of the MET/HGF pathway has been achieved using monoclonal antibodies against the MET receptor and its ligand HGF in addition to MET-specific and multitargeted small-mol. tyrosine-kinase inhibitors with several drugs in late-phase clin. trials including onartuzumab, rilotumumab, tivantinib, and cabozantinib. MET frequently interacts with other key oncogenic tyrosine kinases including epidermal growth-factor receptor (EGFR) and HER-3 and these interactions may be responsible for resistance to anti-EGFR therapies. Similarly, resistance to MET inhibition may be mediated through EGFR activation, or alternatively by increasing levels of MET amplification or acquisition of novel "gatekeeper" mutations. In order to optimize development of effective inhibitors of the MET/HGF pathway clin. trials must be enriched for patients with demonstrable MET-pathway dysregulation for which robustly standardized and validated assays are required.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. targets in oncol. and clin. potential of MeT/hepatocyte growth-factor inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 140 THERE ARE 140 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 193 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1684761 CAPLUS Full-text
DOCUMENT NUMBER: 161:588517
TITLE: Cabozantinib for progressive metastatic medullary thyroid cancer: a review
AUTHOR(S): Colombo, Joshua R.; Wein, Richard O.
CORPORATE SOURCE: Department of Otolaryngology, Head and Neck Surgery, Tufts Medical Center, Boston, MA, USA
SOURCE: Therapeutics and Clinical Risk Management (2014), 10, 395-404, 10 pp.
CODEN: TCRMA6; ISSN: 1178-203X
DIGITAL OBJECT ID: 10.2147/TCRM.S46041
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Medullary thyroid cancer is uncommon and patients typically present with advanced disease. Treatment options for patients with progressive, metastatic medullary thyroid cancer had been limited until recently. Tyrosine kinase inhibitors have garnered increasing interest in this subset of patients. The US Food and Drug Administration recently approved cabozantinib, a tyrosine kinase inhibitor, after promising results were shown in a large Phase III clin. trial. This review summarizes the clin. pharmacol., clin. trials, and safety data for cabozantinib and concludes with a discussion of possible future directions for the treatment of medullary thyroid cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for progressive metastatic medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

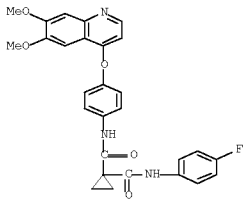


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 194 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1660666 CAPLUS Full-text
DOCUMENT NUMBER: 161:546938
TITLE: Methods and compositions for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): Tactical Therapeutics Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140294806	A1	20141002	US 2013-13986103	20130401
US 9089570	B2	20150728		
CA 2902144	A1	20141009	CA 2014-2902144	20140328
WO 2014165412	A2	20141009	WO 2014-US32253	20140328
WO 2014165412	A3	20150129		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014248377	A1	20150903	AU 2014-248377	20140328
IL 241827	A	20151130	IL 2014-241827	20140328
CN 105120663	A	20151202	CN 2014-80019712	20140328
EP 2981169	A2	20160210	EP 2014-779684	20140328
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2016026824	A	20160309	KR 2015-7022953	20140328
IN 2015DN07750	A	20160122	IN 2015-DN7750	20150828

PRIORITY APPLN. INFO.: US 2013-13986103 A 20130401
WO 2014-US32253 W 20140328
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



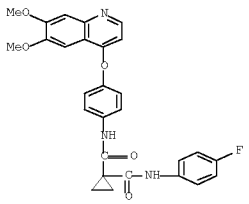
L4 ANSWER 195 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1657302 CAPLUS Full-text
DOCUMENT NUMBER: 161:559304
TITLE: Methods of treating proliferative diseases such as cancer using natural compounds and/or ketogenic diet
INVENTOR(S): Reynolds, Brent; Deleyrolle, Loic
PATENT ASSIGNEE(S): University of Florida Research Foundation, Incorporated, USA
SOURCE: PCT Int. Appl., 115pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014159500	A1	20141002	WO 2014-US23934	20140312
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2912518	A1	20141002	CA 2014-2912518	20140312
AU 2014240467	A1	20151105	AU 2014-240467	20140312
EP 2968260	A1	20160120	EP 2014-775944	20140312
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CN 105377252	A	20160302	CN 2014-80028215	20140312
US 20160038456	A1	20160211	US 2015-14775751	20150914
IN 2015DN09621	A	20160226	IN 2015-DN9621	20151014

PRIORITY APPLN. INFO.: US 2013-61784386 P 20130314
WO 2014-US23934 W 20140312
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The current invention is directed to a treatment of a proliferative disease comprising administering to a subject in need of such treatment, a composition comprising epigallocatechin-3-gallate (EGCG), curcumin, glucosinolates and, optionally Daikon radish sprout, alone or in combination with providing a ketogenic diet or a modified ketogenic diet to the subject. The invention also provides a composition comprising medium chain triglycerides, epigallocatechin-3-gallate, curcumin, compns. comprising glucosinolates and/or derivs. thereof, such as glucoraphanin and its breakdown product sulforaphane (SFN) (which are found at high levels in broccoli sprouts or sprouts of other cruciferous vegetables), and, optionally Daikon radish sprout.
IT 1140909-48-3, Cometriq
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cometriq; methods of treating proliferative diseases such as cancer using natural compds. and/or ketogenic diet)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

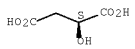
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

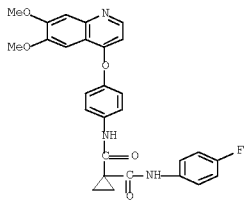


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
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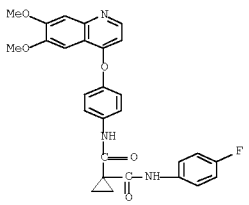
L4 ANSWER 196 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1653556 CAPLUS Full-text
DOCUMENT NUMBER: 161:542164
TITLE: Articles and methods for preventing and treating dermatologic adverse events
INVENTOR(S): Lacouture, Mario E.; Abou-Alfa, Ghassan Khaled
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 22pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014160628	A2	20141002	WO 2014-US31545	20140324
WO 2014160628	A3	20141204		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2978412	A2	20160203	EP 2014-775469	20140324
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160101114	A1	20160414	US 2015-14888392	20151030
PRIORITY APPLN. INFO.:			US 2013-61804907 P	20130325
			WO 2014-US31545 W	20140324

AB The present invention provides articles and methods for preventing or treating dermatol. adverse events.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(articles and methods for preventing and treating dermatol. adverse events)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 197 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1651697 CAPLUS Full-text
DOCUMENT NUMBER: 161:710328
TITLE: Hepatocellular carcinoma: novel molecular targets in carcinogenesis for future therapies
AUTHOR(S): Bertino, Gaetano; Demma, Shirin; Ardiri, Annalisa; Proiti, Maria; Gruttadauria, Salvatore; Toro, Adriana; Malaguarnera, Giulia; Bertino, Nicoletta; Malaguarnera, Michele; Malaguarnera, Mariano; Di Carlo, Isidoro
CORPORATE SOURCE: Hepatology Unit, Department of Medical and Pediatric Sciences, University of Catania, Policlinic, Catania, 95123, Italy
SOURCE: BioMed Research International (2014) 203693/1-203693/15, 16 pp.
CODEN: BRIIDT; ISSN: 2314-6141
DIGITAL OBJECT ID: 10.1155/2014/203693
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background. Hepatocellular carcinoma is one of the most common and lethal malignant tumors worldwide. Over the past 15 years, the incidence of HCC has more than doubled. Due to late diagnosis and/or advanced underlying liver cirrhosis, only limited treatment options with marginal clin. benefit are available in up to 70% of patients. During the last decades, no effective conventional cytotoxic systemic therapy was available contributing to the dismal prognosis in patients with HCC. A better knowledge of mol. hepatocarcinogenesis provides today the opportunity for targeted therapy. Materials and Methods. A search of the literature was made using cancer literature, the PubMed, Scopus, and Web of Science (WOS) database for the following keywords: "hepatocellular carcinoma," "mol. hepatocarcinogenesis," "targeted therapy," and "immunotherapy." Discussion and Conclusion. Treatment decisions are complex and dependent upon tumor staging, presence of portal hypertension, and the underlying degree of liver dysfunction. The knowledge of mol. hepatocarcinogenesis broadened the horizon for patients with advanced HCC. During the last years, several mol. targeted agents have been evaluated in clin. trials in advanced HCC. In the future, new therapeutic options will be represented by a blend of immunotherapy-like vaccines and T-cell modulators, supplemented by molecularly targeted inhibitors of tumor signaling pathways.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatocellular carcinoma as novel mol. targets in carcinogenesis for future therapies)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

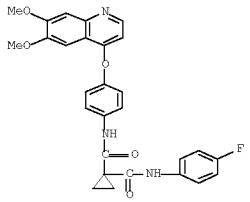


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 198 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1600971 CAPLUS Full-text
DOCUMENT NUMBER: 161:533327
TITLE: c-met cancer biomarkers for patient prognosis and selection for the therapy with c-met antagonist, particularly anti-c-met antibody
INVENTOR(S): Yauch, Robert; Koeppen, Hartmut
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 99pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014150819	A2	20140925	WO 2014-US24316	20140312
WO 2014150819	A3	20150108		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2013-61801276 P	20130315

AB The invention concerns c-met biomarkers for patient selection and prognosis in cancer, as well as methods of therapeutic treatment and diagnostic kits using anti-c-met antibodies.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-met antagonist; c-met cancer biomarkers for patient prognosis and selection for therapy with c-met antagonist, particularly anti-c-met antibody)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 199 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1599013 CAPLUS Full-text
DOCUMENT NUMBER: 161:533781
TITLE: Antibodies for treating angiogenesis-related disorders
INVENTOR(S): Gurewich, Victor
PATENT ASSIGNEE(S): FFE Therapeutics LLC, USA
SOURCE: PCT Int. Appl., 76pp.

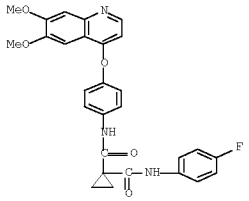
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014151917	A1	20140925	WO 2014-US26675	20140313
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2968550	A1	20160120	EP 2014-769535	20140313
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US 20160024194	A1	20160128	US 2015-14775261	20150911

PRIORITY APPLN. INFO.: US 2013-61785345 P 20130314
WO 2014-US26675 W 20140313
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The author discloses anti-angiogenic monoclonal antibodies and antigen-binding antibody fragments that selectively and specifically bind to an epitope in both fibronectin and either fibrinogen or fibrin fragment E. In one example, administration of the monoclonal antibodies is shown to inhibit tumor growth and vascularization in a colon adenocarcinoma xenograft model.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination therapy with cross-reactive monoclonal antibodies to fibronectin and fibrinogen)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

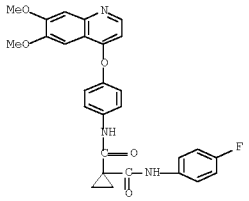
L4 ANSWER 200 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1596401 CAPLUS Full-text
DOCUMENT NUMBER: 161:528901
TITLE: Stapling eIF4E-eIF4G interacting peptides and their therapeutic use in cancer treatment
INVENTOR(S): Brown, Christopher John; Lane, David Philip; Quah, Soo Tng; Lama, Dilraj; Verma, Chandra Shekhar
PATENT ASSIGNEE(S): Agency for Science, Technology and Research, Singapore
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

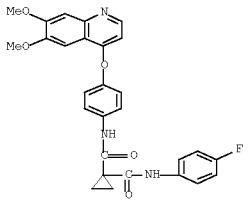
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014149001	A1	20140925	WO 2014-SG94	20140228
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SG 201400336	A1	20150828	SG 2014-336	20140115
CN 105263950	A	20160120	CN 2014-80029531	20140228
EP 2976354	A1	20160127	EP 2014-768664	20140228
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160046672	A1	20160218	US 2015-14778761	20150921

PRIORITY APPLN. INFO.: SG 2013-2065 A 20130321
SG 2014-336 A 20140115
WO 2014-SG94 W 20140228
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 161:528901

AB The present invention relates to crosslinked peptides that are assocd. with human eIF4G and bind to eIF4E, uses thereof and pharmaceutical compns. comprising the peptides. Described below are crosslinked peptides related to a portion of human eIF4E. These crosslinked peptides contain at least two modified amino acids that together form an internal crosslink (also referred to as a staple) that can help to stabilize the alpha-helical secondary structure of a portion of eIF4G1 that is thought to be important for binding of eIF4E to eIF4G. Accordingly, a crosslinked peptide described herein can have improved biol. activity relative to a corresponding peptide that is not crosslinked. The crosslinked eIF4G1 peptides are thought to interfere with binding of eIF4G1 to eIF4G thereby inhibiting the increased translation of mRNAs with highly structured 5'UTRs. The crosslinked eIF4G1 peptide described herein can be used therapeutically, e.g., to treat or prevent a variety of cancers in a subject.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stapling eIF4E-eIF4G interacting peptides and their therapeutic use in cancer treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



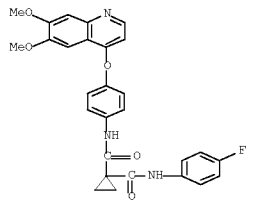
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 201 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1594844 CAPLUS Full-text
DOCUMENT NUMBER: 162:544299
TITLE: Congestive heart failure risk in cancer patients treated with vascular endothelial growth factor tyrosine kinase inhibitors: a systematic review and meta-analysis of 36 clinical trials
AUTHOR(S): Qi, Wei-Xiang; Shen, Zan; Tang, Li-Na; Yao, Yang
CORPORATE SOURCE: Department of Oncology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE: British Journal of Clinical Pharmacology (2014), 78(4), 748-762
CODEN: BCPHBM; ISSN: 1365-2125
DIGITAL OBJECT ID: 10.1111/bcp.12387
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Aims : Congestive heart failure (CHF) assocd. with vascular endothelial growth factor tyrosine-kinase inhibitors (VEGFR-TKIs) has emerged as a relevant problem in clin. and scientific communities. We performed an up-to-date, comprehensive meta-anal. to determine the overall incidence and risk of CHF in cancer patients receiving VEGFR-TKIs. Methods : The databases

of PubMed, Web of Science and abstrs. presented at the American Society of Clin. Oncol. up to August 31 2013 were searched for relevant articles. Statistical analyses were conducted to calculate the summary incidence, odds ratio (OR) and 95% confidence intervals (CIs) by using either random effects or fixed effect models according to the heterogeneity of included studies. Results : A total of 10 553 patients from 36 clin. trials were included. The overall incidence of all grade and high grade CHF associated with VEGFR-TKIs was 3.2% (95% CI 1.8%, 5.8%) and 1.4% (95% CI 0.9%, 2.3%), resp. The use of VEGFR-TKIs significantly increased the risk of developing all grade (OR 2.37, 95% CI 1.76, 3.20, P < 0.001) and high grade (OR 3.51, 95% CI 1.74, 7.05, P < 0.001) CHF. In subgroup analyses, the risk of CHF did not significantly vary with tumor types (P = 0.071 for all grade; P = 0.72 for high grade) and VEGFR-TKIs (P = 0.55 for all grade; P = 0.99 for high grade). Meta-regression indicated that CHF might possibly occur early in the treatment of VEGFR-TKIs. No evidence of publication bias was observed Conclusion : The use of VEGFR-TKIs is associated with a significantly increased risk of developing congestive heart failure in cancer patients. Clinicians should be aware of this risk and provide close monitoring in patients receiving these therapies.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(congestive heart failure risk in cancer patients treated with vascular endothelial growth factor tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

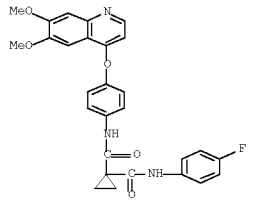
L4 ANSWER 202 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1563739 CAPLUS Full-text
DOCUMENT NUMBER: 161:496846
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Privada Institut de Recerca Biomedica, Spain; Fundacio Privada Institucio Catalana de Recerca i Estudis Avancats
SOURCE: PCT Int. Appl., 97pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014140933	A2	20140918	WO 2014-IB1253	20140314
WO 2014140933	A3	20141231		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2906394	A1	20140918	CA 2014-2906394	20140314
AU 2014229505	A1	20150903	AU 2014-229505	20140314
KR 2015122731	A	20151102	KR 2015-7026432	20140314
EP 2971113	A2	20160120	EP 2014-747411	20140314
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 105324491	A	20160210	CN 2014-80015564	20140314
US 20160032400	A1	20160204	US 2015-14776412	20150914

PRIORITY APPLN. INFO.: US 2013-61801718 P 20130315
WO 2014-IB1253 W 20140314

AB The invention relates to a method for the prognosis of bone metastasis in cancer which comprises using a probe to determine if a gene of interest is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise using a probe to determine the expression level of a gene of interest, or the amplification or translocation of a gene of interest. The invention also relates to a method for predicting early bone metastasis in a subject suffering cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering cancer and for classifying a subject from cancer into a cohort.

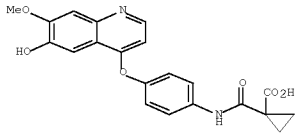
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for prognosis and treatment of cancer metastasis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 203 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1554223 CAPLUS Full-text
DOCUMENT NUMBER: 161:496839
TITLE: Metabolites of n-[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]-n'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven; Nguyen, Linh
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

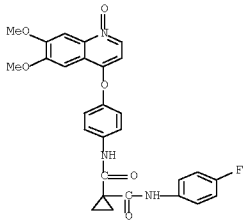
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014145693	A1	20140918	WO 2014-US30498	20140317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2013-61792562 P 20130315
OTHER SOURCE(S): CASREACT 161:496839; MARPAT 161:496839
GI

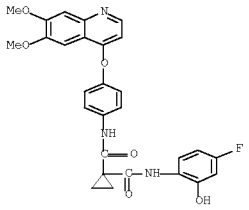


AB The invention relates to metabolites of foretinib as well as uses thereof.

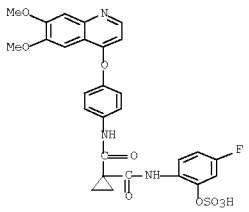
IT 1621681-63-7P 1628530-38-0P 1628530-40-4P 1628530-41-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metabolites of foretinib)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 1628530-38-0 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluoro-2-hydroxyphenyl)- (CA INDEX NAME)



RN 1628530-40-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[4-fluoro-2-(sulfooxy)phenyl]- (CA INDEX NAME)

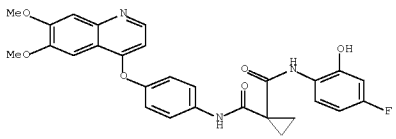


RN 1628530-41-5 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluoro-3-hydroxyphenyl)- (CA INDEX NAME)

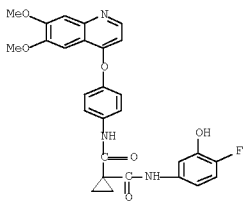
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014145715	A1	20140918	WO 2014-US30524	20140317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2907334	A1	20140918	CA 2014-2907334	20140317
AU 2014232714	A1	20151008	AU 2014-232714	20140317
KR 2015130376	A	20151123	KR 2015-7027712	20140317
IL 241577	A	20151130	IL 2014-241577	20140317
CN 105121412	A	20151202	CN 2014-80021215	20140317
EP 2970126	A1	20160120	EP 2014-721149	20140317
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160031818	A1	20160204	US 2015-14776337	20150914
IN 2015KN03380	A	20160318	IN 2015-KN3380	20151013

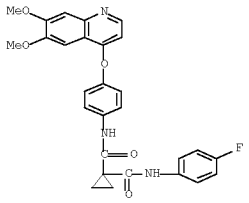
PRIORITY APPLN. INFO.: US 2013-61792413 P 20130315
WO 2014-US30524 W 20140317
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:496838; MARPAT 161:496838
GI



AB The invention relates to metabolites of cabozantinib as well as uses thereof.
IT 1621681-63-7P 1628530-40-4P 1628530-41-5P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)



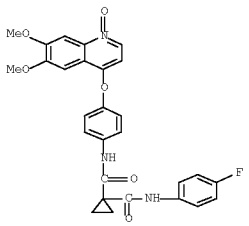
IT 849217-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(metabolites of foretinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



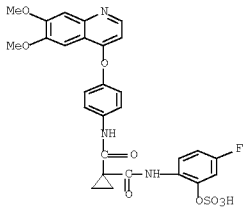
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 204 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1554191 CAPLUS Full-text
DOCUMENT NUMBER: 161:496838
TITLE: Metabolites of
N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl) cyclopropane-1,1-dicarboxamide
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven; Nguyen, Linh
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 65pp.
CODEN: PIXXD2

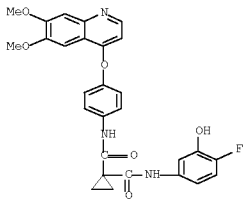
(metabolites of cabozantinib)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



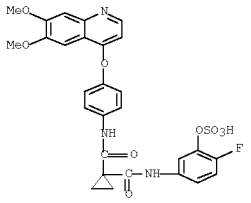
RN 1628530-40-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[4-fluoro-2-(sulfooxy)phenyl]- (CA INDEX NAME)



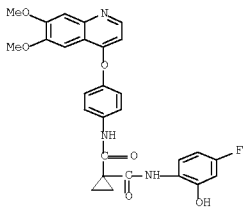
RN 1628530-41-5 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluoro-3-hydroxyphenyl)- (CA INDEX NAME)



IT 1628530-45-9 1628542-34-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolites of cabozantinib)
RN 1628530-45-9 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[4-fluoro-3-(sulfooxy)phenyl]- (CA INDEX NAME)



RN 1628542-34-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, monohydroxy deriv. (CA INDEX NAME)

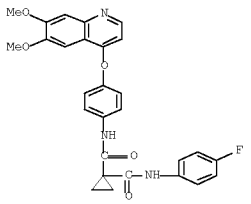


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 205 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1509904 CAPLUS Full-text
DOCUMENT NUMBER: 162:419468
TITLE: Antitumor Agent Cabozantinib Decreases RANKL Expression in Osteoblastic Cells and Inhibits Osteoclastogenesis and PTHrP-Stimulated Bone Resorption
AUTHOR(S): Stern, Paula H.; Alvares, Keith
CORPORATE SOURCE: Department of Pharmacology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
SOURCE: Journal of Cellular Biochemistry (2014), 115(11), 2033-2038
CODEN: JCEBD5; ISSN: 0730-2312
DIGITAL OBJECT ID: 10.1002/jcb.24879
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

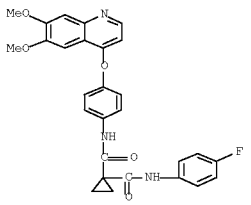
AB Cabozantinib, an inhibitor of vascular endothelial growth factor and hepatocyte growth factor signaling, decreases bone lesions in patients with prostate cancer. To determine direct effects of cabozantinib on bone, resorption in neonatal mouse bone organ culture and on gene expression, proliferation, and phenotypic markers in osteoblast and osteoclast cell lines were examined Cabozantinib, 0.3 and 3 μM, prevented PTHrP-stimulated calcium release from neonatal mouse calvaria. Since the effect on resorption could reflect effects on osteoblasts to prevent osteoclast activation, or direct inhibition of osteoclasts, responses in osteoblastic and osteoclast precursor cell lines were examined Twenty-four-hour treatment of osteoblastic MC3T3-E1 cells with 3 μM cabozantinib decreased expression of receptor activator of NFkB ligand (RANKL) and alkaline phosphatase. Forty-eight-hour treatment of MC3T3-E1 cells with 3 μM cabozantinib inhibited cell proliferation and decreased MTT activity. Effects on alkaline phosphatase activity were biphasic, with small stimulatory effects at concns. below 3 μM. When RAW 264.7 osteoclast precursor cells differentiated with 20 ng/mL RANKL were co-treated for 24 h with 3 μM cabozantinib, expression of RANK, TRAP, cathepsin K, alpha v or beta 3 integrin, or NFATc1 were unaffected. Five-day treatment of RANKL-treated RAW 264.7 cells with 3 μM cabozantinib decreased TRAP and MTT activity. The results suggest that the osteoblast could be the initial target, with subsequent direct and indirect effects on osteoclastogenesis leading to decreased resorption. The multiple effects of cabozantinib on the cell microenvironment of bone are consistent with its effectiveness in reducing lesions from prostate cancer metastases. J. Cell. Biochem. 115: 2033-2038, 2014. © 2014 Wiley Periodicals, Inc.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agent cabozantinib decreases RANKL expression in osteoblastic cells and inhibits osteoclastogenesis and PTHrP-stimulated bone resorption)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



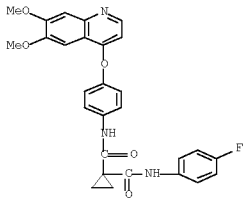
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 206 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1476801 CAPLUS Full-text
DOCUMENT NUMBER: 161:446646
TITLE: Preparation of pyridine compounds as protein tyrosine kinase inhibitors for treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wang, Ruyong; Wang, Liang
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 118pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:



D1—OH

IT 849217-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(metabolites of cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1628530-38-0
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(metabolites of cabozantinib)
RN 1628530-38-0 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluoro-2-hydroxyphenyl)- (CA INDEX NAME)

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CN 104016979	A	20140903	CN 2013-10597520		20131122
PRIORITY APPLN. INFO.:			CN 2012-10480698	A	20121123
			CN 2013-10116667	A	20130403

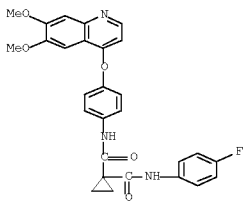
OTHER SOURCE(S): MARPAT 161:446646
GI

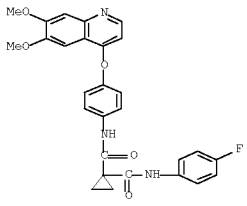
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridinyl compds. of general formula I, pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. For I, each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; X is C6-C10 aryl or 5-10 membered heteroaryl that are optionally substituted; and Y is an (un)substituted bicyclic heterocyclyl. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 6-step reaction that culminated in coupling of intermediates III and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-ol. Example compds. of the invention were also tested in ALK and c-Met kinase inhibition assays. Pharmacokinetic profiles were also examined in rats, as was compound stability in human and rat liver microsomes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyridine compds. as protein tyrosine kinase inhibitors for treatment of proliferative diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 208 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1425621 CAPLUS Full-text
DOCUMENT NUMBER: 161:400645
TITLE: Treatment of cancer using an oncolytic virus and a receptor tyrosine kinase inhibitor
INVENTOR(S): Conner, Joe
PATENT ASSIGNEE(S): Virttu Biologics Limited, UK
SOURCE: PCT Int. Appl., 310pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014128487	A1	20140828	WO 2014-GB50522	20140221
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
GB 2516521	A	20150128	GB 2014-3083	20140221
US 20150374767	A1	20151231	US 2015-14768549	20150818

PRIORITY APPLN. INFO.:			
GB 2013-3184	A	20130222	
WO 2014-GB50522	W	20140221	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

L4 ANSWER 207 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1460877 CAPLUS Full-text
DOCUMENT NUMBER: 162:17927
TITLE: Comparison of the cancer gene targeting and biochemical selectivities of all targeted kinase inhibitors approved for clinical use
AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; de Man, Jos; Tanizawa, Yoshinori; Kawase, Yusuke; Yoshino, Kohichiro; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE: Netherlands Translational Research Center B.V., Oss, Neth.
SOURCE: PLoS One (2014), 9(3), e92146/1-e92146/13, 13 pp.
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0092146
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The anti-proliferative activities of all twenty-five targeted kinase inhibitor drugs that are in clin. use were measured in two large assay panels: (1) a panel of proliferation assays of forty-four human cancer cell lines from diverse tumor tissue origins; and (2) a panel of more than 300 kinase enzyme activity assays. This study provides a head-on comparison of all kinase inhibitor drugs in use, and for six of these drugs, the first kinome profiling data in the public domain. Correlation of drug activities with cancer gene mutations revealed novel drug sensitivity markers, suggesting that cancers dependent on mutant CTNNB1 will respond to trametinib and other MEK inhibitors, and cancers dependent on SMAD4 to small mol. EGFR inhibitor drugs. Comparison of cellular targeting efficacies reveals the most targeted inhibitors for EGFR-, ABL1- and BRAF(V600E)-driven cell growth, and demonstrates that the best targeted agents combine high biochem. potency with good selectivity. For ABL1 inhibitors, we computationally deduce optimized kinase profiles for use in a next generation of drugs. Our study shows the power of combining biochem. and cellular profiling data in the evaluation of kinase inhibitor drug action.

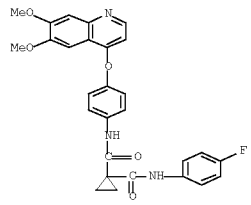
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of cancer gene targeting and biochem. selectivities of all targeted kinase inhibitors approved for clin. use in human)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

AB A method of treating cancer is disclosed, the method comprising simultaneous or sequential administration of an oncolytic virus and a receptor tyrosine kinase (RTK) inhibitor.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of cancer using an oncolytic virus and a receptor tyrosine kinase inhibitor)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



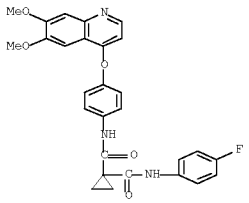
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 209 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1416968 CAPLUS Full-text
DOCUMENT NUMBER: 162:442908
TITLE: High-Grade Undifferentiated Sarcomas of the Uterus: Diagnosis, Outcomes, and New Treatment Approaches
AUTHOR(S): Philip, Charles-Andre; Pautier, Patricia; Duffaud, Florence; Ray-Coquard, Isabelle
CORPORATE SOURCE: Department of Adult Medical Oncology, Centre Leon Berard, Lyon, 69008, Fr.
SOURCE: Current Oncology Reports (2014), 16(10), 1-8
CODEN: CORUAT; ISSN: 1534-6269
DIGITAL OBJECT ID: 10.1007/s11912-014-0405-1
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. High-grade undifferentiated sarcomas (HGUS) are rare malignancies accounting for 6 % of all uterine sarcomas and have a very poor outcome. Histol. classification of HGUS is currently debated as a subgroup with uniform nucleoli, and frequently YWHAE-FAM22 transcript has been described, constituting a potential target for new therapies. In localized HGUS, surgery involving total hysterectomy and bilateral oophorectomy is recommended. Adjuvant radiotherapy has recently been suggested in a retrospective study to decrease local recurrence and improve survival vs. observation in localized HGUS. In metastatic or recurrent disease,

chemotherapy with doxorubicin with or without ifosfamide constitutes the standard of care. Gemcitabine plus docetaxel also seems to be an interesting alternative. Targeted therapies such as pazopanib are now available for soft tissue sarcomas and so could be proposed for uterine sarcoma patients after first- or second-line chemotherapy in the metastatic phase. Further investigations are needed to determine their indications and targets. A European Organization for Research and Treatment of Cancer (EORTC) randomized trial testing maintenance therapy with cabozantinib after first-line chemotherapy in HGUS is ongoing.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-Grade Undifferentiated Sarcomas of the Uterus: Diagnosis, Outcomes, and New Treatment Approaches)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

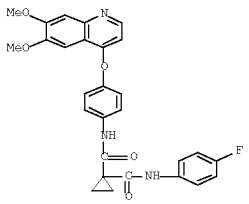
L4 ANSWER 210 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1390694 CAPLUS Full-text
DOCUMENT NUMBER: 161:375913
TITLE: Preparation of pyrazolopyridine compounds as protein kinase modulators useful for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 41pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140234254	A1	20140821	US 2014-14181670	20140215

in seven steps (procedure given). Candidate compds. of I were assayed for their stability in liver microsomes, their oral and i.v. bioavailability, and inhibitory activity against PI3K and mTOR kinase (data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyrazolopyridine compds. as protein kinase modulators useful for treatment of hyperproliferative disorders)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 211 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1389525 CAPLUS Full-text
DOCUMENT NUMBER: 161:379820
TITLE: Efflux inhibitor compositions containing effect transporter protein inhibitors
INVENTOR(S): Bunt, Antonius Martinus Gustave; Tellingen, Olaf Van
PATENT ASSIGNEE(S): Izumi Biosciences LLC, USA; The Netherlands Cancer Institute
SOURCE: U.S. Pat. Appl. Publ., 33pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

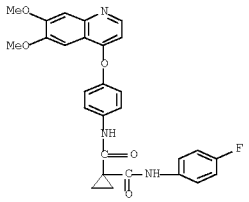
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140235631	A1	20140821	US 2013-13952476	20130726
PRIORITY APPLN. INFO.:			US 2013-61767689 P	20130221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to efflux inhibitor compns. and methods of using these agents for treating conditions where the activity of efflux transporter proteins (e.g., Breast Cancer Resistance Protein (BCRP) and P-Glycoprotein (P-GP)) inhibit effective delivery of a therapeutic agent to a target tissue (e.g., brain, spinal cord, nerves, cerebrospinal fluid, testis, eyeballs, retina, inner ear, placenta, mammary gland, liver, biliary tract, kidney, intestines, lung, adrenal cortex, endometrium, hematopoietic cells, and/or stem cells). E.g., elacridar nanoparticles were prepared

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kinase inhibitor; efflux inhibitor pharmaceuticals containing effect transporter protein inhibitors)

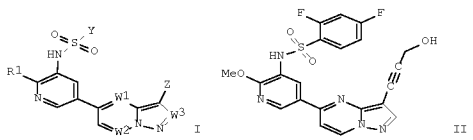
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 212 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1348855 CAPLUS Full-text
DOCUMENT NUMBER: 161:346659
TITLE: Drug selection for non-small cell lung cancer therapy
INVENTOR(S): Singh, Sharat; Kim, Phillip
PATENT ASSIGNEE(S): Nestec S.A., Switz.
SOURCE: PCT Int. Appl., 77pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014122582	A1	20140814	WO 2014-IB58790	20140204
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
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CA 2898294	A1	20140828	CA 2014-2898294	20140215
WO 2014130375	A1	20140828	WO 2014-US16643	20140215
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
AU 2014219256	A1	20150730	AU 2014-219256	20140215
KR 2015118102	A	20151021	KR 2015-7019069	20140215
EP 2958564	A1	20151230	EP 2014-754663	20140215
R:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME			
JP 2016509056	T	20160324	JP 2015-558892	20140215
PRIORITY APPLN. INFO.:			US 2013-61767721 P	20130221
			WO 2014-US16643 W	20140215

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:375913; MARPAT 161:375913
GI



AB The invention provides heteroarom. derivs. and pharmaceutically acceptable salts and formulations thereof useful in modulating the protein kinase activity, especially phosphatidylinositol 3-kinases (PI3K) and mammalian target of rapamycin (mTOR), and in modulating inter- and/or intra-cellular signaling activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Compds. of formula I [wherein W1, W2, and W3 are independently N or CRc; Z is D, CN, N3, etc.; Y is C1-6 alkyl, C3-6 cycloalkyl, C3-C6 heterocyclyl, etc.; R1 is H, Cl, C3-6 cycloalkyl, etc.; each Rc is independently H, D, F, etc.] or stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, prodrugs, or pharmaceutically acceptable salts thereof are claimed and exemplified. Example compound II was prepared

EP 2954068 A1 20151216 EP 2014-706699 20140204
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
US 20160032403 A1 20160204 US 2015-14812979 20150729
PRIORITY APPLN. INFO.: US 2013-61761105 P 20130205
WO 2014-IB58790 W 20140204

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods for therapy selection for a patient with non-small cell lung cancer (NSCLC) based on detecting, quantifying, and comparing the activity of particular signal transduction pathways, and components thereof, which can be represented as the patient's analyte index (e.g., EGFR/cMET index) and can be used to determine whether the patient is likely to respond to a particular therapy such as EGFR inhibitor therapy alone, cMET inhibitor therapy alone, or a combination thereof. The EGFR inhibitor is selected from the group consisting of cetuximab, panitumumab, matuzumab, nimotuzumab, Erbl vaccine, erlotinib, gefitinib, CL-387785 and a combination thereof, wherein the c-MET inhibitor is selected from the group consisting of ARQ197, XL184, GSK1363089/XL880, MP470, MGCD265, SGX523, PF04217903, JNJ38877605, INCB28060, AMG-458, E7050, MK-2461, BMS-777607 and a combination thereof. The invention also provides methods for determining drug resistance in non-small cell lung cancer (NSCLC) patients receiving above mentioned therapy.

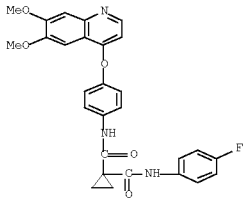
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for non-small cell lung cancer therapy)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

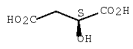
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 213 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1339983 CAPLUS Full-text
DOCUMENT NUMBER: 161:329247
TITLE: Improved treatment for adenoid cystic carcinoma comprising growth factor receptor kinase and MET kinase inhibitors
INVENTOR(S): Stenman, Goeran; Andersson, Mattias
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 116pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014123476	A1	20140814	WO 2014-SE50140	20140204

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

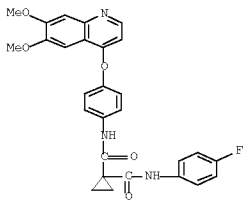
PRIORITY APPLN. INFO.: US 2013-61849920 P 20130205

AB The present application relates to inhibitors of epidermal growth factor receptor (EGFR) kinase, MET kinase, insulin receptor (IR) kinase and insulin-like growth factor 1 (IGF1R) kinase for use in the treatment of neoplastic disease such as adenoid cystic carcinoma (ACC) and dermal cylindroma characterized by MYB activation. In an optional embodiment, the kinase inhibitor inhibits the MET kinase and the EGFR kinase and/or the IGF1R/IR kinase. In an optional embodiment, the kinase inhibitor is BMS-754807. In an optional embodiment, the IGF1R/IR kinase inhibitor is selected from a group consisting of linsitinib and BMS-754807. In an optional embodiment, the EGFR kinase inhibitor is selected from a group consisting of gefitinib, erlotinib, BMS-690514 and cetuximab. In an optional embodiment, the MET kinase inhibitor is selected from a group consisting of crizotinib, BMS-907351, BMS-777607 and BMS-754807.

IT 849217-68-1, BMS 907351
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BMS 907351; improved treatment for adenoid cystic carcinoma comprising growth factor receptor kinase and MET kinase inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

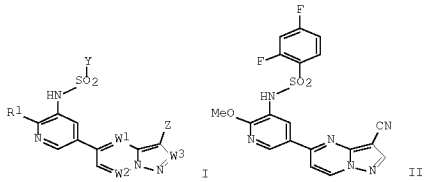
L4 ANSWER 214 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1274352 CAPLUS Full-text
DOCUMENT NUMBER: 161:361023
TITLE: Preparation of aryl-heterocyclic compounds for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 59pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103965199	A	20140806	CN 2014-10041929	20140128

PRIORITY APPLN. INFO.: CN 2013-10040391 A 20130202
CN 2013-10117077 A 20130404

OTHER SOURCE(S): CASREACT 161:361023; MARPAT 161:361023

GI

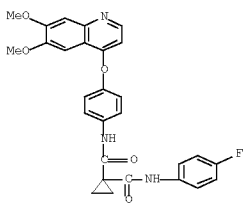


AB The present invention discloses aryl-heterocyclic compd. (with structure as shown in formula I), stereo isomers, geometrical isomers, tautomers, oxynitride, hydrates, solvates, metabolic products, pharmaceutically acceptable salts or prodrugs, pharmaceutical compns. containing thereof and application thereof in preparing agents for inhibiting or regulating the activity of protein kinases in biol. specimens. For example, compound II was prepared in a multi-step synthesis. The present invention also relates to pharmaceutical compns. containing the inventive compound, and application of the pharmaceutical compns. for treating mammal, particular human hyperproliferative disorders.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of aryl-heterocyclic compds. for treatment of hyperproliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



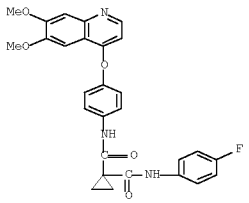
L4 ANSWER 215 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1273412 CAPLUS Full-text

DOCUMENT NUMBER: 162:67014
TITLE: Development of cabozantinib for the treatment of prostate cancer
AUTHOR(S): Vaishampayan, Ulka N.
CORPORATE SOURCE: Department of Oncology, Wayne State University/Karmanos Cancer Institute, Detroit, MI, USA
SOURCE: Core Evidence (2014), 9, 61-67, 7 pp.
CODEN: CEOVAF; ISSN: 1555-1741
DIGITAL OBJECT ID: 10.2147/CE.S67095
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib (XL184) is a multitargeted receptor tyrosine kinase with predominantly MET and vascular endothelial growth factor inhibition properties. It is currently approved by the US Food and Drug Administration for the treatment of progressive metastatic medullary thyroid cancer. The agent has a convenient once-daily oral dosing schedule and has demonstrated encouraging activity in metastatic castrate-resistant prostate cancer (CRPC). A Phase I/II trial demonstrated responses in soft tissue, visceral disease, and bone metastases in CRPC. An objective response rate of 5%, a stable disease rate of 75%, and a median progression-free survival of 6 mo was observed As compared with the 140 mg daily dose used in thyroid cancer, a lower dose of 60 mg daily is currently being utilized in prostate cancer studies due to the fact that toxicity could be reduced without compromising efficacy. Randomized trials are ongoing in comparison with prednisone or with mitoxantrone and prednisone in pretreated metastatic CRPC. Cabozantinib has demonstrated a unique mechanism of action and preliminary efficacy in the crowded therapeutic field of prostate cancer. Since multiple therapies have recently demonstrated overall survival benefit in metastatic CRPC, cabozantinib will likely face some challenges in clin. application. At present, in this rapidly evolving field, it is unclear what proportion of patients with prostate cancer will be eligible to receive this therapy. The cost of cabozantinib is likely to be another deterrent, especially if it remains more expensive than other oral therapies, such as abiraterone and enzalutamide. Defining the role of MET overexpression and RET mutations as biomarkers in prostate cancer may help to guide patient selection, and enrich and enhance the future applications of this targeted novel agent.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of cabozantinib for treatment of prostate cancer in patients)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



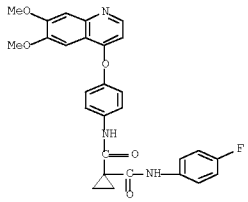
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 216 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1270460 CAPLUS Full-text
DOCUMENT NUMBER: 161:351479
TITLE: Degradation kinetics study of cabozantinib by a novel stability-indicating LC method and identification of its major degradation products by LC/TOF-MS and LC-MS/MS
AUTHOR(S): Wu, Chunyong; Xu, Xue; Feng, Chao; Shi, Yuanyuan; Liu, Wenyuan; Zhu, Xiaoyun; Zhang, Junying
CORPORATE SOURCE: Key Laboratory of Drug Quality Control and Pharmacovigilance, Ministry of Education, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2014), 98, 356-363
CODEN: JPBADA; ISSN: 0731-7085
DIGITAL OBJECT ID: 10.1016/j.jpba.2014.06.008
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB The chem. stability of cabozantinib (CBZ) was investigated using a novel stability-indicating LC method. Forced degradation of CBZ was carried out under acidic, basic, thermal, oxidative and photolytic stress conditions. Hydrolysis and oxidation were the primary pathways for this compound and three major unknown degradation products were characterized by LC/TOF-MS and LC-MS/MS. The major oxidative degradation product was isolated by preparative LC and identified by UV, HRMS and NMR techniques to be N-{4-[(N-oxide-6,7-dimethoxyquinolin-4-yl)oxy]phenyl}-N'-(4-fluorophenyl)- cyclopropane-1,1-dicarboxamide. The developed method was validated as per ICH guidelines and then successfully applied to investigate the degradation kinetics of CBZ. Degradation of CBZ followed first-order kinetics under all exptl. conditions. A V-shaped pH-rate profile over the pH range 2-10 was observed with maximum stability at pH 6. The effect of temperature on the rate of CBZ degradation was characterized using the Arrhenius equation. The activation energy for hydrolysis was 57.31 kJ mol-1 in alkaline solution

IT 849217-68-1, Cabozantinib 1140909-48-3, Cabozantinib (S)-Malate
RL: AMX (Analytical matrix); PEP (Physical, engineering or chemical process); PRP (Properties); ANST (Analytical study); PROC (Process)
(degradation kinetics study of cabozantinib by novel stability-indicating LC method and identification of major degradation products by LC/TOF-MS and LC-MS/MS)

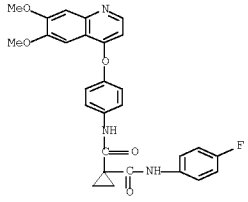
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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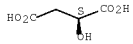
CRN 849217-68-1
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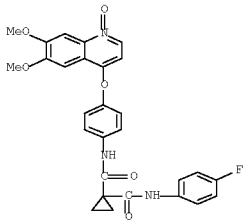
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 1621681-63-7
RL: ANT (Analyte); FMU (Formation, unclassified); PRP (Properties); ANST (Analytical study); FORM (Formation, nonpreparative)
(degradation kinetics study of cabozantinib by novel stability-indicating LC method and identification of major degradation products by LC/TOF-MS and LC-MS/MS)

RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 217 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1237165 CAPLUS Full-text
DOCUMENT NUMBER: 162:55826
TITLE: Recent orphan drugs that are first-in-class
AUTHOR(S): Phillips, M. Ian; Lee, Jongserk R.
CORPORATE SOURCE: Keck Graduate Institute, Center for Rare Disease Therapies, 535 Watson Drive, Claremont, CA, 91711, USA
SOURCE: Expert Opinion on Orphan Drugs (2014), 2(8), 759-763

CODEN: EOODAJ; ISSN: 2167-8707
DIGITAL OBJECT ID: 10.1517/21678707.2014.931806
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

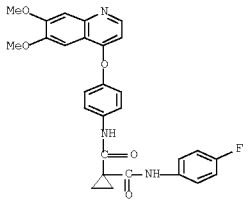
AB A review. Although the pipeline for new drugs seemed to be drying up, the number of new 'first-in-class' drugs appeared to be increasing. First-in-class drugs are those which use a new and unique mechanism for treating a disease or medical condition. They are a subset of new mol. entities (NMEs). The FDA reports that in 2012, 39 NMEs were approved. Twenty of these NMEs (.apprx. 50%) were identified by the FDA as first-in-class drugs. Of the 39 NMEs, 13 were designated orphan drugs and 9 of those orphan drugs were first-in-class. In 2013, there were 27 NMEs of which 9 were first-in-class. In 2013, nos. of NMEs are lower than the 2011 or 2012 but are based on fewer applications than in those years. There were 33% of NMEs that were first-in-class and 33% of the NMEs were orphan drugs. The FDA data indicate that creative new products are being developed for rare diseases.

IT 1140909-48-3, Cometriq
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(movement toward first-in-class drugs, indicating more innovation in drug discovery and utilizing orphan drugs)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

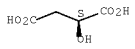
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



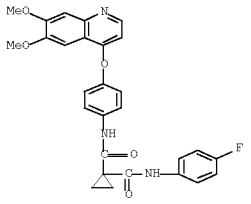
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 218 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1222486 CAPLUS Full-text
DOCUMENT NUMBER: 161:744871
TITLE: Cabozantinib-Induced Thyroid Dysfunction: A Review of Two Ongoing Trials for Metastatic Bladder Cancer and Sarcoma
AUTHOR(S): Yavuz, Sahzene; Apolo, Andrea B.; Kummar, Shivaani; del Rivero, Jaydira; Madan, Ravi A.; Shawker, Thomas; Reynolds, James; Celi, Francesco S.
CORPORATE SOURCE: National Institute of Diabetes and Digestive and Kidney Diseases, Diabetes, Endocrine, and Obesity Branch, National Institutes of Health, Bethesda, MD, USA
SOURCE: Thyroid (2014), 24(8), 1223-1231
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2013.0621
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Background: Thyroid dysfunction is a common adverse event associated with tyrosine kinase inhibitors (TKI), but its underlying pathophysiol. is unclear. Cabozantinib is a novel TKI currently Food and Drug Administration approved for advanced medullary thyroid cancer and tested in clin. trials on solid tumors including prostate, liver, bladder, breast, and ovarian cancer. Methods: We analyzed the thyroid function of patients enrolled in two phase 2 clin. trials using cabozantinib at the National Institutes of Health Clin. Center. Two cases of thyroiditis associated with cabozantinib therapy are presented in detail, and a systematic review of the literature on TKI-associated thyroid dysfunction is also discussed. Results: Between Sept. 2012 and Sept. 2013, 33 patients were treated with cabozantinib, and follow-up thyroid function tests were available for 31 (20 males, 11 females; age 59±1 years). Thyroid dysfunction was recorded in the majority of patients (93.1%), with a predominance of subclin. hypothyroidism. Two cases showed a biphasic pattern of thyroid dysfunction characterized by a transient thyrotoxicosis followed by hypothyroidism. Color Doppler demonstrated an increase in vascularization during the thyrotoxic phase, but no uptake was visualized on nuclear medicine imaging. A systematic review of the literature resulted in the identification of 40 original manuscripts, of which 13 were case series and 6 were case reports describing TKI-associated thyroid dysfunction. Conclusion: TKI therapy often results in clin. significant thyroid dysfunction. Cabozantinib treatment commonly results in thyroid dysfunction varying from subclin. hypothyroidism to symptomatic thyrotoxicosis. Early detection and characterization of cabozantinib-associated thyroid dysfunction and close follow-up are essential to provide adequate management of this common adverse event.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(review of two ongoing trials for metastatic bladder cancer and sarcoma and cabozantinib-induced thyroid dysfunction)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 219 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1212244 CAPLUS Full-text
DOCUMENT NUMBER: 161:731791
TITLE: Cabozantinib: A Review of Its Use in Patients with Medullary Thyroid Cancer
AUTHOR(S): Hoy, Sheridan M.
CORPORATE SOURCE: Springer, Auckland, N. Z.
SOURCE: Drugs (2014), 74(12), 1435-1444
CODEN: DRUGAY; ISSN: 0012-6667
DIGITAL OBJECT ID: 10.1007/s40265-014-0265-x
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

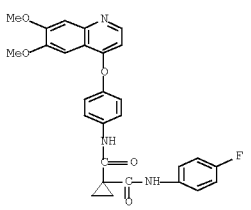
AB A review. Cabozantinib (Cometriq) is an orally administered small mol. inhibitor of multiple tyrosine kinase receptors, including those involved in the pathogenesis of medullary thyroid cancer (MTC) [i.e. rearranged during transfection (RET), MET and vascular endothelial growth factor receptor (VEGFR)-2]. Cabozantinib is indicated for the treatment of adults with progressive, unresectable locally advanced (in the EU) or metastatic (in the EU and USA) MTC. Compared with placebo, cabozantinib significantly prolonged progression-free survival, reflecting a 72 % reduction in the risk of disease progression or death, in patients with unresectable, locally advanced or metastatic MTC participating in a multinational, phase III study. A significantly higher proportion of patients receiving cabozantinib than those receiving placebo achieved an objective response or disease stabilization (i.e. a complete or partial response, or stable disease). The overall survival benefit with cabozantinib is as yet unclear, with no significant benefit observed in two interim analyses (one prespecified, and one unplanned and conducted at the request of the US FDA). The tolerability profile of oral cabozantinib is typical for a small mol. targeting the VEGFR and other tyrosine kinase-mediated pathways, with adverse events associated with the inhibition of the VEGF pathway (e.g. gastrointestinal perforation, hemorrhage, hypertension and venous thrombosis) reported in the phase III study. Treatment-emergent adverse events were generally managed with supportive therapy, dose redns. and/or dose interruptions. Although final overall survival data are awaited, current evidence suggests cabozantinib to be a valuable treatment option for adults with progressive, unresectable locally advanced or metastatic MTC.

IT 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cabozantinib in patients with medullary thyroid cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

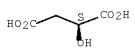
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

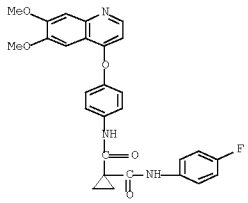
L4 ANSWER 220 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1205266 CAPLUS Full-text
DOCUMENT NUMBER: 161:269288
TITLE: Hydrogen-bond surrogate peptides and peptidomimetics for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer
INVENTOR(S): Arora, Paramjit S.; Pan, Quintin; Mapp, Anna
PATENT ASSIGNEE(S): New York University, USA; The Ohio State University Research Foundation; University of Michigan
SOURCE: PCT Int. Appl., 98pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014113792	A1	20140724	WO 2014-US12331	20140121
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20140205681	A1	20140724	US 2014-14160018	20140121
US 20140220159	A1	20140807	US 2014-14160001	20140121
EP 2964245	A1	20160113	EP 2014-740418	20140121
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PRIORITY APPLN. INFO.: US 2013-61754574 P 20130119
US 2013-61874190 P 20130905
WO 2014-US12331 W 20140121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 161:269288

AB The present invention relates to peptidomimetics for reactivating p53. Methods of using the peptidomimetics are also disclosed. One aspect of the present invention relates to a peptidomimetic, where the peptidomimetic mimics a helix having the formula X1-X2-X2-X3-X2-X2-X1-X4, wherein each X1 is any neg. charged residue, each X2 is any hydrophobic residue, X3 is any pos.-charged residue, and X4 is any polar residue. Addnl., the peptidomimetic may contain one or more bridges linking the side chains of its component amino acids. Another aspect of the present invention relates to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, the method comprising administering to the subject a peptidomimetic of the present invention under conditions effective to treat or prevent the disorder. Another aspect of the present invention relates to a method of inducing apoptosis and decreasing survival and/or proliferation of a cell, the method comprising contacting the cell with a peptidomimetic. In this study, the authors took a novel approach and functionally reactivated p53 in Human papillomaviruses (HPV)-pos. head and neck squamous cell carcinoma (HNSCC) by blocking the interaction between E6 and p300. Ectopic expression of the CH1 domain of p300 squelched E6 to disrupt E6-p300 association resulting in an increase in p53 acetylation, accumulation, and activity. CH1 domain inhibitors reactivated p53 and dramatically potentiated the efficacy of cisplatinum in HPV-pos. HNSCC. Taken together, the authors work revealed a novel druggable approach to reactivate p53 in HPV-pos. HNSCC that is expected to translate to other HPV-pos. carcinomas.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidomimetics for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer and combination with other agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

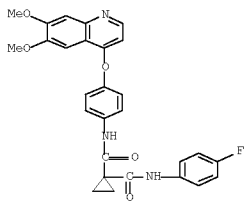
L4 ANSWER 221 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1202788 CAPLUS Full-text
DOCUMENT NUMBER: 161:269285
TITLE: Oligooxopiperazines for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer
INVENTOR(S): Arora, Paramjit S.; Pan, Quintin; Mapp, Anna
PATENT ASSIGNEE(S): New York University, USA; The Ohio State University Research Foundation; The Regents of the University of Michigan
SOURCE: PCT Int. Appl., 95pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014113794	A2	20140724	WO 2014-US12337	20140121
WO 2014113794	A3	20140912		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2898329	A1	20140724	CA 2014-2898329	20140121
US 20140205655	A1	20140724	US 2014-14160037	20140121
AU 2014207311	A1	20150820	AU 2014-207311	20140121
EP 2945631	A2	20151125	EP 2014-741084	20140121
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 105246481	A	20160113	CN 2014-80010794	20140121
JP 2016510327	T	20160407	JP 2015-553892	20140121

PRIORITY APPLN. INFO.: US 2013-61754575 P 20130119
WO 2014-US12337 W 20140121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:269285; MARPAT 161:269285

AB The present invention relates to oligooxopiperazines for reactivating p53. Methods of using the oligooxopiperazines are also disclosed. A first aspect of the present invention relates to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, the method comprising administering to the subject an oligooxopiperazine that substantially mimics helix αB of the C-terminal transactivation domain of Hypoxia-Inducible Factor Iα under conditions effective to treat or prevent the disorder. A second aspect of the present invention relates to a method of inducing apoptosis or decreasing survival and/or proliferation of a cell, the method comprising contacting the cell with an oligooxopiperazine. In this study, the authors took a novel approach and functionally reactivated p53 in Human papillomaviruses (HPV)-pos. head and neck squamous cell carcinoma (HNSCC) by blocking the interaction between E6 and p300. Ectopic expression of the CH1 domain of p300 squelched E6 to disrupt E6-p300 association resulting in an increase in p53 acetylation, accumulation, and activity. CH1 domain inhibitors reactivated p53 and dramatically potentiated the efficacy of cisplatinum in HPV-pos. HNSCC. Taken together, the authors work revealed a novel druggable approach to reactivate p53 in HPV-pos. HNSCC that is expected to translate to other HPV-pos. carcinomas. HMD: helix αB of C-terminal transactivation domain, of HIF-1α, mimics.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligooxopiperazines for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer and combination with other agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 222 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1160177 CAPLUS Full-text
DOCUMENT NUMBER: 161:239766
TITLE: Androgen receptor modulator for treatment of prostate cancer and other conditions
INVENTOR(S): Chen, Isan; Hager, Jeffrey H.; Maneval, Edna Chow; Herbert, Mark R.; Smith, Nicholas D.
PATENT ASSIGNEE(S): Aragon Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 46pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

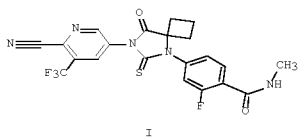
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140199236	A1	20140717	US 2014-14151106	20140109
CA 2898025	A1	20140724	CA 2014-2898025	20140109
WO 2014113260	A1	20140724	WO 2014-US10777	20140109
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US,				

UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

AU 2014207839	A1	20150723	AU 2014-207839		20140109
IL 239741	A	20150831	IL 2014-239741		20140109
KR 2015105464	A	20150916	KR 2015-7021865		20140109
CN 105007920	A	20151028	CN 2014-80015802		20140109
EP 2945628	A1	20151125	EP 2014-701865		20140109
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
JP 2016508991	T	20160324	JP 2015-552756		20140109
AR 94654	A1	20150819	AR 2014-100116		20140113
CR 20150357	A	20150824	CR 2015-357		20150708
MX 2015009090	A	20151005	MX 2015-9090		20150714
PRIORITY APPLN. INFO.:			US 2013-61752842	P	20130115
			WO 2014-US10777	W	20140109

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

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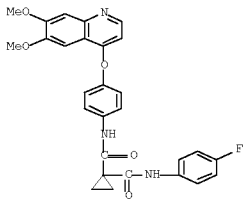
I

AB The invention discloses the androgen receptor modulator I for the treatment of prostate cancer in combination with other therapeutic options and for the treatment of diseases or conditions that are amenable to treatment with the androgen receptor modulator, as well as pharmaceutical compns. and medicaments that include I.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androgen receptor modulator for treatment of prostate cancer and other conditions)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 224 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1134083 CAPLUS Full-text

DOCUMENT NUMBER: 162:254986

TITLE: A Melanoma Cell State Distinction Influences Sensitivity to MAPK Pathway Inhibitors

AUTHOR(S): Konieczkowski, David J.; Johannessen, Cory M.; Abudayyeh, Omar; Kim, Jong Wook; Cooper, Zachary A.; Piris, Adriano; Frederick, Dennie T.; Barzily-Rokni, Michal; Straussman, Ravid; Haq, Rizwan; Fisher, David E.; Mesirov, Jill P.; Hahn, William C.; Flaherty, Keith T.; Wargo, Jennifer A.; Tamayo, Pablo; Garraway, Levi A.

CORPORATE SOURCE: Broad Institute of Harvard and MIT, Cambridge, MA, USA

SOURCE: Cancer Discovery (2014), 4(7), 816-827
CODEN: CDAIB2; ISSN: 2159-8274

DIGITAL OBJECT ID: 10.1158/2159-8290.CD-13-0424

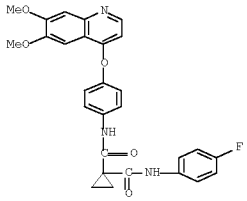
PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Most melanomas harbor oncogenic BRAFv600 mutations, which constitutively activate the MAPK pathway. Although MAPK pathway inhibitors show clin. benefit in BRAFV600-mutant melanoma, it remains incompletely understood why 10% to 20% of patients fail to respond. Here, we show that RAF inhibitor-sensitive and inhibitor-resistant BRAFv600-mutant melanomas display distinct transcriptional profiles. Whereas most drug-sensitive cell lines and patient biopsies showed high expression and activity of the melanocytic lineage transcription factor MITF, intrinsically resistant cell lines and biopsies displayed low MITF expression but higher levels of NF-κ signaling and the receptor tyrosine kinase AXL. In vitro, these MITF-low/NF-κβ-high melanomas were resistant to inhibition of RAF and MEK singly or in combination, and ERK. Moreover, in cell lines, NF- activation antagonized MITF expression and induced both resistance marker genes and drug resistance. Thus, distinct cell states characterized by MITF or NF-κβ activity may influence intrinsic resistance to MAPK pathway inhibitors in BRAFv600-mutant melanoma.

IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 223 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1154296 CAPLUS Full-text

DOCUMENT NUMBER: 161:209516

TITLE: Predictive biomarker and method for combination therapy of EGFR and c-MET inhibitors in non-small cell lung cancer with wild type EGFR

INVENTOR(S): Lee, Mun Ja; Kim, Hyeon Jeong; Kang, Han Na

PATENT ASSIGNEE(S): JEUK Co., Ltd., S. Korea

SOURCE: Repub. Korea, 20pp.
CODEN: KRXXFC

DOCUMENT TYPE: Patent

LANGUAGE: Korean

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 1418970	B1	20140711	KR 2013-29977	20130320
PRIORITY APPLN. INFO.:			KR 2013-29977	20130320

AB The title method comprises the steps of: detg. the p53 genotypes of patients, separating out the patients having cooperation tumor effect probability of combination therapy according to EGFR and c-MET inhibitors. Therefore, the condition of p53 can be used as predicative factor for combination therapy of EGFR and c-MET inhibitors.

IT 849217-68-1, Cabozantinib, co-use with EGFR inhibitors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MET inhibitor; predictive biomarker and method for combination therapy of EGFR and c-MET inhibitors in non-small cell lung cancer with wild type EGFR)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

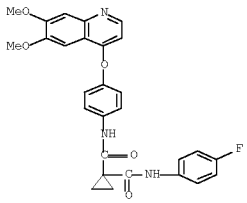
(RAF inhibitor resistant human melanoma cells carrying mutant BRAF showed low MITF and high NFκB levels which influence intrinsic resistance to MAPK pathway inhibitors)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

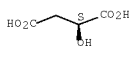
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 225 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1064742 CAPLUS Full-text

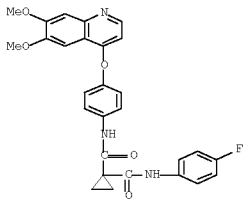
DOCUMENT NUMBER: 161:455975

TITLE: A targeted next-generation sequencing assay detects a high frequency of therapeutically targetable alterations in primary and metastatic breast cancers:

implications for clinical practice
AUTHOR(S): Vasan, Neil; Yelensky, Roman; Wang, Kai; Moulder, Stacy; Dzimitrowicz, Hannah; Avritscher, Rony; Wang, Bauang; Wu, Yun; Cronin, Maureen T.; Palmer, Gary; Symmans, W. Fraser; Miller, Vincent A.; Stephens, Phiup; Pusztai, Lajos
CORPORATE SOURCE: Yale University School of Medicine, Connecticut, New Haven, USA
SOURCE: Oncologist (2014), 19(5), 453-458
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2013-0377
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English

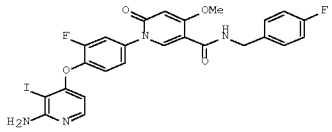
AB Background. The aim of this study was to assess the frequency of potentially actionable genomic alterations in breast cancer that could be targeted with approved agents or investigational drugs in clin. trials using a next-generation sequencing-based genomic profiling assay performed in a Clin. Laboratory Improvement Amendments-certified and College of American Pathologists-accredited com. laboratory Methods. Fifty-one breast cancers were analyzed, including primary tumor biopsies of 33 stage I-II and 18 stage IV cancers (13 soft tissue, 3 liver, and 2 bone metastases). We assessed 3,230 exons in 182 cancer-related genes and 37 introns in 14 genes often rearranged in cancer for base substitutions, indels, copy number alterations, and gene fusions. The average median sequencing depth was 1,154×. Results. We observed 158 genomic alterations in 55 genes in 48 of 51 (94%) tumors (mean 3.1, range 0-9). The average number of potentially therapeutically relevant alterations was similar in primary (1.6, range 0-4) and in heavily pretreated metastatic cancers (2.0, range 0-4) (p = .24). The most common actionable alterations were in PIK3CA (n = 9, phosphatidylinositol 3-kinase [PI3K]/mammalian target of rapamycin [mTOR] inhibitors), NF1 (n = 7, PI3K/mTOR/mitogen-activated protein kinase inhibitors), v-akt murine thymoma viral oncogene homolog 1-3 (n = 7, PI3K/mTOR/AKT inhibitors), BRCA1/2 (n = 6, poly[ADP-ribose] polymerase inhibitors), and CCND1,2 and CCNE (n = 8)/cycline dependent kinase (CDK)6 (n = 1) (CDK4/6 inhibitors), KIT (n = 1, imatinib/sunitinib), ALK (n = 1, crizotinib), FGFR1,2 (n = 5, fibroblast growth factor receptor inhibitors), and EGFR (n = 2, epidermal growth factor receptor inhibitors). Our sequencing assay also correctly identified all six cases with HER2 (ERBB2) amplification by fluorescence in situ hybridization when tumor content was adequate. In addition, two known activating HER2 mutations were identified, both in unamplified cases. Conclusion. Overall, 84% of cancers harbored at least one genomic alteration linked to potential treatment options. Systematic evaluation of the predictive value of these genomic alterations is critically important for further progress in this field.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeted next-generation sequencing assay detects a high frequency of therapeutically targetable alterations in primary and metastatic breast cancers and its implications for clin. practice)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

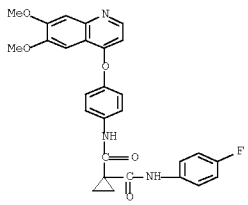
L4 ANSWER 226 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1049484 CAPLUS Full-text
DOCUMENT NUMBER: 161:246290
TITLE: Design, synthesis and evaluation of highly selective pyridone-based class II MET inhibitors
AUTHOR(S): She, Nengfang; Zhuo, Linsheng; Jiang, Wen; Zhu, Xiaolei; Wang, Jia; Ming, Zhihui; Zhao, Xinge; Cong, Xin; Huang, Wei
CORPORATE SOURCE: Key Laboratory of Pesticide and Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Wuhan, 430079, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2014), 24(15), 3351-3355
CODEN: BMCLE8; ISSN: 0960-894X
DIGITAL OBJECT ID: 10.1016/j.bmcl.2014.05.097
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 161:246290
GI



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AB The high incidence of MET oncogene activation in human malignancies has prompted researchers to develop MET inhibitors. As part of our efforts to developing effective and safe therapeutic agents against MET-dependent tumors, a pyridone-based class II MET inhibitor, namely, 1-(4-((2-amino-3-iodopyridin-4-yl)-oxy)-3-fluorophenyl)-N-(4-fluorobenzyl)- 4-methoxy-6-oxo-1,6-dihydropyridine-3-carboxamide (3s, I), was identified. Knowledge of the binding mode of class II MET inhibitors led to the design of new inhibitors that utilize 2-pyridone to conformationally restrain key pharmacophoric groups within the mol. Integrated mol. docking and SAR studies resulted in the discovery of a novel class of pyridone MET inhibitors with high potency (IC50 of 0.005 μM) and efficient selectivity (>5000 fold) to VEGFR-2, c-Kit and RET kinases.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(docking and kinase selectivity study; design, synthesis and evaluation of highly selective pyridone-based class II MET inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

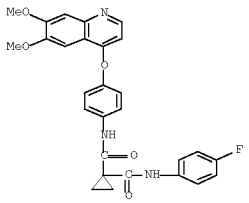


REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 227 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1006107 CAPLUS Full-text
DOCUMENT NUMBER: 161:238658
TITLE: Advanced thyroid cancers: new era of treatment
AUTHOR(S): Mohammed, Amrallah A.; El-Shentenawy, Ayman
CORPORATE SOURCE: Oncology Center, King Abdullah Medical City-Holy Capital, Makkah, 21995, Saudi Arabia
SOURCE: Medical Oncology (New York, NY, United States) (2014), 31(7), 1-8
CODEN: MONCEZ; ISSN: 1357-0560
DIGITAL OBJECT ID: 10.1007/s12032-014-0049-x
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Since chemotherapy has been shown to be unsuccessful in case of advanced thyroid carcinomas, the research for new therapies is fundamental. Clin. trials of many tyrosine kinase inhibitors as well as anti-angiogenic inhibitors suggest that patients with thyroid cancer could have an advantage with new target therapy. Recently, Food and Drug Administration approved two targeted therapies, vandetanib and cabozantinib for the treatment of metastatic thyroid carcinomas with acceptable outcome. We summarized the results and the toxic effects associated with these treatments reported in clin. trials. Future trials should aim at combinations of targeted agents with or without other treatment modalities to obtain a more effective result in thyroid carcinoma treatment.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new era of treatment for advanced thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

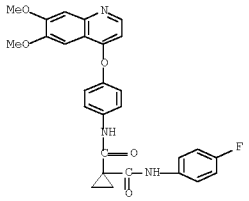
L4 ANSWER 228 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:969861 CAPLUS Full-text
DOCUMENT NUMBER: 161:455940
TITLE: Role of salvage targeted therapy in differentiated thyroid cancer patients who failed first-line sorafenib
AUTHOR(S): Dadu, Ramona; Devine, Catherine; Hernandez, Mike; Waguespack, Steven G.; Busaidy, Naifa L.; Hu, Mimi I.; Jimenez, Camilo; Habra, Mouhammad A.; Sellin, Rena V.; Ying, Anita K.; Cote, Gilbert J.; Sherman, Steven I.; Cabanillas, Maria E.
CORPORATE SOURCE: Departments of Endocrine Neoplasia and Hormonal Disorders, Baylor College of Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Journal of Clinical Endocrinology and Metabolism (2014), 99(6), 2086-2094
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2013-3588
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Context: Sorafenib, a tyrosine kinase inhibitor, is a common first-line therapy for advanced differentiated thyroid cancer (DTC). However, responses are not durable and drug toxicity remains a problem. Objective: The objective of the study was to determine the efficacy of salvage therapy after first-line sorafenib failure. Design: This was a retrospective review at M. D. Anderson Cancer Center from Jan. 2005 to May 2013. Patients: The study included patients with metastatic DTC who received salvage therapy after their initial sorafenib failure (group 2). Patients who received first-line sorafenib only (group 1) were evaluated for comparison of overall survival (OS). Outcome Measures: Progression-free survival, best response, and median OS were measured. Results: Sixty-four patients with metastatic, radioactive iodine refractory DTC were included; 35 were in group 1 and 25 were in group 2, and the groups were well balanced. Median OS of all 64 patients receiving first line sorafenib was 37 mo; median OS was significantly longer with salvage therapy compared with sorafenib alone (58 vs 28 mo, P = .013). In group 2, 17 patients were evaluable for best response, although two patients had toxicity with sorafenib, which was discontinued before restaging. Best responses with first-line sorafenib were partial response in 2 of 15 (13%), stable disease in 10 of 15 (67%), and progressive disease in 3 of 15 (20%) patients. With salvage therapy, partial responses were seen in 7 of 17 (41%) and stable disease in 10 of 17 (59%) patients. Median progression-free survival was 7.4 mo with first-line sorafenib and 11.4 mo with salvage therapy. Salvage therapy included sunitinib (n = 4), pazopanib (n = 3), cabozantinib (n = 4), lenvatinib (n = 3), and vemurafenib (n = 3). Conclusions: Other targeted agents are effective salvage treatments after sorafenib failure, despite similar mechanisms of action, and should be offered to patients who are able to receive salvage therapy.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salvage targeted treatment with sunitinib, pazopanib, cabozantinib, lenvatinib and vemurafenib was effective in treatment of patient with metastatic differentiated thyroid cancer who failed first-line sorafenib therapy)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 229 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:951549 CAPLUS Full-text
DOCUMENT NUMBER: 161:86164
TITLE: Preparation of pyridine compounds as protein tyrosine kinase inhibitors for treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wang, Ruyong; Wang, Liang
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 158pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014089324	A1	20140612	WO 2013-US73367	20131205

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

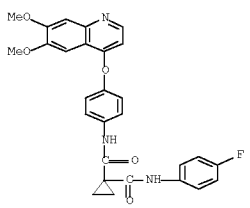
PRIORITY APPLN. INFO.: US 2012-61734903 P 20121207
US 2013-61880184 P 20130920
OTHER SOURCE(S): CASREACT 161:86164; MARPAT 161:86164
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridinyl compds. of general formula I, pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. For I, each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; X is C6-C10 aryl or 5-10 membered heteroaryl that are optionally substituted; and Y is an (un)substituted bicyclic heterocyclyl. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 6-step reaction that culminated in coupling of intermediates III and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-ol. Example compds. of the invention were tested in ALK and c-Met kinase inhibition assays. Pharmacokinetic profiles were also examined in rats, as was compound stability in human and rat liver microsomes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyridine compds. as protein tyrosine kinase inhibitors for treatment of proliferative diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



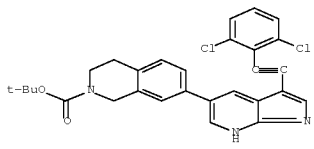
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 230 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:951212 CAPLUS Full-text
DOCUMENT NUMBER: 161:94410
TITLE: Alkynyl compounds and methods of use
INVENTOR(S): Xi, Ning; Li, Xiaobo; Zhou, Shiqing
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014089280	A1	20140612	WO 2013-US73286	20131205

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

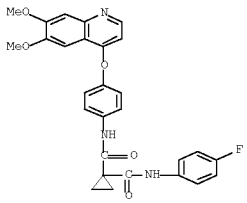
PRIORITY APPLN. INFO.: US 2012-61734897 P 20121207
OTHER SOURCE(S): CASREACT 161:94410; MARPAT 161:94410
GI



AB The present invention provides novel substituted alkynyl compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkynyl compds. and methods of use)

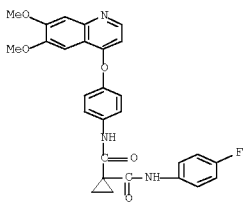
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 231 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:943695 CAPLUS Full-text
DOCUMENT NUMBER: 161:196584
TITLE: Adverse events of targeted therapies
AUTHOR(S): Klastersky, Jean A.
CORPORATE SOURCE: Institut Jules Bordet, Centre des Tumeurs de l'Universite Libre de Bruxelles, Brussels, Belg.
SOURCE: Current Opinion in Oncology (2014), 26(4), 395-402
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0000000000000096
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Purpose of review: There is currently an explosion in the no. of so-called targeted therapies. As new indications for these agents multiply, there is also an increase of new and less new side-effects. Recent findings: Given this rapidly evolving field, any literature on that topic is rapidly obsolete and needs re-evaluation. Summary: Targeted therapies are associated with a wide spectrum of adverse events, which cannot always be easily separated from the complications linked to cancer, its therapy, and comorbidities. A high awareness of these events might improve the patient's quality of life and contribute to the recognition of new syndromes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adverse events of targeted therapies)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

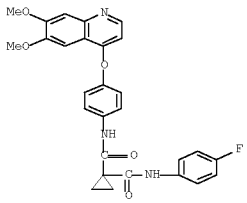
cabozantinib reduced the number of metastatic lesions in the lung and liver in the exptl. metastatic mouse model. Patients with HCC with high level of p-MET are associated with resistance to adjuvant sorafenib treatment. The dual blockade of VEGFR2 and MET by cabozantinib has significant antitumor activities in HCC, and the activation of MET in HCC may be a promising efficacy-predicting biomarker. Clin Cancer Res; 20(11); 2959-70. ©2014 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib suppresses tumor growth and metastasis in hepatocellular carcinoma by dual blockade of VEGFR2 and MET)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 233 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:923002 CAPLUS Full-text
DOCUMENT NUMBER: 161:99226
TITLE: Heterocyclic alkynyl compound, and its use and application as cell proliferation inhibitor and for regulating the activity of protein kinases
INVENTOR(S): Xi, Ning; Li, Xiaobo; Zhou, Shiqing
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 64pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

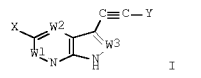
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103833753	A	20140604	CN 2013-10590780	20131121
PRIORITY APPLN. INFO.:			CN 2012-10477798 A	20121122



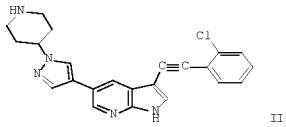
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 232 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:926742 CAPLUS Full-text
DOCUMENT NUMBER: 161:316322
TITLE: Cabozantinib Suppresses Tumor Growth and Metastasis in Hepatocellular Carcinoma by a Dual Blockade of VEGFR2 and MET
AUTHOR(S): Xiang, Qingfeng; Chen, Weiqiang; Ren, Meng; Wang, Jingnan; Zhang, Hongwu; Deng, David Y. B.; Zhang, Lei; Shang, Changzhen; Chen, Yajin
CORPORATE SOURCE: Departments of Hepatopancreatobiliary Surgery, Sun Yat-sen University, Guangzhou, Peop. Rep. China
SOURCE: Clinical Cancer Research (2014), 20(11), 2959-2970
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-2620
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB MET signaling was suggested a potential role in hepatocellular carcinoma (HCC) and associated with prometastasis during antiangiogenesis therapy. We investigated the potential association between MET expression and therapeutic response to sorafenib in patients with HCC. Antitumor effects of cabozantinib, a dual inhibitor of MET and VEGFR2, were examined in cultured HCC cells as well as in vivo models. Total MET and phosphorylated MET (p-MET) were measured in 29 resected HCC specimens, and correlated with response to sorafenib as postoperative adjuvant therapy. In the second set of expts. using cultured HCC cells, and mouse xenograft and metastatic models, effects of cabozantinib were examined High level of p-MET in resected HCC specimens was associated with resistance to adjuvant sorafenib therapy. In cultured HCC cells that expressed p-MET, cabozantinib inhibited the activity of MET and its downstream effectors, leading to G1-phase arrest. Cabozantinib inhibited tumor growth in p-MET-pos. and p-MET-neg. HCC by decreasing angiogenesis, inhibiting proliferation, and promoting apoptosis, but it exhibited more profound efficacy in p-MET-pos. HCC xenografts. Cabozantinib blocked the hepatocyte growth factor (HGF)-stimulated MET pathway and inhibited the migration and invasion of the HCC cells. Notably,

CN 2013-10116694 A 20130403
OTHER SOURCE(S): MARPAT 161:99226
GI

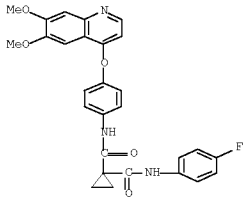


I



II

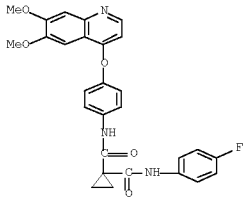
AB The present invention provides new substituted alkynyl compds. with the formula of I [W1-4 independently = N or CRc, wherein Rc = H, D, F, Cl, Br, etc.; X = Ph, pyridinyl, pyrrolyl, pyrazolyl, etc.; Y = (un)substituted aryl or heteroaryl], pharmaceutically acceptable salts thereof, pharmaceutical formulation thereof, and their use in regulating the activity of protein kinases and regulating the signal response in cells or between cells. Thus, e.g., II was prepared in a multi-step synthesis. Compds. of the invention were tested for their stability and Alk, c-Met kinase inhibitory activity, e.g., II showed IC50 value of 58 nM against Alkaline The present invention also relates to pharmaceutical compns. comprising a compound of the present invention, and using the pharmaceutical composition for treating a mammal, particularly to human hyperproliferative disorders.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; heterocyclic alkynyl compound, and its use and application as cell proliferation inhibitor and for regulating the activity of protein kinases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 234 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:913474 CAPLUS Full-text
DOCUMENT NUMBER: 161:46548
TITLE: Cabozantinib capsule composition and its production method
INVENTOR(S): Wang, Luanqiu; Wang, Xinyao
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103830203	A	20140604	CN 2014-10078549	20140305
PRIORITY APPLN. INFO.:			CN 2014-10078549	20140305

AB The invention provides a cabozantinib capsule compn. and its prodn. method. The cabozantinib capsule composition is composed of cabozantinib 10-60wt%, carrier 15-70 wt%, organic solvent 10-30wt%, surfactant 0.5-3.0wt%, micronized silica gel 1.0-3.0wt% and starch 5.0-20wt%. The carrier comprises one or more of glycerol monostearate, polyethylene glycol 6000, cetyl alc. and octyl alc. The organic solvent comprises one or more of ethanol, methanol and acetone. The surfactant comprises one or more of sodium dodecyl sulfate, Tween 80 and lecithin. The production method includes adding carrier into organic solvent, heating to 60°C, adding cabozantinib and surfactant, vacuum drying at 40°C, comminution by gas stream to obtain powder with grain size of 1-8 μm, adding micronized silica gel and starch, mixing, and packaging in. The produced cabozantinib capsule preparation has good oral absorption, high dissoln. rate, high bioavailability, and can remarkably inhibit the growth of tumor volume The invention has simple preparation process, low cost, and applicability for com. process.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for producing cabozantinib capsule composition)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



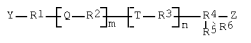
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 235 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:873778 CAPLUS Full-text
DOCUMENT NUMBER: 161:77594
TITLE: Hydrophilic linkers and their uses for conjugation of drugs to cell binding molecules
INVENTOR(S): Zhao, R. Yongxin
PATENT ASSIGNEE(S): Hangzhou Dac Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 102pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

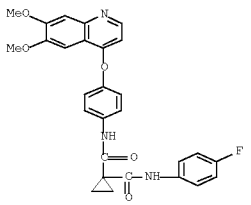
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014080251	A1	20140530	WO 2012-IB56700	20121124
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2891280	A1	20140530	CA 2012-2891280	20121124
AU 2012395148	A1	20150521	AU 2012-395148	20121124
EP 2922818	A1	20150930	EP 2012-888899	20121124
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

JP 2016501859	T	20160121	JP 2015-543532	20121124
US 20150250896	A1	20150910	US 2015-14432073	20150327
PRIORITY APPLN. INFO.:			WO 2012-IB56700 W	20121124

OTHER SOURCE(S): CASREACT 161:77594; MARPAT 161:77594
GI



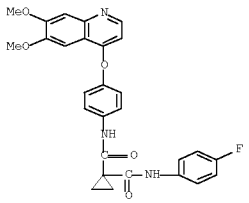
AB Prepn. of cell binding agent-drug conjugates comprising hydrophilic linker of formula (I), wherein:Y represents a functional group that enables reaction with a cell-binding agent; Q and T are either -P(=O)(OM)-, or -S(O)-;m and n are integer from 0 to 5, but not 0 at the same time; In addition, when m = I, n = 0, Q is not -P(=O)(OM)-; or when n = I, m = 0, T is not -P(=O)(OM)-;Z represents a functional group that enables linkage of a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ether, ester, carbamate, carbonate, amine (secondary, tertiary, or quartary), imine, cycloheteroalkyane, heteroarom., alkoxime or amide bond; R1, R2, R3, R4, R5 and R6, are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl, or 1-6 carbon atoms of esters, ether, amide, or polyethyleneoxy unit of formula (OCH2CH2)p, wherein p is an integer from 0 to about 1000, or combination thereof and methods of using such linkers and conjugates in pharmaceutical dosage forms for combination therapy of cancer, autoimmune and infectious diseases are provided.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(hydrophilic linkers and their uses in preparation of cell binding agent-drug conjugates useful in combination therapy of cancer, autoimmune and infectious diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 236 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:814874 CAPLUS Full-text
DOCUMENT NUMBER: 161:466864
TITLE: Aerodigestive Fistula Formation as a Rare Side Effect of Antiangiogenic Tyrosine Kinase Inhibitor Therapy for Thyroid Cancer
AUTHOR(S): Blevins, Dean P.; Dadu, Ramona; Hu, Mimi; Baik, Christina; Balachandran, Diwakar; Ross, William; Gunn, Brandon; Cabanillas, Maria E.
CORPORATE SOURCE: Department of Internal Medicine, University of Texas Health Science Center at Houston, Houston, TX, USA
SOURCE: Thyroid (2014), 24(5), 918-922
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2012.0598
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background: In the past decade, targeted therapy with antiangiogenic drugs has become standard of care for most types of metastatic, progressive thyroid cancer. While these drugs were thought initially to be less toxic than traditional chemotherapy, they can have rare but serious and fatal toxicities. Once such toxicity that has been reported in other tumor types is upper airway fistula formation, which can be life-threatening. Summary: Here, we describe three patients treated with antiangiogenic tyrosine kinase inhibitors at two academic institutions who developed aerodigestive fistula. All three patients had risk factors for fistula formation, which included external beam radiation and/or large tumor with invasion of the tracheal wall. Conclusions: Fistula formation is a known but rare side effect of antiangiogenic tyrosine kinase inhibitors. Knowledge of the risk factors that may predispose thyroid cancer patients to this serious adverse event is vital prior to prescribing antiangiogenics. Particular caution should be observed when using these drugs in patients undergoing radiation therapy or surgery, or in patients whose tumor is invading vital structures of the neck, as they may be at higher risk of developing this rare complication. In these patients, antiangiogenic tyrosine kinase inhibitors should be used cautiously, patients should be aware of the risk, and physicians should monitor patients for symptoms of fistula.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aerodigestive fistula formation as a rare side effect of antiangiogenic tyrosine kinase inhibitor therapy for thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 237 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:794981 CAPLUS Full-text
DOCUMENT NUMBER: 160:740120
TITLE: Preparation of heteroaromatic compounds as protein kinase modulators for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 57pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140134133	A1	20140515	US 2013-14076256	20131110
CA 2889346	A1	20140522	CA 2013-2889346	20131110
WO 2014078211	A1	20140522	WO 2013-US69366	20131110

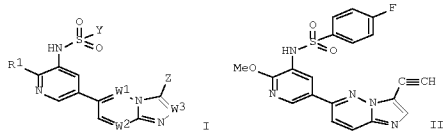
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

AU 2013345107	A1	20150430	AU 2013-345107	20131110
AU 2013345107	B2	20160225		
CN 104755085	A	20150701	CN 2013-80054625	20131110
KR 2015083833	A	20150720	KR 2015-7008264	20131110
EP 2919784	A1	20150923	EP 2013-855522	20131110

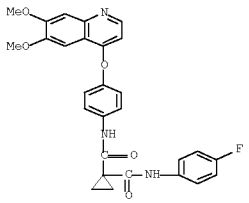
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2015536994	T	20151224	JP 2015-541973	20131110
PRIORITY APPLN. INFO.:			US 2012-61726139 P	20121114
			WO 2013-US69366 W	20131110

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:740120; MARPAT 160:740120
GI



AB The invention provides heteroarom. derivs. and pharmaceutically acceptable salts and formulations thereof useful in modulating the protein kinase activity, especially phosphatidylinositol 3-kinases (PI3K) and mTOR kinase, and in modulating inter- and/or intra-cellular signaling activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Compds. of formula I [wherein W1, W2, and W3 are independently N or CRc; Z is D CN, N3, etc.; Y is C1-C6 alkyl, C3-C6 cycloalkyl, C3-C6 heterocyclyl, etc.; R1 is H, Cl, C3-C6 cycloalkyl, etc.; each Rc is independently H, D, F, etc.] or stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, prodrugs, or pharmaceutically acceptable salts thereof are claimed and exemplified. For example, II was prepared in five steps (procedure given). Candidate compds. of I were assayed for their stability in liver microsomes, their oral and i.v. bioavailability, and inhibitory activity against PI3K and mTOR kinase (data given).
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of heteroarom. compds. as protein kinase modulators for
treatment of hyperproliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 238 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:718961 CAPLUS Full-text
DOCUMENT NUMBER: 160:630742
TITLE: Replication-competent retroviral vectors for gene therapy using mini-promoters
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Lin, Amy H.; Logg, Christopher R.; Kasahara, Noriyuki
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: PCT Int. Appl., 89pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014066700	A1	20140501	WO 2013-US66709	20131024

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2909324	A1	20150826	EP 2013-849839	20131024

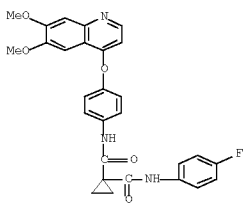
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

CN 104884627	A	20150902	CN 2013-80067486	20131024
JP 2015533510	T	20151126	JP 2015-539817	20131024
US 20150273029	A1	20151001	US 2015-14438564	20150424
PRIORITY APPLN. INFO.:			US 2012-61718610 P	20121025
			WO 2013-US66709 W	20131024

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Compact replicating retroviral vectors using a minimal promoter to express a therapeutic gene with a size of 0.9-1.9 kb are described. An internal ribosome entry sequence may be used for polycistronic expression cassettes. The vectors do not use the prior art SCP1, Ad, or CMV core promoters. Development and optimization of vectors is described.
IT 1140909-48-3, XL-184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in cancer therapy with retroviral gene therapy vectors; retroviral vectors for gene therapy using mini-promoters)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

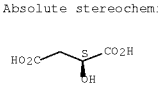
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



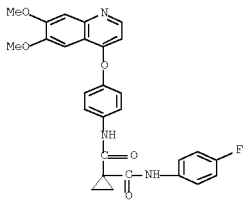
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 239 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:711027 CAPLUS Full-text

DOCUMENT NUMBER: 160:643049
TITLE: Cabozantinib dispersible tablet and preparation method thereof
INVENTOR(S): Peng, Zongyu; Li, Ran; Zheng, Feibo
PATENT ASSIGNEE(S): Qingdao Cancer Hospital, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

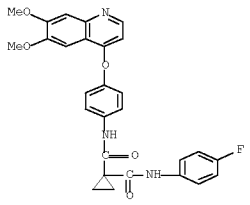
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103751140	A	20140430	CN 2014-10017920	20140115
PRIORITY APPLN. INFO.:			CN 2014-10017920	20140115

AB The invention discloses Cabozantinib dispersible tablet and prepn. method and application thereof. The inventive Cabozantinib dispersible tablet consists of the following component according to weight percentage: Cabozantinib 10-60%, filler 10-40%, disintegrant 10-50%, acidulant 10-50%, binder 0.1-10%, and lubricant and glidant 0.1-20%. Compared with the common tablet, the inventive dispersible tablet contains no surfactant, its solubility, dispersivity, and disintegrability are good, and it can be completely disintegrated within 1 min. The prepared Cabozantinib dispersible tablet has high dissoln. rate, high bioavailability, rapid distribution in vivo, stable quality, and good taste. The preparation method is simple, and suitable for industrial production
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib dispersible tablet)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

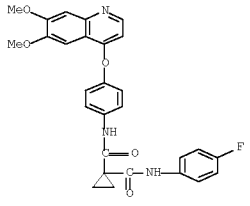


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 240 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:679549 CAPLUS Full-text
DOCUMENT NUMBER: 161:30896
TITLE: Cabozantinib: a new molecular targeted antitumor drug
AUTHOR(S): Zhang, Xiu-ying; Liu, Yao; Bai, Qiu-jiang; Wang, Nan
CORPORATE SOURCE: Department of Pharmacy, Kailuan General Hospital, Tangshan, Hebei Province, 063000, Peop. Rep. China
SOURCE: Yiyao Daobao (2013), 32(11), 1468-1470
CODEN: YDIAAL; ISSN: 1004-0781
DIGITAL OBJECT ID: 10.3870/yydb.2013.11.021
PUBLISHER: Yiyao Daobao Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Cabozantinib, a new mol. targeted antitumor drug, was introduced with several subsections as follow: action mechanisms, pharmacokinetics, adverse reactions, drug interactions, clin. trials, and conclusions.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib: a new mol. targeted antitumor drug)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 241 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:653844 CAPLUS Full-text
DOCUMENT NUMBER: 161:257408
TITLE: Preclinical Evaluation of Imaging Biomarkers for Prostate Cancer Bone Metastasis and Response to Cabozantinib
AUTHOR(S): Graham, Timothy J.; Box, Gary; Tunariu, Nina; Crespo, Mateus; Spinks, Terry J.; Miranda, Susana; Attard, Gerhardt; de Bono, Johann; Eccles, Suzanne A.; Davies, Faith E.; Robinson, Simon P.
CORPORATE SOURCE: Division of Radiotherapy and Imaging, Institute of Cancer Research and Royal Marsden NHS Trust, Surrey, SM2 5NG, UK
SOURCE: Journal of the National Cancer Institute (2014), 106(4), ???
CODEN: JNCIEQ; ISSN: 0027-8874
DIGITAL OBJECT ID: 10.1093/jnci/dju033
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background Prostate cancer is incurable once it has metastasized to the bone. Appropriate preclin. models are lacking. The therapeutic efficacy of the multikinase inhibitor cabozantinib was assessed in an orthotopic xenograft model of castration-resistant prostate cancer (CRPC) bone metastasis using noninvasive, multimodality functional imaging. Methods NOD/SCID mice were injected intratibially with luciferase-expressing ERG (v-ets avian erythroblastosis virus E26 oncogene homolog) rearranged VCaP human prostate carcinoma cells. The response of VCaP xenografts (n = 7 per group) to cabozantinib was investigated using bioluminescence imaging and anatomical and diffusion weighted magnetic resonance imaging. This enabled quantitation of tumor volume and apparent diffusion coefficient (ADC). Bone uptake of technetium-methylene diphosphonate (99mTc-MDP) was assessed by single-photon emission computed tomog. Ex vivo micro computed tomog. was used to quantify bone volume and correlated with appropriate histopathol. Statistical significance was determined using the two-sided Mann-Whitney test or Wilcoxon signed rank test. Results VCaP xenografts were predominantly osteosclerotic with some osteolytic activity. Fluorescent in situ hybridization anal. confirmed retention of ERG oncogene rearrangements. Cabozantinib induced a statistically significant 52% reduction in tumor luminance (P = .02) and stasis in tumor volume after 15 days of treatment. Tumor ADC statistically significantly increased with cabozantinib and was associated with extensive necrosis (after 10 days, mean tumor ADC ± SD = 556±43×10-6 mm2/s vs pretreatment ADC = 485±43×10-6 mm2/s; P = .02). Tumor-associated uptake of 99mTc-MDP was statistically significantly reduced after 3 days of treatment (P = .02), sustained over 15 days treatment, and associated with a statistically significant (P = .048) reduction in bone growth on the tibial cortex, yet a highly statistically significant (P = .001) increase in trabecular bone volume Conclusions The intratibial VCaP model faithfully emulates clin. disease. Cabozantinib exerts potent effects on both tumor and tumor-induced bone matrix remodeling, and quantitation of ADC provides a clin. translatable imaging biomarker for early, sensitive assessment of treatment response in CRPC bone metastasis.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(noninvasive, multimodality functional imaging was effective in imaging biomarkers in response to cabozantinib in xenografted mouse model of human bone metastatic castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 242 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:628215 CAPLUS Full-text
DOCUMENT NUMBER: 160:542029
TITLE: Method for the diagnosis, prognosis and treatment of prostate cancer metastasis
INVENTOR(S): Gomis, Roger; Jean-Mairet, Joel
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 140pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014057357	A2	20140417	WO 2013-IB2866	20131009
WO 2014057357	A3	20140530		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2888122	A1	20140417	CA 2013-2888122	20131009
US 20140105918	A1	20140417	US 2013-14050262	20131009
AU 2013328385	A1	20150507	AU 2013-328385	20131009
EP 2906718	A2	20150819	EP 2013-821939	20131009
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR,				

HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

KR 2015105297	A	20150916	KR 2015-7012297		20131009
CN 104995313	A	20151021	CN 2013-80060218		20131009
JP 2016500517	T	20160114	JP 2015-536237		20131009
MX 2015004610	A	20151022	MX 2015-4610		20150410
US 20150362495	A1	20151217	US 2015-14435128		20150410
PRIORITY APPLN. INFO.:			US 2012-61713318	P	20121012
			WO 2013-IB2866	W	20131009

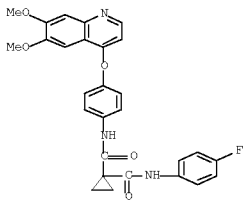
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to a method for the diagnosis or the prognosis of metastasis in prostate cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for the diagnosis or the prognosis of metastasis in prostate cancer, as well as to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which, comprise determining the c-MAF expression level. Finally, the invention relates to the use of a c-MAF inhibitor as therapeutic target for treating the prostate cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MAF gene for diagnosis, prognosis and treatment of prostate cancer metastasis)

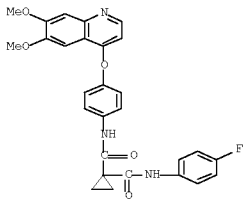
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 243 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2014:581585 CAPLUS Full-text
DOCUMENT NUMBER:	160:555604
TITLE:	Phage display derived peptides highly specific against Mdm2/Mdm4 and methods for treating cancer
INVENTOR(S):	Joseph, Thomas Leonard; Verma, Chandra Shekhar; Lane, David Phillip; Brown, Christopher John
PATENT ASSIGNEE(S):	Agency for Science, Technology and Research, Singapore
SOURCE:	PCT Int. Appl., 61pp. CODEN: PIXXD2



REFERENCE COUNT:	5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 244 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

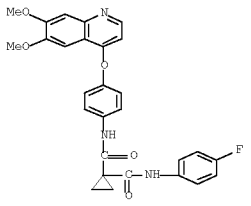
ACCESSION NUMBER:	2014:565947 CAPLUS Full-text
DOCUMENT NUMBER:	161:208503
TITLE:	First-, second-, third-line therapy for mRCC: benchmarks for trial design from the IMDC
AUTHOR(S):	Ko, J. J.; Choueiri, T. K.; Rini, B. I.; Lee, J.-L.; Kroeger, N.; Srinivas, S.; Harshman, L. C.; Knox, J. J.; Bjarnason, G. A.; MacKenzie, M. J.; Wood, L.; Vaishampayan, U. N.; Agarwal, N.; Pal, S. K.; Tan, M.-H.; Rha, S. Y.; Yuasa, T.; Donskov, F.; Bamias, A.; Heng, D. Y. C.
CORPORATE SOURCE:	Tom Baker Cancer Center, University of Calgary, Calgary, AB, Can.
SOURCE:	British Journal of Cancer (2014), 110(8), 1917-1922 CODEN: BJCAAI; ISSN: 0007-0920
DIGITAL OBJECT ID:	10.1038/bjc.2014.25
PUBLISHER:	Nature Publishing Group
DOCUMENT TYPE:	Journal; (online computer file)
LANGUAGE:	English

AB Background: Limited data exist on outcomes for metastatic renal cell carcinoma (mRCC) patients treated with multiple lines of therapy. Benchmarks for survival are required for patient counselling and clin. trial design. Methods: Outcomes of mRCC patients from the International mRCC Database Consortium database treated with 1, 2, or 3+ lines of targeted therapy (TT) were compared by proportional hazards regression. Overall survival (OS) and progression-free survival (PFS) were calculated using different population inclusion criteria. Results: In total, 2705 patients were treated with TT of which 57% received only first-line TT, 27% received two lines of TT, and 16% received 3+ lines of TT. Overall survival of patients who received 1, 2, or 3+ lines of TT were 14.9, 21.0, and 39.2 mo, resp., from first-line TT (P<0.0001). On multivariable anal., 2 lines and 3+ lines of therapy were each associated with better OS (HR=0.738 and 0.626, P<0.0001). Survival outcomes for the subgroups were as follows: for all patients, OS 20.9 mo and PFS 7.2 mo; for those similar to eligible patients in the first-line ADAPT trial, OS 14.7 mo and PFS 5.6 mo; for those similar to patients in first-line TIVO-1 trial, OS 24.8 mo and PFS 8.2 mo; for those similar to patients in second-line INTORSECT trial, OS 13.0 mo and PFS 3.9 mo; and for those similar to patients in the third-line GOLD trial, OS 18.0 mo and PFS 4.4 mo. Conclusions: Patients who are able to receive more lines of TT live longer. Survival benchmarks provide context and perspective when interpreting and designing clin. trials.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(first-, second-, third-line therapy for metastatic renal cell carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT:	7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT:	27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 245 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER:	2014:542996 CAPLUS Full-text
DOCUMENT NUMBER:	161:267984
TITLE:	Bone-targeted therapies in metastatic castration-resistant prostate cancer: evolving paradigms
AUTHOR(S):	El-Amm, Joelle; Freeman, Ashley; Patel, Nihar; Aragon-Ching, Jeanny B.
CORPORATE SOURCE:	Division of Hematology/Oncology, Department of Medicine, George Washington University Medical Center, Washington, DC, 20037, USA
SOURCE:	Prostate Cancer (2013) 210686/1-210686/11, 11 pp. CODEN: PCRACU; ISSN: 2090-312X
DIGITAL OBJECT ID:	10.1155/2013/210686
PUBLISHER:	Hindawi Publishing Corp.
DOCUMENT TYPE:	Journal; General Review; (online computer file)
LANGUAGE:	English

AB A review. Majority of patients with metastatic castrate resistant prostate cancer (mCRPC) develop bone metastases which results in significant morbidity and mortality as a result of skeletal-related events (SREs). Several bone-targeted agents are either in clin. use or in development for

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014055039	A1	20140410	WO 2013-SG428	20131001
WO 2014055039	A9	20141106		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2904000	A1	20150812	EP 2013-844064	20131001

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

US 20150246946	A1	20150903	US 2015-14432729	20150331
PRIORITY APPLN. INFO.:			SG 2012-7302	A 20121001
			WO 2013-SG428	W 20131001

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 160:555604

AB By using a phage display derived peptide as an initial template, compds. have been developed that are highly specific against Mdm2/Mdm4. These compds. exhibit greater potency in p53 activation and protein-protein interaction assays than a compound derived from the p53 wild-type sequence. Unlike nutlin, a small mol. inhibitor of Mdm2/Mdm4, the phage derived compds. can arrest cells resistant to p53 induced apoptosis over a wide concentration range without cellular toxicity, suggesting they are highly suitable for cyclo-therapy. In one embodiment, there is disclosed the peptide comprising or consisting o f the amino acid sequence of SEQ ID NO 1 (TSFXaaiEYWXaa3LLXaai), wherein Xaa3 can be N or A and wherein in case Xaa3 is N, Xaai is not A and/or Xaa2 is not S. In one embodiment, Xaa3 can be any type of amino acid other than A and wherein in case Xaa3 is N, Xaaj is not A and/or Xaa2 is not S. Those peptides have been shown to inhibit the p53:Mdm2 interactions with a nanomolar affinity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL184; phage display derived peptides highly specific against Mdm2/Mdm4 and methods for treating cancer)

RN 849217-68-1 CAPLUS

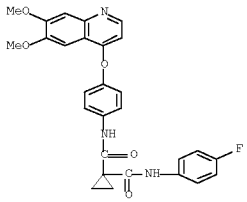
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

prevention of SREs. Bisphosphonates were the first class of drugs investigated for prevention of SREs and zoledronic acid is the only bisphosphonate that is FDA-approved for this indication. Another bone-targeted agent is denosumab which is a fully humanized monoclonal antibody that binds to the RANK-L thereby inhibiting RANK-L mediated bone resorption.While several radiopharmaceuticals were a approved for pain palliation in mCRPC including strontium and samarium, alpharadin is the first radiopharmaceutical to show significant overall survival benefit. Contemporary therapeutic options including enzalutamide and abiraterone have effects on pain palliation and SREs as well. Other novel bone-targeted agents are currently in development, including the receptor tyrosine kinase inhibitors cabozantinib and dasatinib. Emerging therapeutics in mCRPC has resulted in great strides in preventing one of the most significant sources of complications of bone metastases.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evolving paradigms of bone-targeted therapies in metastatic castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 246 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:479457 CAPLUS Full-text

DOCUMENT NUMBER: 160:515456

TITLE: Synthesis method of antitumor therapeutic drug of cabozantinib

INVENTOR(S): Cai, Jianping; Chen, Zengfei; Zhang, Lifeng; Fang, Ying

PATENT ASSIGNEE(S): Suzhou Moer Pharmaceutical Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

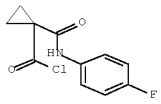
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103664778	A	20140326	CN 2013-10631287	20131127

PRIORITY APPLN. INFO.: CN 2013-10631287 20131127

OTHER SOURCE(S): CASREACT 160:515456; MARPAT 160:515456

GI

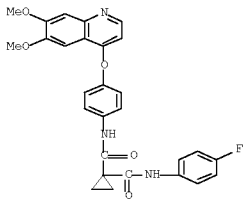


AB The invention discloses a synthesis method of antitumor therapeutic drug of cabozantinib., comprising: using 4-(6, 7- dimethoxy quinoline -4- oxy)-phenylamine to react with 1-((4- fluorophenyl) carbamoyl) cyclopropyl acyl halide, an acid-binding agent in organic solvent at -5~20 ℃ for 0.5~2h to obtain cabozantinib; the inventive method uses cheap raw materials, has mild conditions, simple and convenient operation, stable process, good repeatability, high molar yield, low cost, so invention is an applicable method for com. production of cabozantinib. Cabozantinib was prepared via chlorination of 6,7-dimethoxyquinolin-4-ol; the resulting 4-chloro-6,7-dimethoxyquinoline underwent condensation with 4-aminophenol or 4-nitrophenol to give the corresponding ethers, which underwent redn and/or acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropylcarbonyl halides to give cabozantinib. The said 1-[(4-fluorophenyl)carbamoyl]cyclopropylcarbonyl halides were prepared via condensation of 1,1-cyclopropanedicarboxylic acid with p-fluoroaniline followed by halogenation. The inventive method uses cheap raw materials, has mild conditions, simple and convenient operation, stable process, good repeatability, high molar yield, low cost, so invention is an applicable method for com. production of cabozantinib.

IT 849217-68-1, Cabozantinib
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor drug cabozantinib starting from (dimethoxy)quinolinol and cyclopropanedicarboxylic acid by using etherification and amidation as the key steps)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 247 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:478399 CAPLUS Full-text

DOCUMENT NUMBER: 160:501685

TITLE: Process for the preparation of cabozantinib and its intermediate

INVENTOR(S): Shi, Xiangfei; Zhao, Rui; Meng, Qingyi; Zhang, Xiquan

PATENT ASSIGNEE(S): Chia Tai Tianqing Pharmaceutical Group Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 18pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

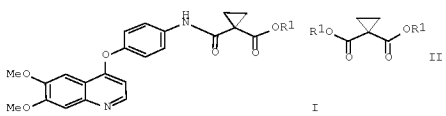
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103664776	A	20140326	CN 2012-10374723	20120926

PRIORITY APPLN. INFO.: CN 2012-10374723 20120926

OTHER SOURCE(S): MARPAT 160:501685

GI

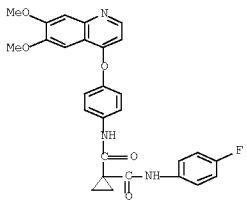


AB The invention relates to process for the prepn. of cabozantinib and its intermediate of formula I from 1,1-cyclopropane dicarboxylic acid diester of formula II [R1 = C1-10 alkyl]. For example, cabozantinib was prepared by hydrolysis of compound II [R1 = Et] to afford 1-(ethoxycarbonyl)cyclopropanecarboxylic acid, which underwent amidation reaction with 4-aminophenol followed by arylation with 4-chloro-6,7-dimethoxyquinoline to afford compound I [R1 = Et], which underwent hydrolysis followed by amidation with 4-fluoroaniline to afford cabozantinib.

IT 849217-68-1P, Cabozantinib
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of cabozantinib and its intermediate)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 248 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:448281 CAPLUS Full-text

DOCUMENT NUMBER: 160:480988

TITLE: Inhibition of viral infection-triggered asthma with c-kit inhibitor

INVENTOR(S): Umetsu, Dale T.; Chang, Ya-Jen; De Kruyff, Rosemarie Helena; Baumgarth, Nicole

PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA

SOURCE: PCT Int. Appl., 128pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014043442	A1	20140320	WO 2013-US59609	20130913

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR,

HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2895170 A1 20150722 EP 2013-836850 20130913

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

US 20150297593 A1 20151022 US 2015-14428272 20150313

PRIORITY APPLN. INFO.: US 2012-61701296 P 20120914

WO 2013-US59609 W 20130913

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods, compns., and kits featuring a c-Kit kinase inhibitor for use in preventing or treating virus-induced respiratory pathol.

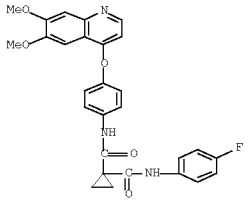
IT 849217-68-1, Cabozantinib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(c-kit inhibitors for treatment of viral infection-triggered asthma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 249 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:443739 CAPLUS Full-text

DOCUMENT NUMBER: 160:485576

TITLE: Combination therapy for prevention or treatment of c-met or angiogenesis factor induced diseases

INVENTOR(S): Jeong, Yun Ju; Kim, Kyung Ah; Song, Yun Jeong; Lee, Ji Min; Lee, Hyo Seon; Choi, Jae Hyun; Lee, Saet Byoul

PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea

SOURCE: Eur. Pat. Appl., 168pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

EP 2708556 A1 20140319 EP 2013-184072 20130912

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

KR 2014035266 A 20140321 KR 2013-108913 20130911

US 20140086926 A1 20140327 US 2013-14025403 20130912

PRIORITY APPLN. INFO.: KR 2012-101177 A 20120912

KR 2013-108913 A 20130911

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The authors disclose combination therapy for prevention or treatment of c-Met-induced or angiogenesis factor-induced diseases. The therapy comprises the co-administration of an angiogenesis inhibitor and an anti-c-Met antibody. In one example, the metastatic potential (migration) of HUVEC cells is shown to be inhibited by the combined effects of an anti-c-Met antibody and an anti-VEGF antibody.

IT 1140909-48-3, XL 184

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in combination therapy with anti-MET receptor antibodies)

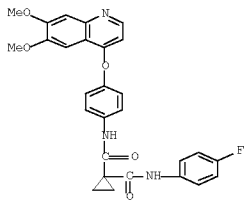
RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1

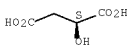
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6

CMF C4 H6 O5



Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 250 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:431636 CAPLUS Full-text

DOCUMENT NUMBER: 163:325757

TITLE: Effects of Cabozantinib on Pain and Narcotic Use in Patients with Castration-resistant Prostate Cancer: Results from a Phase 2 Nonrandomized Expansion Cohort

AUTHOR(S): Basch, Ethan; Autio, Karen A.; Smith, Matthew R.; Bennett, Antonia V.; Weitzman, Aaron L.; Scheffold, Christian; Sweeney, Christopher; Rathkopf, Dana E.; Smith, David C.; George, Daniel J.; Higano, Celestia S.; Harzstark, Andrea L.; Sartor, A. Oliver; Gordon, Michael S.; Vogelzang, Nicholas J.; de Bono, Johann S.; Haas, Naomi B.; Corn, Paul G.; Schimmoller, Frauke; Scher, Howard I.

CORPORATE SOURCE: Cancer Outcomes Research Program, Lineberger Cancer Center, University of North Carolina, Chapel Hill, NC, USA

SOURCE: European Urology (2015), 67(2), 310-318

CODEN: EUURAV; ISSN: 0302-2838

DIGITAL OBJECT ID: 10.1016/j.eururo.2014.02.013

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Pain neg. affects quality of life for cancer patients. Preliminary data in metastatic castration-resistant prostate cancer (mCRPC) suggested a benefit of the oral tyrosine kinase inhibitor cabozantinib to pain palliation. Prospective evaluation of cabozantinib's benefits on pain and narcotic use in mCRPC.This was a nonrandomized expansion (NRE) cohort (n = 144) of a phase 2 randomized discontinuation trial in docetaxel-refractory mCRPC patients. Pain and interference of symptoms with sleep and general activity were electronically self-reported daily for 7-d intervals at baseline and regularly scheduled throughout the study. Mean per-patient scores were calculated for each interval. Narcotic use was recorded daily during the same intervals.Open-label cabozantinib (100 mg or 40 mg). The following stringent response definition was used: clin. meaningful pain reduction (≥30% improvement in mean scores from baseline) confirmed at a later interval without concomitant increases in narcotics. Only patients with moderate or severe baseline pain were analyzed.Sixty-five patients with moderate or severe baseline pain were evaluable. Of these, 27 (42%) experienced pain palliation according to the stringent response definition. Thirty-seven patients (57%) had clin. meaningful pain relief at two consecutive intervals, reported ≥6 wk apart in the majority. Forty-four patients (68%) had palliation at one or more intervals; 36 (55%) decreased narcotics use during one or more intervals. Clin. meaningful pain reduction was associated with significant ($p \leq 0.001$) improvements in sleep quality and general activity. A limitation of this study was its open-label design. Cabozantinib demonstrated clin. meaningful pain palliation, reduced or eliminated patients' narcotic use, and improved patient functioning, thus meriting prospective validation in phase 3 studies.We evaluated the potential of cabozantinib to improve symptoms in patients with metastatic prostate cancer that no longer responds to standard therapies. We saw a promising reduction in pain and reduced need for narcotic painkillers. Larger, well-controlled trials are necessary to confirm these findings.

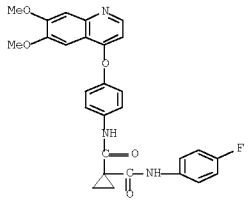
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phase 2 nonrandomized expansion cohort study on effects of cabozantinib on pain and narcotic use in patients with castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 251 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:410366 CAPLUS Full-text

DOCUMENT NUMBER: 160:451706

TITLE: Inhibitors of Met, VEGFR and Ret for use in the treatment of lung adenocarcinoma

INVENTOR(S): Aftab, Dana T.

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 80pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

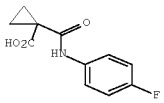
WO 2014039971 A1 20140313 WO 2013-US58768 20130909

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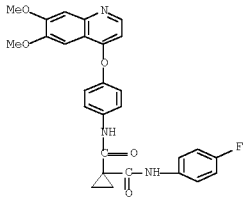
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US 20140121239 A1 20140501 US 2013-14021614 20130909
CN 104703600 A 20150610 CN 2013-80052164 20130909
EP 2892532 A1 20150715 EP 2013-765886 20130909
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JP 2015530389 T 20151015 JP 2015-531283 20130909
US 20150238477 A1 20150827 US 2015-14426580 20150306
PRIORITY APPLN. INFO.: US 2012-61698143 P 20120907
WO 2013-US58768 W 20130909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:451706; MARPAT 160:451706
GI



AB This invention is directed to the treatment of cancer in a patient, particularly a patient with lung adenocarcinoma, and more particularly a patient with KIF5B-RET fusion-pos. non-small cell lung cancer, with an inhibitor of MET, VEGF, and RET.

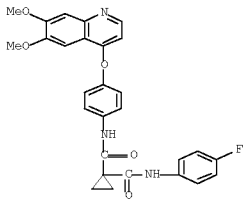
IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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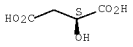
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

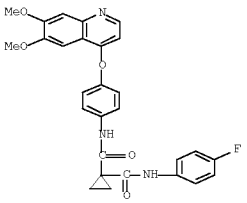
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3P
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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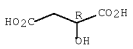
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 252 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:327215 CAPLUS Full-text
DOCUMENT NUMBER: 160:370140
TITLE: Preparation of substituted azaindole prodrugs, salts, pharmaceutical compositions thereof and methods of use in treating cancer and other proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Tingjin; Tang, Yin; Sun, Mingming; Wang, Qian
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 53pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140056849	A1	20140227	US 2013-13975371	20130826
CA 2882157	A1	20140306	CA 2013-2882157	20130826
WO 2014035846	A2	20140306	WO 2013-US56548	20130826
WO 2014035846	A3	20150625		

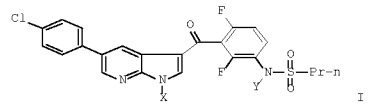
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

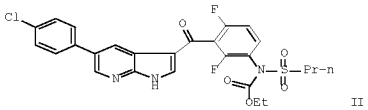
AU 2013309143	A1	20150212	AU 2013-309143	20130826
EP 2888260	A2	20150701	EP 2013-832403	20130826

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

PRIORITY APPLN. INFO.: US 2012-61693335 P 20120827
WO 2013-US56548 W 20130826
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:370140; MARPAT 160:370140
GI



I



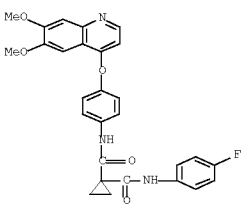
II

AB The present invention provides substituted azaindole prodrugs of vemurafenib, methods of making said prodrugs, pharmaceutical compns. of said prodrugs and methods of using said prodrugs and pharmaceutical compns. thereof to treat or prevent diseases or disorders such as cancer. The prodrugs have general formula I, wherein each of X and Y is independently H, -C(:O)R3, -C(:O)OR4, -C(R1R2)OC(:O)R3, -C(R1R2)OC(:O)OR4 or -C(R1R2)OP(:O)(OR4)(OR4a), with the proviso that when Y is H, X is not -C(:O)CH3 or H; each R1 and R2 is independently H, D, C1-6alkyl, etc.; each R3 is independently H, D, C1-10alkyl, etc.; and each R4 and R4a is independently H, C1-10alkyl, C3-8cycloalkyl, etc. Example compound II was prepared by reacting vemurafenib with Et chloroformate. Various prodrugs of the invention were studied for their stability in liver microsomes, their oral and i.v. bioavailability, and their antitumor properties.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted azaindole prodrugs., salts, pharmaceutical compns. thereof and methods of use in treating cancer and other proliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 254 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:211001 CAPLUS Full-text

DOCUMENT NUMBER: 161:316087

TITLE: Cabozantinib and Prostate Cancer: Inhibiting Seed and Disrupting Soil?

AUTHOR(S): Lee, Richard J.; Smith, Matthew R.

CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA

SOURCE: Clinical Cancer Research (2014), 20(3), 525-527
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-2636

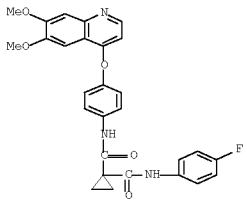
PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Treatment with cabozantinib, an inhibitor of MET and VEGFR2 signaling, has demonstrated clin. benefit in early trials in men with metastatic prostate cancer. Preclin. evidence suggests that cabozantinib can kill cancer cell seeds while disrupting angiogenesis and stromal cells in the metastatic soil.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cabozantinib in treatment of prostate cancer)



L4 ANSWER 253 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:211024 CAPLUS Full-text

DOCUMENT NUMBER: 161:316285

TITLE: Cabozantinib Inhibits Prostate Cancer Growth and Prevents Tumor-Induced Bone Lesions

AUTHOR(S): Dai, Jinlu; Zhang, Honglai; Karatsinides, Andreas; Keller, Jill M.; Kozloff, Kenneth M.; Aftab, Dana T.; Schimmoller, Frauke; Keller, Evan T.

CORPORATE SOURCE: Departments of Urology and Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA

SOURCE: Clinical Cancer Research (2014), 20(3), 617-630
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-0839

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

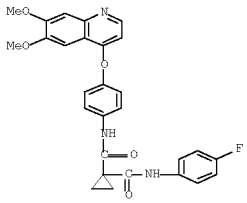
LANGUAGE: English

AB Purpose: Cabozantinib, an orally available multityrosine kinase inhibitor with activity against mesenchymal epithelial transition factor (MET) and VEGF receptor 2 (VEGFR2), induces resolution of bone scan lesions in men with castration-resistant prostate cancer bone metastases. The purpose of this study was to determine whether cabozantinib elicited a direct antitumor effect, an indirect effect through modulating bone, or both. Exptl. Design: Using human prostate cancer xenograft studies in mice, we determined the impact of cabozantinib on tumor growth in soft tissue and bone. In vitro studies with cabozantinib were performed using (i) prostate cancer cell lines to evaluate its impact on cell growth, invasive ability, and MET and (ii) osteoblast cell lines to evaluate its impact on viability and differentiation and VEGFR2. Results: Cabozantinib inhibited progression of multiple prostate cancer cell lines (Ace-1, C4-2B, and LuCaP 35) in bone metastatic and soft tissue murine models of prostate cancer, except for PC-3 prostate cancer cells in which it inhibited only s.c. growth. Cabozantinib directly inhibited prostate cancer cell viability and induced apoptosis in vitro and in vivo and inhibited cell invasion in vitro. Cabozantinib had a dose-dependent biphasic effect on osteoblast activity and inhibitory effect on osteoclast production in vitro that was reflected in vivo. It blocked MET and VEGFR2 phosphorylation in prostate cancer cells and osteoblast-like cells, resp. Conclusion: These data indicate that cabozantinib has direct antitumor activity, and that its ability to modulate osteoblast activity may contribute to its antitumor efficacy. Clin Cancer Res; 20(3); 617-30. ©2013 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib inhibits prostate cancer growth and prevents tumor-induced bone lesions)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 255 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:175942 CAPLUS Full-text

DOCUMENT NUMBER: 160:310859

TITLE: Preparation of substituted pyrazolone compounds as protein tyrosine kinase modulators useful in treatment of proliferative diseases

INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming

PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.

SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

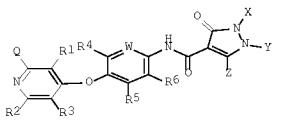
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022117	A1	20140206	WO 2013-US51175	20130719

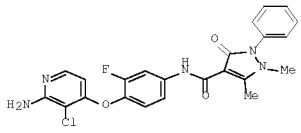
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US 20150050239 A1 20150219 US 2013-13945925 20130719
US 8969388 B2 20150303
EP 2879676 A1 20150610 EP 2013-825325 20130719
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JP 2015523390 T 20150813 JP 2015-524334 20130719
PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
WO 2013-US51175 W 20130719
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:310859; MARPAT 160:310859
GI



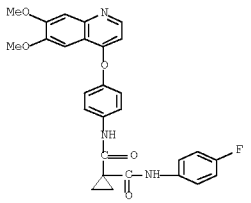
I



II

AB The invention provides substituted pyrazolone compds.of formula I, stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, and pharmaceutical preparation for regulating the activity of protein kinases and adjusting the signal response in the cell or between cells. The invention also relates to pharmaceutical compns. comprising the compds. and a method for treating hyperproliferative disorder of mammal, particularly human using the compns. Compds. of formula I [wherein Q is H, NH2 and derivative, OH and derivs., -NHCOR, etc.; W is (un)substituted CH or N; X, Y, and Z are independently H, D, C1-6 alkyl, C3-8 cycloalkyl-C1-4 alkylene, etc.; R1-R6 are independently H, D, F, Cl, Br, CN, etc.; R is H, C1-6 alkyl, C3-8 cycloalkyl-C1-4 alkylene, C3-7 heterocycloalkyl, etc.] and their stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, are claimed and exemplified. For example, II was prepared in a multistep process (procedure given). I were evaluated for stability in liver microsomes and pharmacokinetic properties in mice, rats, dogs, and monkeys (data given). Binding of I to receptor tyrosine kinases was determined using KINOMEscan where II exhibited binding constant (Kd) values of 23 nM for KDR tyrosine kinase and 4.4 nM for c-Met tyrosine kinase.

IT [illegible]
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolone compds. useful as protein tyrosine kinase modulators for treatment of proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

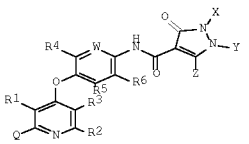


L4 ANSWER 256 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:175941 CAPLUS Full-text
DOCUMENT NUMBER: 160:310858
TITLE: Preparation of substituted pyrazolone compounds as protein tyrosine kinase modulators for treatment of proliferative disease
INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 110pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

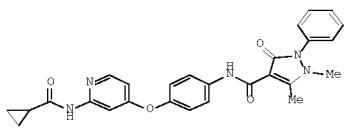
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022116	A2	20140206	WO 2013-US51174	20130719
WO 2014022116	A3	20150716		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL,

SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
CA 2876246 A1 20140206 CA 2013-2876246 20130719
AU 2013296897 A1 20141218 AU 2013-296897 20130719
AU 2013296897 B2 20150917
US 20150050239 A1 20150219 US 2013-13945925 20130719
US 8969388 B2 20150303
EP 2879677 A2 20150610 EP 2013-826459 20130719
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
JP 2015530975 T 20151029 JP 2015-524333 20130719
PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
WO 2013-US51174 W 20130719
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:310858; MARPAT 160:310858
GI



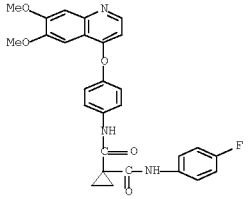
I



II

AB The invention provides substituted pyrazolone compds.of formula I, stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, and pharmaceutical preparation for regulating the activity of protein kinases and adjusting the signal response in the cell or between cells. The invention also relates to pharmaceutical compns. comprising the compds. and a method for treating hyperproliferative disorder of mammal, particularly human using the compns. Compds. of formula I [wherein Q is D, NH2 and derivs., -NHCOR, etc.; W is (un)substituted CH or N; each X, Y, and Z is independently H, D, C1-6 alkyl, C3-8 cycloalkyl, etc.; each R1-R6 is independently H, D, F, Cl, Br, CN, etc.; R is D, C3-8 cycloalkyl, -C1-4 alkylene -C6-10 aryl, etc.] and their stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, are claimed and exemplified. For example, II was prepared in a multistep process (procedure given). Candidate compds. of I were evaluated for stability in liver microsomes and pharmacokinetic properties in mice, rats, dogs, and monkeys (data given). Binding of I to receptor tyrosine kinases was determined using KINOMEscan where II exhibited binding constant (Kd) values of 2.9 nM for KDR tyrosine kinase and 0.21 nM for c-Met tyrosine kinase.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolone compds. useful as protein tyrosine kinase modulators for treatment of proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



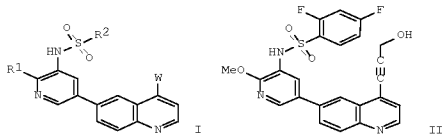
L4 ANSWER 257 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:173876 CAPLUS Full-text
DOCUMENT NUMBER: 160:294980
TITLE: Preparation of N-[3-(quinolin-6-yl)pyridin-5-yl] benzenesulfonamides as PI3 kinase modulators
INVENTOR(S): Xi, Ning; Li, Zhuo; Wang, Tingjin; Wu, Zuping; Wen, Qiuling
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022128	A1	20140206	WO 2013-US51405	20130719

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61676966 P 20120729
OTHER SOURCE(S): CASREACT 160:294980; MARPAT 160:294980
GI

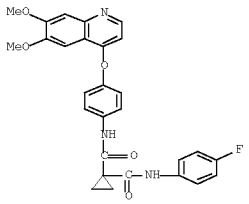


I II

AB This invention relates to the field of lipid kinases and modulators thereof. In particular, the invention relates to compds. I [W = D, CN, N3, (un)substituted C5-12 spirobicyclyl or C=CX; X = H, D, alkyl, cycloalkyl, etc.; R1 = H, D, Cl, alkyl, etc.; R2 = alkyl, cycloalkyl, aryl, etc.] as modulators of phosphatidylinositol 3-kinases (PI3 kinases or PBKs) signaling pathways, and methods of their use. Twenty-nine compds. I were prepared and disclosed. E.g., a multi-step synthesis of II, starting from 5-bromo-2-chloro-3-nitropyridine, was described. Exemplified compds. I exhibited potent activities in the PI3Kα(h) and mTOR(h) assays (data given for representative compds. I). The invention also provides pharmaceutically acceptable compns. comprising compds. I and methods of using the compns. in modulating of PI3K signaling pathways and their related disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-[3-(quinolin-6-yl)pyridin-5-yl] benzenesulfonamides as PI3 kinase modulators)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L4 ANSWER 258 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:151402 CAPLUS full-text
DOCUMENT NUMBER: 160:242457
TITLE: In-frame fusion of genes CEP55 and RET associated with diffuse-type gastric cancer and their use in drug discovery and cancer therapy
INVENTOR(S): Shibata, Tatsuhiro; Hosoda, Fumie
PATENT ASSIGNEE(S): National Cancer Center, Japan
SOURCE: PCT Int. Appl., 53pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014017491	A1	20140130	WO 2013-JP69929	20130723

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CN 104619841	A	20150513	CN 2013-80039589	20130723
EP 2878672	A1	20150603	EP 2013-822713	20130723

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO,

RS, SE, SI, SK, SM, TR, BA, ME

US 20150177246	A1	20150625	US 2015-14417052	20150123

PRIORITY APPLN. INFO.: JP 2012-165694 A 20120726
WO 2013-JP69929 W 20130723

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

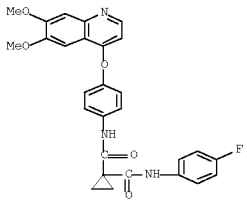
AB Through transcriptome an in-frame fusion of 2 genes (CEP55 and RET) of human chromosome 10 was found in patients with diffuse-type gastric cancer. The fused genes can be used for evaluation of the effectiveness of an antitumor agent such as RET tyrosine kinase inhibitors. Antibody to CEP55 or RET protein is also claimed.

IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RET tyrosine kinase inhibitors; in-frame fusion of genes CEP55 and RET associated with diffuse-type gastric cancer and their use in drug discovery and cancer therapy)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

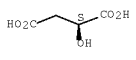
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 259 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:146206 CAPLUS full-text
DOCUMENT NUMBER: 160:225648
TITLE: Efflux inhibitor compositions and methods of treatment using the same
INVENTOR(S): Bunt, Antonius Martinus Gustave; Van Tellingen, Olaf
PATENT ASSIGNEE(S): Neth.
SOURCE: PCT Int. Appl., 74pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014018932	A2	20140130	WO 2013-US52402	20130726
WO 2014018932	A3	20140320		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2880236	A1	20140130	CA 2013-2880236	20130726
AU 2013295549	A1	20150319	AU 2013-295549	20130726
EP 2877159	A2	20150603	EP 2013-745549	20130726

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

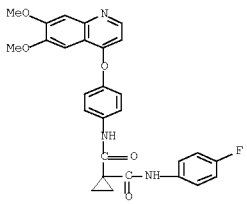
CN 104736144	A	20150624	CN 2013-80050643	20130726
JP 2015523400	T	20150813	JP 2015-524485	20130726
MX 2015001194	A	20151123	MX 2015-1194	20150126
IN 2015MN00408	A	20150904	IN 2015-MN408	20150225

PRIORITY APPLN. INFO.: US 2012-61676689 P 20120727
WO 2013-US52402 W 20130726

AB The present invention relates to efflux inhibitor compns. and methods of using these agents for treating conditions where the activity of efflux transporter proteins (e.g., Breast Cancer Resistance Protein (BCRP) and P-Glycoprotein (P-GP)) inhibit effective delivery of a therapeutic agent to a target tissue (e.g., brain, spinal cord, nerves, cerebrospinal fluid, testis, eyeballs, retina, inner ear, placenta, mammary gland, liver, biliary tract, kidney, intestines, lung, adrenal cortex, endometrium, hematopoietic cells, and/or stem cells).

IT 849217-68-1, Cabozantinib
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

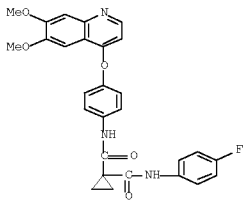
(efflux inhibitor compns. and methods of treatment using same)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

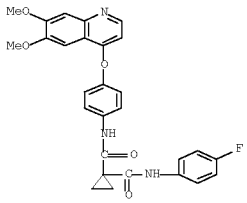
L4 ANSWER 260 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:127915 CAPLUS Full-text
DOCUMENT NUMBER: 160:362955
TITLE: Novel tyrosine kinase inhibitors for renal cell carcinoma
AUTHOR(S): Dorff, Tanya B.; Pal, Sumanta K.; Quinn, David I.
CORPORATE SOURCE: Department of Medicine, USC Norris Comprehensive Cancer Center, USC Keck School of Medicine, Los Angeles, CA, 90033, USA
SOURCE: Expert Review of Clinical Pharmacology (2014), 7(1), 67-73
CODEN: ERCPAG; ISSN: 1751-2433
DIGITAL OBJECT ID: 10.1586/17512433.2014.862496
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Although targeted therapy against VEGF and mTOR have revolutionized the treatment of advanced renal cell carcinoma (RCC), addnl. agents are required due to toxicity and resistance to currently available drugs. Some next-generation tyrosine kinase inhibitors have focused on VEGF, narrowing the spectrum of receptors which are inhibited and enhancing binding affinity. However, targeting novel receptors with tyrosine kinase inhibition of addnl. receptor targets has also emerged as an important future therapeutic strategy for RCC, both clear cell and variant histol. New pathways being targeted include FGF, angiopoietin and MET. In this review, we highlight five novel tyrosine kinase inhibitors in development for RCC: tivozanib; dovitinib; regorafenib; cabozantinib; and tivantinib.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel tyrosine kinase inhibitors for renal cell carcinoma)

therapeutic value in cancer therapy. Focus on the selectivity of both types of inhibitors, with potent selectivity or multi-targets, have demonstrated antitumor efficacy. The network pharmacol. and clin. trials integrated would provide powerful tools to further evaluate the superiority of both inhibitors in continued efficacy and toxicity.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(application of c-MET kinase inhibitors for the treatment of medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

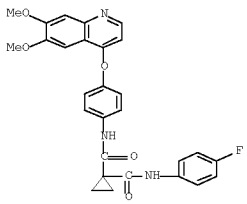
L4 ANSWER 262 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:2007812 CAPLUS Full-text
DOCUMENT NUMBER: 160:380536
TITLE: Newly approved antitumor drugs by FDA in 2012
AUTHOR(S): Yang, Minglun
CORPORATE SOURCE: Department of Pharmacy, Linqu County People's Hospital, Linqu, Shandong Province, 262600, Peop. Rep. China
SOURCE: Yaoxue Fuwu Yu Yanjiu (2013), 13(4), 304-306
CODEN: YFYYAH; ISSN: 1671-2838
DIGITAL OBJECT ID: 10.5428/pcar20130420
PUBLISHER: Yaoxue Fuwu Yu Yanjiu Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Newly approved antitumor drugs by FDA in 2012 were introduced.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(newly approved antitumor drugs by FDA in 2012)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



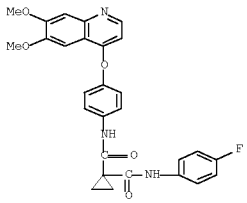
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 261 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:93138 CAPLUS Full-text
DOCUMENT NUMBER: 160:289739
TITLE: c-MET kinase inhibitors: a patent review (2011 - 2013)
AUTHOR(S): Zhu, Kongkai; Kong, Xiangqian; Zhao, Dan; Liang, Zhongjie; Luo, Cheng
CORPORATE SOURCE: Center for Systems Biology, Soochow University, Jiangsu, 215006, Peop. Rep. China
SOURCE: Expert Opinion on Therapeutic Patents (2014), 24(2), 217-230
CODEN: EOTPEG; ISSN: 1354-3776
DIGITAL OBJECT ID: 10.1517/13543776.2014.864279
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Introduction: The receptor tyrosine kinase c-MET displays aberrant activation in the malignant phenotype of various tumors, and thus, has drawn considerable attention as drug target for cancer therapy. Many c-MET inhibitors are now under clin. investment, and one of them - Cabozantinib - has been approved by US FDA in 2012 for the treatment of medullary thyroid cancer, which further proved the feasibility of c-MET inhibition method in cancer therapy. Areas covered: This article briefly outlines the role of c-MET in oncogenesis and provides a broad overview of the assays used to characterize new inhibitors. Then, a series of representative small-mol. inhibitors of c-MET, especially from the published patent literature from 2011 to 2013, are recorded. Herein, the challenges in the kinase inhibitor design, such as the inhibitor selectivity and resistance mutations, are also discussed. Expert opinion: Up to now, at least 17 inhibitors of c-MET are under clin. evaluation, and several agents exhibit encouraging results. Thus, inhibiting c-MET signaling has major

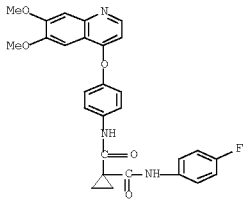
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 263 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:2006727 CAPLUS Full-text
DOCUMENT NUMBER: 160:380516
TITLE: Pharmacological and clinical studies of cabozantinib
AUTHOR(S): Zheng, Xi-yuan; Jiang, Han-jie; Pu, Xiao-ping
CORPORATE SOURCE: Department of Molecular and Cellular Pharmacology, School of Pharmaceutical Sciences, Peking University, Beijing, 100191, Peop. Rep. China
SOURCE: Zhongguo Xinyao Zazhi (2013), 22(17), 1990-1993
CODEN: ZXZHA6; ISSN: 1003-3734
PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Cabozantinib, a new drug for medullary thyroid cancer treatment, is a potent inhibitor of MET, RET, and vascular endothelial factor receptor 2 (VEGFR2) as well as other tyrosine kinases that have been implicated in tumor development and progression. The mechanism, pharmacokinetics, drug interaction, clin. evaluation, and safety of cabozantinib were reviewed.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. and clin. studies of cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

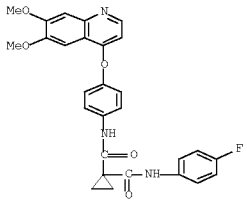


L4 ANSWER 264 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1965166 CAPLUS Full-text
DOCUMENT NUMBER: 160:155703
TITLE: Metastatic castration-resistant prostate cancer reveals intrapatient similarity and interpatient heterogeneity of therapeutic kinase targets
AUTHOR(S): Drake, Justin M.; Graham, Nicholas A.; Lee, John K.; Stoyanova, Tanya; Faltermeier, Claire M.; Sud, Sudha; Titz, Bjorn; Huang, Jiaoti; Pienta, Kenneth J.; Graeber, Thomas G.; Witte, Owen N.
CORPORATE SOURCE: Department of Microbiology, Immunology, and Molecular Genetics, David Geffen School of Medicine, University of California, Los Angeles, CA, 90095, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2013), 110(49), E4762-E4769,SE4762/1-SE4762/23
CODEN: PNASA6; ISSN: 0027-8424
DIGITAL OBJECT ID: 10.1073/pnas.1319948110
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In prostate cancer, multiple metastases from the same patient share similar copy number, mutational status, erythroblast transformation specific (ETS) rearrangements, and methylation patterns supporting their clonal origins. Whether actionable targets such as tyrosine kinases are also similarly expressed and activated in anatomically distinct metastatic lesions of the same patient is not known. We evaluated active kinases using phosphotyrosine peptide enrichment and quant. mass spectrometry to identify druggable targets in metastatic castration-resistant prostate cancer obtained at rapid autopsy. We identified distinct phosphopeptide patterns in metastatic tissues compared with treatment-naive primary prostate tissue and prostate cancer cell line-derived xenografts. Evaluation of metastatic castration-resistant prostate cancer samples for tyrosine phosphorylation and upstream kinase targets revealed SRC, epidermal growth factor receptor (EGFR), rearranged during transfection (RET), anaplastic lymphoma kinase (ALK), and MAPK1/3 and other activities while exhibiting intrapatient similarity and interpatient heterogeneity. Phosphoproteomic analyses and identification of kinase activation states in metastatic castration-resistant prostate cancer patients have allowed for the prioritization of kinases for further clin. evaluation.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphokinase profiling for drug targets of metastatic castration-resistant prostate cancer reveals intrapatient similarity and interpatient heterogeneity)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

L4 ANSWER 265 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1898455 CAPLUS Full-text
DOCUMENT NUMBER: 160:555100
TITLE: In Vitro and In Vivo Activity of Cabozantinib (XL184), an Inhibitor of RET, MET, and VEGFR2, in a Model of Medullary Thyroid Cancer
AUTHOR(S): Bentzien, Frauke; Zuzow, Marcus; Heald, Nathan; Gibson, Anna; Shi, Yongchang; Goon, Leanne; Yu, Peiwen; Engst, Stefan; Zhang, Wentao; Huang, Donghui; Zhao, Lora; Vysotskaia, Valentina; Chu, Felix; Bautista, Rajana; Cancilla, Belinda; Lamb, Peter; Joly, Alison H.; Yakes, F. Michael
CORPORATE SOURCE: ., Exelixis, Inc., South San Francisco, CA, USA
SOURCE: Thyroid (2013), 23(12), 1569-1577
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2013.0137
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: A limited no. of approved therapeutic options are available to metastatic medullary thyroid cancer (MTC) patients, and the response to conventional chemotherapy and/or radiotherapy strategies is inadequate. Sporadic and inherited mutations in the tyrosine kinase RET result in oncogenic activation that is associated with the pathogenesis of MTC. Cabozantinib is a potent inhibitor of MET, RET, and vascular endothelial factor receptor 2 (VEGFR2), as well as other tyrosine kinases that have been implicated in tumor development and progression. The object of this study was to determine the in vitro biochem. and cellular inhibitory profile of cabozantinib against RET, and in vivo antitumor efficacy using a xenograft model of MTC.Methods: Cabozantinib was evaluated in biochem. and cell-based assays that determined the potency of the compound against wild type and activating mutant forms of RET. Addnl., the pharmacodynamic modulation of RET and MET and in vivo antitumor activity of cabozantinib was examined in a MTC tumor model following subchronic oral administration.Results: In biochem. assays, cabozantinib inhibited multiple forms of oncogenic RET kinase activity, including M918T and Y791F mutants. Addnl., it inhibited proliferation of TT tumor cells that harbor a C634W activating mutation of RET that is most often associated with MEN2A and familial MTC. In these same cells grown as xenograft tumors in nude mice, oral administration of cabozantinib resulted in dose-dependent tumor growth inhibition that correlated with a reduction in circulating plasma calcitonin levels. Moreover, immunohistochem. analyses of tumors revealed that cabozantinib reduced levels of phosphorylated MET and RET, and decreased tumor cellularity, proliferation, and vascularization.Conclusions: Cabozantinib is a potent inhibitor of RET and prevalent mutationally activated forms of RET known to be associated with MTC, and effectively inhibits the growth of a MTC tumor cell model in vitro and in vivo.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of in vitro and in vivo antitumor efficacy of cabozantinib in preclin. model of medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



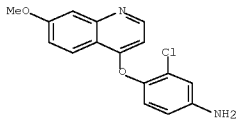
OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 266 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1873443 CAPLUS Full-text
DOCUMENT NUMBER: 160:50465
TITLE: Substituted quinoline compounds and use as Antitumor agents
INVENTOR(S): Xi, Ning; Wang, Tingjin; Zeng, Shan; Sun, Mingming; Wang, Kunrui
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013180949	A1	20131205	WO 2013-US41036	20130515

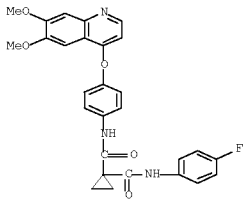
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61652210 P 20120527
OTHER SOURCE(S): CASREACT 160:50465; MARPAT 160:50465
GI



AB The present invention provides novel substituted quinoline compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted quinoline compds. and methods of use)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

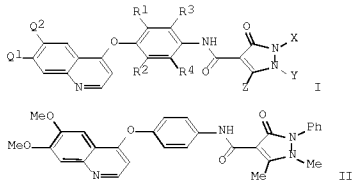


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

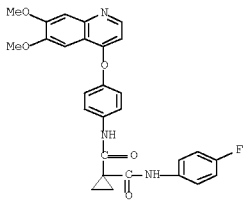
L4 ANSWER 267 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1866363 CAPLUS Full-text
DOCUMENT NUMBER: 160:33885
TITLE: Substituted quinoline compound useful in treatment of hyperproliferative diseases and its preparation
INVENTOR(S): Xi, Ning; Wang, Tingjin; Zeng, Shan; Sun, Mingming; Wang, Kunrui
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 57pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103420986	A	20131204	CN 2013-10179608	20130515
PRIORITY APPLN. INFO.:			CN 2012-10154478 A	20120518
			CN 2013-10118880 A	20130403

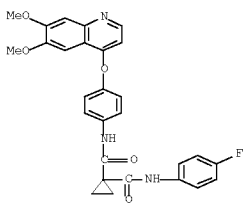
OTHER SOURCE(S): CASREACT 160:33885; MARPAT 160:33885
GI



AB The invention relates to substituted quinoline compds. of formula I as protein kinase regulator useful in treatment of proliferative diseases and their preparation Compound I, wherein R1, R2, R3, and R4 are independently H, D, F, Cl, or Br; Q1 and Q2 are independently H, D, C1-6 alkyl, etc.; X and Z are independently H, D, C1-6 alkyl, etc.; Y is H, D, C2-6 alkynyl, etc.; their stereoisomers, N-oxides, solvates, pharmaceutically acceptable salts, are claimed. Compound II was prepared by multi-step procedure (procedure given). The present invention also relates to the pharmaceutical compns. containing the inventive compds., and method of application of the pharmaceutical composition for treatment of a mammal, especially hyperproliferative disease.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted quinoline compound useful in treatment of hyperproliferative diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 268 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1864045 CAPLUS Full-text
DOCUMENT NUMBER: 161:30833
TITLE: An update on clinical trials of targeted therapies in thyroid cancer
AUTHOR(S): Haraldsdottir, Sigurdis; Shah, Manisha H.
CORPORATE SOURCE: The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA
SOURCE: Current Opinion in Oncology (2014), 26(1), 36-44
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0000000000000029
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Purpose of review: Several new targeted therapies with multikinase inhibitors targeting vascular endothelial growth factor (VEGF), rearranged during transfection and v-raf murine sarcoma viral oncogene homolog B1 pathways have been tested in clin. trials for radioiodine-refractory differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC) in the past 10 years. Recent findings: Results of the first phase III trial of VEGF-targeted therapy (sorafenib) in DTC were presented in June 2013, and two phase III trials with VEGF and rearranged during transfection-targeted therapies (vandetanib and cabozantinib) in MTC have led to approval by US Food and Drug Administration in the past 2 years. Whereas such therapies increase median progression-free survival compared to placebo, there is no therapy proven to improve overall survival yet. Significant potential adverse event risks associated with such therapies need to be recognized. Dissemination of knowledge about targeted therapies is critical for various medical specialists as patient care for thyroid cancers is best delivered in a multidisciplinary setting. Summary: Successful development of targeted systemic therapies in DTC and MTC in the past 5 years is incredibly exciting in the field and patients with advanced DTC/MTC now have new standard-of-care therapy options.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(update on clin. trials of targeted therapies in thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

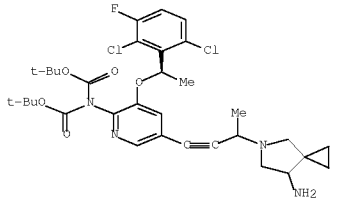


OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 269 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1837363 CAPLUS Full-text
DOCUMENT NUMBER: 160:28188
TITLE: Substituted alkynyl pyridine compounds and methods of use
INVENTOR(S): Xi, Ning; Yin, Lihua; Li, Xiaobo; Yu, Na; Wu, Yanjun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013177092	A1	20131128	WO 2013-US41918	20130521
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2012-61650513 P 20120523
OTHER SOURCE(S): CASREACT 160:28188; MARPAT 160:28188
GI

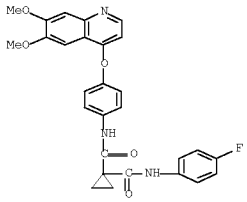


AB The present invention provides novel substituted alkynyl pyridine compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted alkynyl pyridine compds. and methods of use)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 270 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1836624 CAPLUS Full-text

DOCUMENT NUMBER: 160:28252

TITLE: Compounds and methods of use thereof for treating neurodegenerative disorders

INVENTOR(S): Zack, Donald J.; Welsbie, Derek Stuart; Yang, Zhiyong

PATENT ASSIGNEE(S): The Johns Hopkins University, USA

SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013177367	A2	20131128	WO 2013-US42367	20130523

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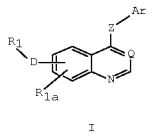
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EP 2852388	A2	20150401	EP 2013-793466	20130523
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US 20150164906	A1	20150618	US 2014-14403523	20141124

PRIORITY APPLN. INFO.:

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WO 2013-US42367	W	20130523

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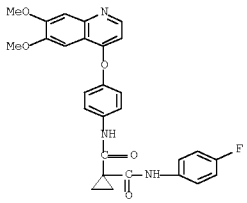
I

AB In some embodiments, the presently disclosed subject matter provides a method for treating or preventing a neurodegenerative disease, disorder, or condition in a subject in need thereof, the method comprising administering to the subject a 15 therapeutically effective amount of a compound of Formula I (wherein D is selected from the group consisting of O, S(O)0-2, and NR1b; R1a is selected from the group consisting of H, substituted or unsubstituted alkyl, halogen, OR1b, NO2, NR1bR1c; wherein: R1b and R1c are each independently selected from the group consisting of H or substituted or unsubstituted alkyl, aryl, etc.; R1 is H, substituted alkyl, aryl, etc.; Q is CR2a or N wherein R2a is H, alkyl or cyano; Z is O, NR1b and S(O)0-2; and Ar is substituted aryl or substituted heteroaryl), or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, thereby treating or preventing the neurodegenerative disease, disorder, or condition.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. and methods of use thereof for treating neurodegenerative disorders in relation to use of other agents and diagnosis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 271 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1823382 CAPLUS Full-text

DOCUMENT NUMBER: 161:178446

TITLE: Ocular adverse events of molecularly targeted agents approved in solid tumours: A systematic review

AUTHOR(S): Huillard, Olivier; Bakalian, Silvin; Levy, Christine; Desjardins, Laurence; Lumbroso-Le Rouic, Livia; Pop, Simona; Sablin, Marie-Paule; Le Tourneau, Christophe

CORPORATE SOURCE: Department of Medical Oncology, Clinical Trial Unit, Institut Curie, Paris, Fr.

SOURCE: European Journal of Cancer (2014), 50(3), 638-648
CODEN: EJCAEL; ISSN: 0959-8049

DIGITAL OBJECT ID: 10.1016/j.ejca.2013.10.016

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; (online computer file)

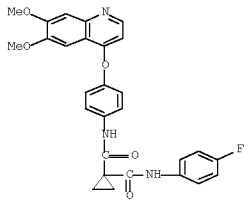
LANGUAGE: English

AB When using molecularly targeted agents (MTAs), oncologists and patients face new and sometimes unexpected toxicities. Though ocular adverse events (OAEs) are not uncommon with chemotherapy, they are rarely severe or dose limiting. Ocular toxicity profile may differ with MTAs, indeed severe and dose limiting toxicities have been described with targeted therapies currently under investigation. Our study aimed to review OAEs experienced with MTAs approved in solid tumors. This review revealed that many OAEs, frequent and potentially severe, exist and concern most MTAs. The suggestion is prompt referral of patients with severe pain and/or visual impairment to the ophthalmologist since these symptoms can be associated with potentially severe OAE and need ophthalmic assessment. Oncologists must be aware of such events and their potential severity for better treatment and better diagnosis in daily practice as well as in clin. trials.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ocular adverse events of molecularly targeted agents approved in solid tumors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 272 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1802363 CAPLUS Full-text

DOCUMENT NUMBER: 160:509021

TITLE: Multivoxel 1H MR spectroscopy is superior to contrast-enhanced MRI for response assessment after anti-angiogenic treatment of orthotopic human glioma xenografts and provides handles for metabolic targeting

AUTHOR(S): Hamans, Bob; Navis, Anna Catharina; Wright, Alan; Wesseling, Pieter; Heerschap, Arend; Leenders, William

CORPORATE SOURCE: Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.

SOURCE: Neuro-Oncology (Cary, NC, United States) (2013), 15(12), 1615-1624
CODEN: NEURJR; ISSN: 1522-8517

DIGITAL OBJECT ID: 10.1093/neuonc/not129

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; (online computer file)

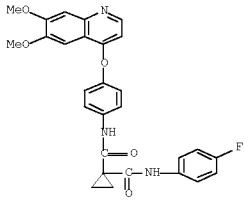
LANGUAGE: English

AB Background Anti-angiogenic treatment of glioblastoma characteristically results in therapy resistance and tumor progression via diffuse infiltration. Monitoring tumor progression in these patients is thwarted because therapy results in tumor invisibility in contrast-enhanced (CE) MRI. To address this problem, we examined whether tumor progression could be monitored by metabolic mapping using 1H MR spectroscopic imaging (MRSI). Methods We treated groups of BALB/c nu/nu mice carrying different orthotopic diffuse-infiltrative glioblastoma xenografts with bevacizumab (anti-vascular endothelial growth factor [VEGF] antibody, n = 13), cabozantinib (combined VEGF receptor 2/c-Met tyrosine kinase inhibitor, n = 11), or placebo (n = 15) and compared CE-MRI with MRS-derived metabolic maps before, during, and after treatment. Metabolic maps and CE-MRIs were subsequently correlated to histol. and immunohistochem. Results In vivo imaging of choline/n-acetyl aspartate ratios via multivoxel MRS is better able to evaluate response to therapy than CE-MRI. Lactate imaging revealed that diffuse infiltrative areas in glioblastoma xenografts did not present

with excessive glycolysis. In contrast, glycolysis was observed in hypoxic areas in angiogenesis-dependent compact regions of glioma only, especially after anti-angiogenic treatment. Conclusion Our data present MRSI as a powerful and feasible approach that is superior to CE-MRI and may provide handles for optimizing treatment of glioma. Furthermore, we show that glycolysis is more prominent in hypoxic areas than in areas of diffuse infiltrative growth. The Warburg hypothesis of persisting glycolysis in tumors under normoxic conditions may thus not be valid for diffuse glioma.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolic mapping via multivoxel magnetic resonance spectroscopy imaging than contrast-enhanced MRI showed better tumor progression after antiangiogenic Avastin and Exelixis treatment in mouse xenografted with human glioma cell)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



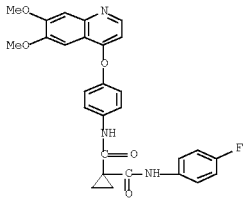
OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 273 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1792084 CAPLUS Full-text
DOCUMENT NUMBER: 159:737215
TITLE: Cabozantinib in progressive medullary thyroid cancer
AUTHOR(S): Elisei, Rossella; Schlumberger, Martin J.; Mueller, Stefan P.; Schoffski, Patrick; Brose, Marcia S.; Shah, Manisha H.; Licitra, Lisa; Jarzab, Barbara; Medvedev, Viktor; Kreissl, Michael C.; Niederle, Bruno; Cohen, Ezra E. W.; Wirth, Lori J.; Ali, Haythem; Hessel, Colin; Yaron, Yifah; Ball, Douglas; Nelkin, Barry; Sherman, Steven I.
CORPORATE SOURCE: University of Pisa, Pisa, Italy
SOURCE: Journal of Clinical Oncology (2013), 31(29), 3639-3646
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.48.4659
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: Cabozantinib, a tyrosine kinase inhibitor (TKI) of hepatocyte growth factor receptor (MET), vascular endothelial growth factor receptor 2, and rearranged during transfection (RET), demonstrated clin. activity in patients with medullary thyroid cancer (MTC) in phase I. Patients and Methods: We conducted a double-blind, phase III trial comparing cabozantinib with placebo in 330 patients with documented radiog. progression of metastatic MTC. Patients were randomly assigned (2:1) to cabozantinib (140 mg per day) or placebo. The primary end point was progression-free survival (PFS). Addnl. outcome measures included tumor response rate, overall survival, and safety. Results: The estimated median PFS was 11.2 mo for cabozantinib vs. 4.0 mo for placebo (hazard ratio, 0.28; 95% CI, 0.19 to 0.40; P < .001). Prolonged PFS with cabozantinib was observed across all subgroups including by age, prior TKI treatment, and RET mutation status (hereditary or sporadic). Response rate was 28% for cabozantinib and 0% for placebo; responses were seen regardless of RET mutation status. Kaplan-Meier ests. of patients alive and progression-free at 1 yr are 47.3% for cabozantinib and 7.2% for placebo. Common cabozantinib-associated adverse events included diarrhea, palmar-plantar erythrodysesthesia, decreased weight and appetite, nausea, and fatigue and resulted in dose redns. in 79% and holds in 65% of patients. Adverse events led to treatment discontinuation in 16% of cabozantinib-treated patients and in 8% of placebo-treated patients. Conclusion: Cabozantinib (140 mg per day) achieved a statistically significant improvement of PFS in patients with progressive metastatic MTC and represents an important new treatment option for patients with this rare disease. This dose of cabozantinib was associated with significant but manageable toxicity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in progressive medullary thyroid cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 110 THERE ARE 110 CAPLUS RECORDS THAT CITE THIS RECORD (112 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 274 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1772555 CAPLUS Full-text
DOCUMENT NUMBER: 159:738209
TITLE: Methods for determining nucleotide sequence
INVENTOR(S): Iafrate, Anthony John; Le, Long Phi; Zheng, Zongli
PATENT ASSIGNEE(S): The General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013169339	A1	20131114	WO 2013-US30201	20130311
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2873176	A1	20131114	CA 2013-2873176	20130311
US 20130303461	A1	20131114	US 2013-13793564	20130311
EP 2847353	A1	20150318	EP 2013-787745	20130311
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104603287	A	20150506	CN 2013-80037100	20130311
JP 2015517307	T	20150622	JP 2015-511444	20130311
PRIORITY APPLN. INFO.:			US 2012-61645364 P	20120510
			US 2012-61679302 P	20120803
			WO 2013-US30201 W	20130311

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

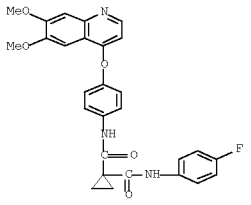
AB The technol. described herein is directed to methods of detg. oligonucleotide sequences, e.g. by enriching target sequences prior to sequencing the sequences. The invention provides the sequences of the DNA primers used for sequencing anal. The target sequence may be genomic DNA, RNA or cDNA with or without gene rearrangement.

IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for determining nucleotide sequence)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

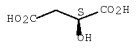
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

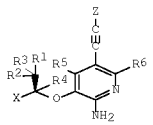


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

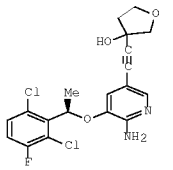
L4 ANSWER 275 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1771791 CAPLUS Full-text
DOCUMENT NUMBER: 159:742705
TITLE: Substituted alkynyl pyridine compounds as protein kinase regulator useful in treatment various diseases and their preparation
INVENTOR(S): Xi, Ning; Yin, Lihua; Li, Xiaobo; Yu, Na; Wu, Yanjun
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 65pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103387535	A	20131113	CN 2013-10173770	20130510

PRIORITY APPLN. INFO.: CN 2012-10141993 A 20120510
CN 2013-10116652 A 20130403
OTHER SOURCE(S): CASREACT 159:742705; MARPAT 159:742705
GI



I



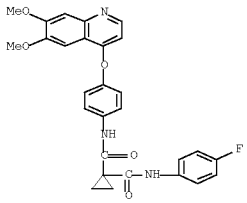
II

AB The invention relates to substituted alkynyl pyridine compds. of formula I as protein kinase regulator useful in treatment of various diseases and their preparation Compds. I, wherein R1, R2, R3, R4, R5 and R6 are independently H, D or F; X is C6-10 aryl or heteroaryl containing 5-10 atoms; Z is C1-6 alkyl, C3-6 cycloalkyl, C3-6 heterocyclic radical, etc.; their stereoisomers, solvates, N-oxidants, pharmaceutically acceptable salts, are claimed. Compound II was prepared by multi-step procedure (procedure given). The invention compds. were evaluated for their ALK(h) kinase activity. From assay, it was determined that II exhibited the IC50 value of 52 nM against ALK(h).

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted alkynyl pyridine compds. as protein kinase regulator useful in treatment of various diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

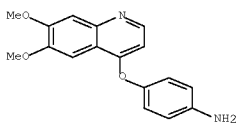


(2 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 277 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1734775 CAPLUS Full-text
DOCUMENT NUMBER: 159:691817
TITLE: A dual MET-VEGF modulator for treating osteolytic bone metastases
INVENTOR(S): Aftab, Dana T.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013166296	A1	20131107	WO 2013-US39284	20130502
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2844254	A1	20150311	EP 2013-722238	20130502
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015515988	T	20150604	JP 2015-510456	20130502
US 20150133494	A1	20150514	US 2014-14398188	20141031

PRIORITY APPLN. INFO.: US 2012-61641837 P 20120502
WO 2013-US39284 W 20130502
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 159:691817; MARPAT 159:691817
GI



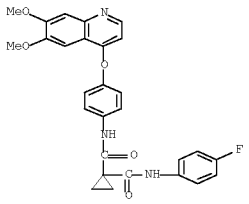
L4 ANSWER 276 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1746648 CAPLUS Full-text
DOCUMENT NUMBER: 160:200751
TITLE: Cabozantinib: a novel agent with a dual mechanism of action for castration-resistant prostate carcinoma
AUTHOR(S): Pinto, Alvaro
CORPORATE SOURCE: Medical Oncology Department, University Hospital La Paz-IdiPAZ, Madrid, Spain
SOURCE: Cancer Chemotherapy and Pharmacology (2014), 73(2), 219-222
CODEN: CCPHDZ; ISSN: 0344-5704
DIGITAL OBJECT ID: 10.1007/s00280-013-2343-2
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. The landscape of castration-resistant prostate carcinoma has changed completely in the last few years, with the approval of four new agents with proven benefit in overall survival. Abiraterone, cabazitaxel, enzalutamide and radium-223 dichloride have been added to the armamentarium of available agents for the treatment of these patients. We still lack information about which agent works best in an individual patient and how to optimally use them in a sequential strategy. Cabozantinib, a targeted agent against MET and vascular endothelial growth factor receptor-2, has shown promising results and could become the first targeted therapy to be approved for castration-resistant prostate carcinoma. This paper reviews the clin. development of cabozantinib in prostate cancer and future research possibilities for this drug.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib, a novel agent with a dual mechanism of action for castration-resistant prostate carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



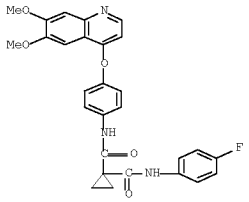
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD

AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and osteolytic bone metastases, with a dual inhibitor of MET and VEGF.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



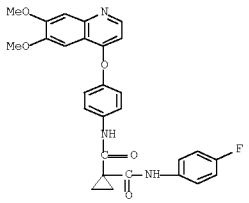
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

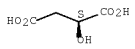
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

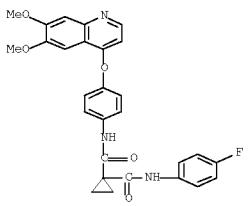
Absolute stereochemistry. Rotation (-).



IT [redacted]
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

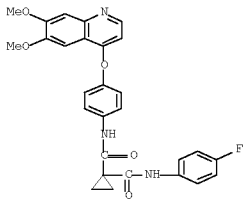
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

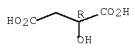
L4 ANSWER 279 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1698309 CAPLUS Full-text
DOCUMENT NUMBER: 159:662217
TITLE: Detection of RET fusions in cancer
INVENTOR(S): Doebele, Robert; Garcia, Marileila Varella; Le, Anh T.; Xu, Liangguo



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

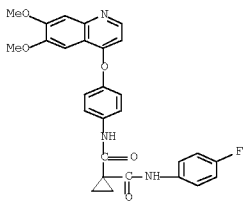
L4 ANSWER 278 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1717033 CAPLUS Full-text
DOCUMENT NUMBER: 160:363229
TITLE: Cabozantinib inhibits growth of androgen-sensitive and castration-resistant prostate cancer and affects bone remodeling
AUTHOR(S): Nguyen, Holly M.; Ruppender, Nazanin; Zhang, Xiaotun; Brown, Lisha G.; Gross, Ted S.; Morrissey, Colm; Gulati, Roman; Vessella, Robert L.; Schimmoller, Frauke; Aftab, Dana T.; Corey, Eva
CORPORATE SOURCE: Department of Urology, University of Washington, Seattle, WA, USA
SOURCE: PLoS One (2013), 8(10), e78881
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0078881
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is an inhibitor of multiple receptor tyrosine kinases, including MET and VEGFR2. In a phase II clin. trial in advanced prostate cancer (PCa), cabozantinib treatment improved bone scans in 68% of evaluable patients. Our studies aimed to determine the expression of cabozantinib targets during PCa progression and to evaluate its efficacy in hormone-sensitive and castration-resistant PCa in preclin. models while delineating its effects on tumor and bone. Using immunohistochem. and tissue microarrays containing normal prostate, primary PCa, and soft tissue and bone metastases, our data show that levels of MET, P-MET, and VEGFR2 are increasing during PCa progression. Our data also show that the expression of cabozantinib targets are particularly pronounced in bone metastases. To evaluate cabozantinib efficacy on PCa growth in the bone environment and in soft tissues we used androgen-sensitive LuCaP 23.1 and castration-resistant C4-2B PCa tumors. In vivo, cabozantinib inhibited the growth of PCa in bone as well as growth of s.c. tumors. Furthermore, cabozantinib treatment attenuated the bone response to the tumor and resulted in increased normal bone volume In summary, the expression pattern of cabozantinib targets in primary and castration-resistant metastatic PCa, and its efficacy in two different models of PCa suggest that this agent has a strong potential for the effective treatment of PCa at different stages of the disease.
IT [redacted], Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET, VEGFR2, RET expressions were found higher while cabozantinib by inhibiting these targets, it safely, effectively inhibited tumor growth, improved bone remodeling in human androgen-sensitive, metastatic CRPC tumor xenografted mouse)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

PATENT ASSIGNEE(S): University of Colorado, USA
SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013163428	A1	20131031	WO 2013-US38215	20130425

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61638452 P 20120425
AB Disclosed are methods and assay systems for the identification of chromosomal rearrangements involving the RET kinase gene in cellular samples. Further described are methods for identifying cancer patients who are predicted to respond, or not respond to the therapeutic administration of a chemotherapeutic regimen including one or more kinase inhibitor(s), to treat cancer in the patient.
IT [redacted], Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detection of RET fusions in cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



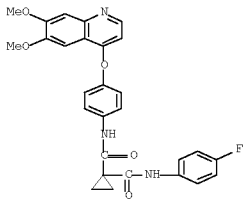
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 280 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1679191 CAPLUS Full-text
DOCUMENT NUMBER: 160:82446
TITLE: Commentary on "Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial." Smith DC, Smith MR, Sweeney C, Elfiky AA, Logothetis C, Corn PG, Vogelzang NJ, Small EJ, Harzstark AL, Gordon MS, Vaishampayan UN, Haas NB, Spira AI, Lara PN Jr, Lin CC, Srinivas S, Sella A, SchoffskiSchoeffski P, Scheffold C, Weitzman AL, Hussain M, University of Michigan, Ann Arbor, MI
AUTHOR(S): Trump, Donald L.
CORPORATE SOURCE: Neth.
SOURCE: Urologic Oncology: Seminars and Original Investigations (2013), 31(8), 1848
CODEN: UOSOAA; ISSN: 1078-1439
DIGITAL OBJECT ID: 10.1016/j.urolonc.2013.07.012
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib (XL184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. Patients received 100 mg of cabozantinib daily. Those with stable disease per RECIST at 12 wk were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 wk and progression-free survival (PFS) after random assignment. One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 wk was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 wk (95% CI, 10.7 to 62.4 wk) with cabozantinib and 5.9 wk (95% CI, 5.4 to 6.6 wk) with placebo (hazard ratio, 0.12; P<.001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by≥50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot syndrome (8%). Cabozantinib has clin. activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and redns. in bone turnover markers, pain, and narcotic use.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in patients with advanced prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

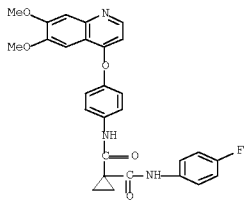
L4 ANSWER 281 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1655693 CAPLUS Full-text
DOCUMENT NUMBER: 159:632725
TITLE: Menainv and cancer invasion and metastasis diagnosis and antitumor screening
INVENTOR(S): Gertler, Frank B.; Hughes-Alford, Shannon K.; Lauffenburger, Douglas A.; Neil, Jason; White, Forest; Condeelis, John S.; Oudin, Madeleine J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA; Albert Einstein College of Medicine of Yeshiva University
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013158485	A1	20131024	WO 2013-US36336	20130412
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150044234	A1	20150212	US 2014-14390113	20141002
PRIORITY APPLN. INFO.:			US 2012-61625985 P	20120418
			US 2013-61778767 P	20130313
			WO 2013-US36336 W	20130412

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods and compns. are provided for diagnosing or inhibiting invasion or metastasis of a cancer in a subject based on MenaINV. A method is provided of identifying an agent as an inhibitor of sarcoma or carcinoma cell invasion or as an inhibitor of metastasis of a carcinoma or sarcoma, comprising contacting a preparation comprising a growth factor receptor and a protein tyrosine phosphatase 1b (PTP1b) in the presence of an amount of MenaINV and an amount of Mena and quantifying the association of the growth factor receptor and PTP1b in the presence of the agent and in the absence of the agent. An agent that increases the association of growth factor receptor and PTP1b in the presence of the agent as compared to in the absence of the agent is identified as an inhibitor of sarcoma or carcinoma cell invasion or of metastasis, and an agent that does not increase, or decreases, the association of growth factor receptor and PTP1b in the presence of the agent as compared to in the absence of the agent is not identified as an inhibitor of sarcoma or carcinoma cell invasion or metastasis. A further method is provided of identifying an agent as an inhibitor of sarcoma or carcinoma cell invasion or of metastasis of a carcinoma or sarcoma, the method comprising contacting a preparation comprising an amount of MenaINV, an amount of Mena, and a protein, wherein the protein is phosphorylated, with the agent and PTP1b and quantifying phosphorylation of the protein at the site or sites. A decrease in phosphorylation in (a) the presence of the agent and PTP1b as compared to (b) in the absence of the agent and presence of PTP1b identifies the agent as an inhibitor of sarcoma or carcinoma cell invasion or metastasis, and wherein an increase in, or no change in, phosphorylation in (i) the presence of the agent and PTP1b as compared to (ii) in the absence of the agent and presence of PTP1b does not identify the agent as an inhibitor of sarcoma or carcinoma cell invasion or metastasis.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Menainv and cancer invasion and metastasis diagnosis and antitumor screening)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 282 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1629334 CAPLUS Full-text
DOCUMENT NUMBER: 159:602931
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Arnal, Anna; Tarragona, Maria; Pavlovic, Milica; Planet, Evarist; Gomis, Roger
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 150pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013153458	A2	20131017	WO 2013-IB1204	20130315
WO 2013153458	A3	20140227		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2650682	A1	20131016	EP 2012-382139	20120409
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CA 2891609	A1	20131017	CA 2013-2891609	20130315
AU 2013246618	A1	20141106	AU 2013-246618	20130315
KR 2015014919	A	20150209	KR 2014-7031148	20130315
EP 2836837	A2	20150218	EP 2013-731875	20130315
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104797935	A	20150722	CN 2013-80027292	20130315
JP 2015520606	T	20150723	JP 2015-505034	20130315
US 20150293100	A1	20151015	US 2014-14391085	20141007
MX 2014012233	A	20150617	MX 2014-12233	20141009
PRIORITY APPLN. INFO.:			EP 2012-382139 A	20120409
			US 2012-61621949 P	20120409
			US 2012-61724807 P	20121109
			US 2012-61732175 P	20121130
			US 2012-61732174 P	20121130
			WO 2013-IB1204 W	20130315

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

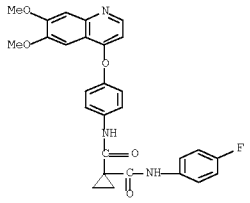
AB The present invention relates to a method for the prognosis of bone metastasis in triple neg. (including basal-like) breast cancer or, alternatively, ER+

breast cancer (including luminal A and β) which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of triple neg. (including basal-like) breast cancer metastasis or, alternatively, ER+ breast cancer (including luminal A and B) metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for the prognosis and treatment of cancer metastasis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 283 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1622779 CAPLUS Full-text

DOCUMENT NUMBER: 160:260019

TITLE: Novel Modeling of Cancer Cell Signaling Pathways Enables Systematic Drug Repositioning for Distinct Breast Cancer Metastases

AUTHOR(S): Zhao, Hong; Jin, Guangxu; Cui, Kemi; Ren, Ding; Liu, Timothy; Chen, Peikai; Wong, Solomon; Li, Fuhai; Fan, Yubo; Rodriguez, Angel; Chang, Jenny; Wong, Stephen T. C.

CORPORATE SOURCE: Department of Systems Medicine and Bioengineering; NCI Center for Modeling Cancer Development, The Methodist Hospital Research Institute, Weill Cornell Medical College; Methodist Cancer Center, The Methodist Hospital, Dan L. Duncan Cancer Center, Baylor College of Medicine, Houston, TX, USA

SOURCE: Cancer Research (2013), 73(20), 6149-6163
CODEN: CNREA8; ISSN: 0008-5472

DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-12-4617

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

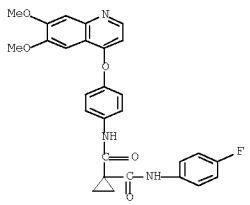
LANGUAGE: English

AB A new type of signaling network element, called cancer signaling bridges (CSB), has been shown to have the potential for systematic and fast-tracked drug repositioning. On the basis of CSBs, we developed a computational model to derive specific downstream signaling pathways that reveal previously unknown target-disease connections and new mechanisms for specific cancer subtypes. The model enables us to reposition drugs based on available patient gene expression data. We applied this model to repurpose known or shelved drugs for brain, lung, and bone metastases of breast cancer with the hypothesis that cancer subtypes have their own specific signaling mechanisms. To test the hypothesis, we addressed specific CSBs for each metastasis that satisfy (i) CSB proteins are activated by the maximal number of enriched signaling pathways specific to a given metastasis, and (ii) CSB proteins are involved in the most differential expressed coding genes specific to each breast cancer metastasis. The identified signaling networks for the three types of breast cancer metastases contain 31, 15, and 18 proteins and are used to reposition 15, 9, and 2 drug candidates for the brain, lung, and bone metastases. We conducted both in vitro and in vivo preclin. expts. as well as anal. on patient tumor specimens to evaluate the targets and repositioned drugs. Of special note, we found that the Food and Drug Administration-approved drugs, sunitinib and dasatinib, prohibit brain metastases derived from breast cancer, addressing one particularly challenging aspect of this disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel developed cancer signaling bridges-based computational model enabled systematic drug repositioning for brain, lung and bone metastasis in human breast cancer cell and in xenografted mouse model)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 284 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1619978 CAPLUS Full-text

DOCUMENT NUMBER: 159:634400

TITLE: Method for the prognosis and treatment of cancer metastasis

INVENTOR(S): Gomis Cabre, Roger; Planet, Evarist; Pavlovic, M. Milica

PATENT ASSIGNEE(S): Fundacio Privada Institut de Recerca Biomedica, Spain; Fundacio Privada Institucio Catalana de Recerca i Estudis Avancats

SOURCE: Eur. Pat. Appl., 51pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2650682	A1	20131016	EP 2012-382139	20120409
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CA 2891609	A1	20131017	CA 2013-2891609	20130315
WO 2013153458	A2	20131017	WO 2013-IB1204	20130315
WO 2013153458	A3	20140227		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2013246618	A1	20141106	AU 2013-246618	20130315
KR 2015014919	A	20150209	KR 2014-7031148	20130315
EP 2836837	A2	20150218	EP 2013-731875	20130315
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104797935	A	20150722	CN 2013-80027292	20130315
JP 2015520606	T	20150723	JP 2015-505034	20130315
US 20150293100	A1	20151015	US 2014-14391085	20141007
MX 2014012233	A	20150617	MX 2014-12233	20141009

PRIORITY APPLN. INFO.:

EP 2012-382139	A	20120409
US 2012-61621949	P	20120409
US 2012-61724807	P	20121109
US 2012-61732174	P	20121130
US 2012-61732175	P	20121130
WO 2013-IB1204	W	20130315

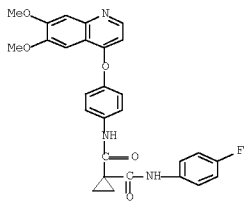
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to a method for the prognosis of bone metastasis in triple neg. (including basal-like) breast cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level. The invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of triple neg. (including basal-like) breast cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.

IT 849217-68-1, CAbozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for the prognosis and treatment of cancer metastasis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 285 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1549396 CAPLUS Full-text

DOCUMENT NUMBER: 159:577130

TITLE: Preparation of spirobicyclyl substituted pyrazolyl pyridinamine compounds as tyrosine kinase inhibitors for treating hyperproliferative disorders

INVENTOR(S): Xi, Ning; Li, Minxiong; Zhou, Xuan; Wu, Yanjun

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 90pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013148537	A1	20131003	WO 2013-US33633	20130325

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

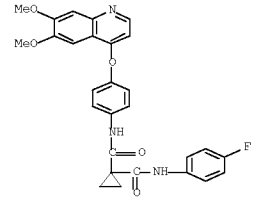
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61617626 P 20120329
OTHER SOURCE(S): CASREACT 159:577130; MARPAT 159:577130
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

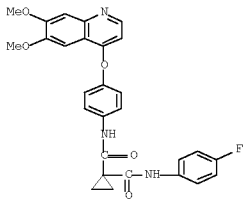
AB The present invention provides spirobicyclic compds. of general formula I (wherein R1-R6 are independently H, D, or F; each X and Y is independently (un)substituted C6-10aryl or (un)substituted 5-10 membered heteroaryl; Z is (un)substituted C5-12spirobicyclyl or (un)substituted -(C1-4alkylene)-(C5-12spirobicyclyl)-, with provisos), pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Synthetic procedures for preparing I are exemplified. For example, II was prepared in a 12-step synthesis that culminated in reaction of intermediates III and IV. II inhibited ALK kinase and c-Met kinase with IC50 values of 15 and 9 nM, resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of spirobicyclyl substituted pyrazolyl pyridinamine compds. as tyrosine kinase inhibitors for treating hyperproliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 287 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 286 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1459937 CAPLUS Full-text
DOCUMENT NUMBER: 159:472093
TITLE: Preparation of substituted pyrazolylpyridinamine compounds as protein tyrosine kinase modulators for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning; Wang, Tingjin; Yi, Lei
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 141pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013138210	A1	20130919	WO 2013-US30096	20130311

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61610473 P 20120314
US 2012-61617626 P 20120329
OTHER SOURCE(S): CASREACT 159:472093; MARPAT 159:472093
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides substituted pyrazolylpyridinamine compds. of formula I as protein tyrosine kinase modulators capable of regulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion for use in the treatment of hyperproliferative disorders. Compds. of formula I [wherein each R1, R2, R3, R4, R5, and R6 are independently H, D, or F; Z is substituted C3-7 heterocyclyl, substituted (C1-4 alkylene)-(C3-7 heterocyclyl), (un)substituted C5-12 fused bicyclyl, etc.;] stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, or pharmaceutically acceptable salts or prodrugs thereof are claimed and prepared For example, II was prepared by the reaction of 4-iodo-1-(4-((tetrahydro-2H-pyran-2-yl)oxy)tetrahydrofuran-3-yl)-1H-pyrazole with III followed by removal of the tetrahydro-2H-pyran and deprotection of the amine group to afford II in 80% yield. Pharmacodynamic and pharmacokinetic assays were performed on II. II inhibited ALK kinase and c-Met kinase with IC50 of 5 nM and 4 nM resp., demonstrated 82% inhibition of glioblastoma tumor growth when dosed orally at 60 mg/kg to mice, and exhibited a half-life of 35.37 min in human microsomes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolylpyridinamine compds. as protein tyrosine kinase modulators for treatment of hyperproliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

ACCESSION NUMBER: 2013:1270627 CAPLUS Full-text
DOCUMENT NUMBER: 159:384885
TITLE: Epithelial membrane protein 2 (EMP2) regulates angiogenesis in cancer cells through induction of VEGF
INVENTOR(S): Wadehra, Madhuri; Braun, Jonathan; Gordon, Lynn K.
PATENT ASSIGNEE(S): University of California, USA; United States Dept. of Veterans Affairs
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013119693	A1	20130815	WO 2013-US24968	20130206

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2863986	A1	20130815	CA 2013-2863986	20130206
AU 2013203424	A1	20130822	AU 2013-203424	20130206
EP 2812354	A1	20141217	EP 2013-747090	20130206

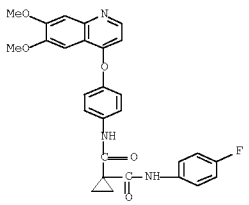
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2015508066	T	20150316	JP 2014-555854	20130206
US 20150079089	A1	20150319	US 2014-14376724	20140805

PRIORITY APPLN. INFO.: US 2012-61595617 P 20120206
WO 2013-US24968 W 20130206
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

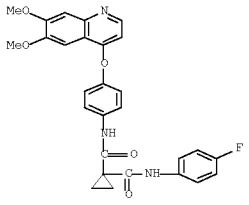
AB The authors disclose the targeting of epithelial membrane protein 2 (EMP2) for the treatment and prevention of endometrial cancer. In one example, EMP2 expression directly correlated with VEGF protein levels as well as with secreted protein expression by endometrial adenocarcinoma cells. Ribozyme-mediated reduction of EMP2 resulted in undetectable levels of VEGF.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with anti-EMP2 antibodies for treatment of uterine cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 288 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1255893 CAPLUS Full-text
DOCUMENT NUMBER: 159:660795
TITLE: Ponatinib is a potent inhibitor of wild-type and drug-resistant gatekeeper mutant RET kinase
AUTHOR(S): Mologni, Luca; Redaelli, Sara; Morandi, Andrea; Plaza-Menacho, Ivan; Gambacorti-Passerini, Carlo
CORPORATE SOURCE: Dept. of Health Sciences, University of Milano-Bicoccavia Cadore, Monza, 20900, Italy
SOURCE: Molecular and Cellular Endocrinology (2013), 377(1-2), 1-6
CODEN: MCEND6; ISSN: 0303-7207
DIGITAL OBJECT ID: 10.1016/j.mce.2013.06.025
PUBLISHER: Elsevier Ireland Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB RET kinase is aberrantly activated in thyroid cancers and in rare cases of lung and colon cancer, and has been validated as a mol. target in these tumors. Vandetanib was recently approved for the treatment of medullary thyroid cancer. However, vandetanib is ineffective in vitro against RET mutants carrying bulky aminoacids at position 804, the gatekeeper residue, similarly to drug-resistant BCR-ABL mutants in chronic myeloid leukemia. Ponatinib is a multi-target kinase inhibitor that was recently approved for treatment-refractory Philadelphia-pos. leukemia. We show here potent inhibition of oncogenic RET by ponatinib, including the drug-insensitive V804M/L mutants. Ponatinib inhibited the growth of RET+ and BCR-ABL+ cells with similar potency, while not affecting RET-neg. cells. Both in biochem. and in cellular assays ponatinib compared favorably with known RET inhibitors, such as vandetanib, cabozantinib, sorafenib, sunitinib and motesanib, used as reference compds. We suggest that ponatinib should be considered for the treatment of RET+ tumors, in particular those expressing vandetanib-resistant V804M/L mutations.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 290 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1227139 CAPLUS Full-text
DOCUMENT NUMBER: 159:329544
TITLE: Methods for predicting tumor response to targeted therapies with signal transduction pathway inhibitors using biomarkers
INVENTOR(S): Cohen, Jonathan M.; Derrien-Colemyn, Alexandrine Josephe; Gillespie, John Williams; Park, Soon Sik
PATENT ASSIGNEE(S): 20/20 Gene Systems, Inc., USA
SOURCE: PCT Int. Appl., 146pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013116735	A1	20130808	WO 2013-US24456	20130201

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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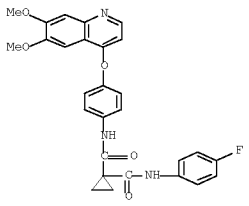
US 20140378500	A1	20141225	US 2014-14375827	20140731

PRIORITY APPLN. INFO.:

US 2012-61593688	P	20120201
US 2012-61654400	P	20120601
US 2012-61660305	P	20120615
US 2012-61660692	P	20120616
US 2012-61665943	P	20120629
US 2012-61699760	P	20120911
US 2012-61699874	P	20120912
WO 2013-US24456	W	20130201

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method for identifying cancer patients that are likely to be responders or non-responders to a signal transduction pathway inhibitor is described. The present invention is directed to methods and tests that help predict the likelihood that a tumor will respond to a targeted therapy so that those cancer patients most likely to benefit can receive that drug in a timely manner and those patients unlikely to benefit from a particular drug can instead be prescribed alternative therapies. The test comprises a panel of two or more biomarkers that are part of a signal transduction pathway. The biomarkers included in the panel, in combination, express differently in tumors that respond the drug from those that do not respond. The drugs to which these tests predict response may be designed or determined to target the signal transduction pathway of which the biomarker panel is associated Examples of such drugs are those that target angiogenesis pathways like VEGF or cellular growth pathways like mTOR. Alternatively, the drugs might target something other than the pathway with which the biomarkers are associated but activation of that pathway might otherwise limit or defeat the effectiveness of that drug. Examples of such drugs are those that block cellular receptors but for which activation of downstream signaling pathways nevertheless maintains cellular growth.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for predicting tumor response to targeted therapies with signal transduction pathway inhibitors using biomarkers)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

(multi-target tyrosine kinase inhibitor ponatinib exposure inhibited both wild-type and drug-resistant gatekeeper mutant RET kinase activity and inhibited growth of RET+ and BCR-ABL+ human cancer but not RET-cancer or normal cell)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



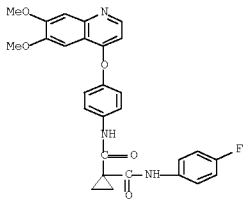
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 289 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1254595 CAPLUS Full-text
DOCUMENT NUMBER: 159:353569
TITLE: Combination therapy comprising selective VEGFR-2 inhibitors and MEK inhibitors
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 106pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2626066	A1	20130814	EP 2012-154880	20120210

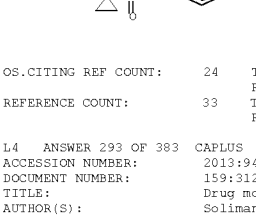
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

PRIORITY APPLN. INFO.: EP 2012-154880 20120210
AB The present invention relates to a combination therapy comprising selective inhibitors of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase and inhibitors of MAP kinase kinase (MEK). Accordingly, a pharmaceutical composition is provided that comprises a selective inhibitor of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase or a pharmaceutically acceptable salt, solvate and/or hydrate thereof, and an inhibitor or a pharmaceutically acceptable salt, solvate and/or hydrate thereof, for use in medicine, especially in the treatment of cancer, like lung cancer, such as non-small cell lung cancer, lung adenocarcinoma or small cell lung cancer. Also a method for identifying patients that are particularly susceptible to such a combination therapy is subject of the present invention. The method comprises the evaluation of the expression level of VEGFR-2 and/or VEGF. An increase in said expression level indicates susceptibility to the combination therapy.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy comprising selective VEGFR-2 inhibitors and MEK inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



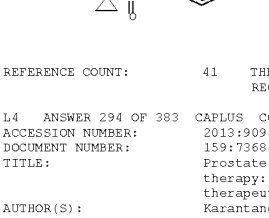
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 291 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1191423 CAPLUS Full-text
DOCUMENT NUMBER: 159:508181
TITLE: Cabozantinib (XL184) for the treatment of locally advanced or metastatic progressive medullary thyroid cancer
AUTHOR(S): Viola, David; Cappagli, Virginia; Elisei, Rossella
CORPORATE SOURCE: Endocrinology Unit, Department of Clinical & Experimental Medicine, WHO Collaborating Center for the Study & Treatment of Thyroid Diseases & other Endocrine & Metabolic Disorders, University of Pisa, Via Paradisa 2, Pisa, 56124, Italy
SOURCE: Future Oncology (2013), 9(8), 1083-1092
CODEN: FOUNBN; ISSN: 1479-6694
DIGITAL OBJECT ID: 10.2217/fon.13.128
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (XL184) is an oral multiple receptor tyrosine kinase inhibitor manufactured by Exelixis Inc., CA, USA. It mainly inhibits three tyrosine kinase receptors: MET, VEGFR2 and RET. In both preclin. and clin. studies it has been shown to inhibit tumor angiogenesis, invasiveness and metastases. The most frequent side effects are fatigue, diarrhea, decreased appetite, nausea, weight loss and palmar-plantar erythrodysesthesia. A Phase III clin. trial (EXAM study) of XL184 vs. placebo in advanced and progressive medullary thyroid cancer showed a 28 vs. 0% overall response rate and a progression-free survival of 11.2 vs. 4.0 mo (hazard ratio: 0.28; 95% CI: 0.19-0.40; $p < 0.0001$) in patients treated with cabozantinib and placebo, resp. The drug has been approved by the US FDA for the treatment of advanced/progressive metastatic medullary thyroid cancer in the USA. The EMA is now evaluating its approval in Europe.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of locally advanced or metastatic progressive medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (24 CITINGS)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

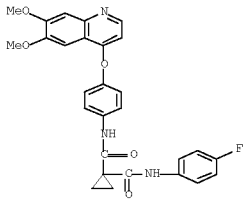
L4 ANSWER 293 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:948019 CAPLUS Full-text
DOCUMENT NUMBER: 159:312293
TITLE: Drug monographs: cabozantanib and omacetaxine
AUTHOR(S): Solimando, Dominic A., Jr.; Ho, Kristin V.; Waddell, J. Aubrey
CORPORATE SOURCE: Walter Reed National Military Medical Center, Bethesda, MD, USA
SOURCE: Hospital Pharmacy (2013), 48(5), 373-377
CODEN: HOPHAZ; ISSN: 0018-5787
DIGITAL OBJECT ID: 10.1310/hpj4805-373
PUBLISHER: Thomas Land Publishers, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The complexity of cancer chemotherapy requires pharmacists be familiar with the complicated regimens and highly toxic agents used. This column reviews various issues related to preparation, dispensing, and administration of antineoplastic therapy, and the agents, both com. available and investigational, used to treat malignant diseases. Questions or suggestions for topics should be addressed to Dominic A. Solimando, Jr, President, Oncol. Pharmacy Services, Inc, 4201 Wilson Blvd #110-545, Arlington, VA 22203, e-mail: OncRxSvc@aol.com; or J. Aubrey Waddell, Professor, University of Tennessee College of Pharmacy; Oncol. Pharmacist, Pharmacy Department, Blount Memorial Hospital, 907 E. Lamar Alexander Parkway, Maryville, TN 37804, e-mail: waddfour@charter.net.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug monographs of cabozantinib and omacetaxine)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 294 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:909480 CAPLUS Full-text
DOCUMENT NUMBER: 159:736844
TITLE: Prostate cancer progression after androgen deprivation therapy: mechanisms of castrate resistance and novel therapeutic approaches
AUTHOR(S): Karantanos, T.; Corn, P. G.; Thompson, T. C.
CORPORATE SOURCE: Department of Genitourinary Medical Oncology-Research, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Oncogene (2013), 32(49), 5501-5511
CODEN: ONCNES; ISSN: 0950-9232
DIGITAL OBJECT ID: 10.1038/onc.2013.206

After long-term cabozantinib treatment, PDA cells had altered anti- and pro-apoptotic signaling, but still responded to cabozantinib, as apoptosis only slightly decreased and viability only slightly increased suggesting a low resistance-inducing potential of cabozantinib. In parallel, c-Met expression and the pluripotency transcription factor SOX2 were downregulated, which might counteract development of full therapy resistance in long-term treated subclones. In single-treatment studies, cabozantinib increased efficacy of gemcitabine. Most importantly, cabozantinib strongly induced apoptosis and reduced viability in PDA cell lines, which are completely resistant toward gemcitabine. In primary, CSC-enriched spheroidal cultures cabozantinib downregulated CSC markers SOX2, c-Met and CD133 and induced apoptosis. These findings suggest that the clin. use of cabozantinib may be more effective than current chemotherapeutics.
IT 849217-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel c-mesenchymal-epithelial transition factor inhibitor cabozantinib overcomes gemcitabine resistance and stem cell signaling in pancreatic cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 292 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1087476 CAPLUS Full-text
DOCUMENT NUMBER: 159:649618
TITLE: The novel c-Met inhibitor cabozantinib overcomes gemcitabine resistance and stem cell signaling in pancreatic cancer
AUTHOR(S): Hage, C.; Rausch, V.; Giese, N.; Giese, T.; Schoensiegel, F.; Labsch, S.; Nwaeburu, C.; Mattern, J.; Gladkich, J.; Herr, I.
CORPORATE SOURCE: Department of Experimental Medicine, Molecular OncoSurgery Group, University of Heidelberg and German Cancer Research Center, Heidelberg, Germany
SOURCE: Cell Death & Disease (2013), 4(May), e627
CODEN: CDDEA4; ISSN: 2041-4889
DIGITAL OBJECT ID: 10.1038/cddis.2013.158
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Pancreatic ductal adenocarcinoma (PDA) is one of the most lethal malignancies. Cancer stem cells (CSCs), which are not targeted by current therapies, may be the reason for pronounced therapy resistance. A new treatment option in phase II trials is cabozantinib that inhibits the pancreatic CSC surface marker and tyrosine kinase receptor c-Met. The purpose of this study was to evaluate the effect of cabozantinib to stem-like features and therapy resistance. Established PDA cell lines, a gemcitabine-resistant subclone, non-malignant pancreatic ductal cells and primary spheroidal cultures from patient tumors were analyzed by MTT-assay, flow cytometry, colony and spheroid formation assays, western blotting, qRT-PCR, antibody protein array, immunohistochem. and morphol. features. Cabozantinib inhibited viability and spheroid formation and induced apoptosis in malignant cells with minor effects in non-malignant cells.

PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

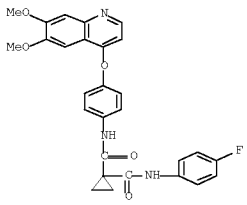
AB A review. Prostate cancer is the second-leading cause of cancer-related mortality in men in Western societies. Androgen receptor (AR) signaling is a critical survival pathway for prostate cancer cells, and androgen-deprivation therapy (ADT) remains the principal treatment for patients with locally advanced and metastatic disease. Although a majority of patients initially respond to ADT, most will eventually develop castrate resistance, defined as disease progression despite serum testosterone levels of <20 ng/dL. The recent discovery that AR signaling persists during systemic castration via intratumoral production of androgens led to the development of novel anti-androgen therapies including abiraterone acetate and enzalutamide. Although these agents effectively palliate symptoms and prolong life, metastatic castration-resistant prostate cancer remains incurable. An increased understanding of the mechanisms that underlie the pathogenesis of castrate resistance is therefore needed to develop novel therapeutic approaches for this disease. The aim of this review is to summarize the current literature on the biol. and treatment of castrate-resistant prostate cancer.

IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cabozatinib; prostate cancer progression after androgen deprivation therapy in relation to mechanisms of castrate resistance and novel therapeutic approaches)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

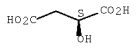
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



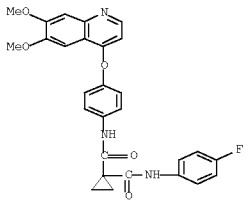
OS.CITING REF COUNT: 67 THERE ARE 67 CAPLUS RECORDS THAT CITE THIS RECORD (67 CITINGS)
REFERENCE COUNT: 158 THERE ARE 158 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 295 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:907853 CAPLUS Full-text
DOCUMENT NUMBER: 160:94029
TITLE: Response to Cabozantinib in Patients with RET Fusion-Positive Lung Adenocarcinomas
AUTHOR(S): Drilon, Alexander; Wang, Lu; Hasanovic, Adnan; Suehara, Yoshiyuki; Lipson, Doron; Stephens, Phil; Ross, Jeffrey; Miller, Vincent; Ginsberg, Michelle; Zakowski, Maureen F.; Kris, Mark G.; Ladanyi, Marc; Rizvi, Naiyer
CORPORATE SOURCE: Department of Medicine Thoracic Oncology Service, Lenox Hill Hospital, New York, NY, USA
SOURCE: Cancer Discovery (2013), 3(6), 630-635
CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID: 10.1158/2159-8290.CD-13-0035
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The discovery of RET fusions in lung cancers has uncovered a new therapeutic target for patients whose tumors harbor these changes. In an unselected population of non-small cell lung carcinomas (NSCLCs), RET fusions are present in 1%to2% of cases. This incidence increases substantially, however, in never-smokers with lung adenocarcinomas that lack other known driver oncogenes. Although preclin. data provide exptl. support for the use of RET inhibitors in the treatment of RET fusion-pos. tumors, clin. data on response are lacking. We report preliminary data for the first three patients treated with the RET inhibitor cabozantinib on a prospective phase II trial for patients with RET fusion-pos. NSCLCs (NCT01639508). Confirmed partial responses were observed in 2 patients, including one harboring a novel TRIM33-RET fusion. A third patient with a KIF5B-RET fusion has had prolonged stable disease approaching 8 mo (31 wk). All three patients remain progression-free on treatment.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response to cabozantinib in patients with RET fusion-pos. lung adenocarcinomas)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



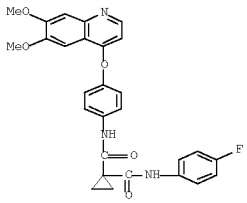
OS.CITING REF COUNT: 83 THERE ARE 83 CAPLUS RECORDS THAT CITE THIS RECORD (85 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 296 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:884114 CAPLUS Full-text
DOCUMENT NUMBER: 161:430953
TITLE: Tumour angiogenesis: an elusive target in castration-resistant prostate cancer
AUTHOR(S): Galsky, Matthew D.; Oh, William K.
CORPORATE SOURCE: The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA
SOURCE: Lancet Oncology (2013), 14(8), 681-682
CODEN: LOANBN; ISSN: 1470-2045
DIGITAL OBJECT ID: 10.1016/S1470-2045(13)70239-0
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB In this article, tumor angiogenesis an attractive target in castration-resistant prostate cancer is studied. Indeed, impressive single-agent activity has been reported with cabozantinib, a small mol. inhibitor of the tyrosine kinases MET and VEGFR2. The author reports on randomly allocated 1050 patients with castration-resistant prostate cancer to treatment with docetaxel plus prednisone with or without bevacizumab-the median overall survival for patients receiving bevacizumab was 22.6 mo compared with 21.5 mo for patients treated with placebo (hazard ratio 0.91, 95% CI 0.78-1.05; stratified log-rank p=0.181).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on tumor angiogenesis as elusive target in castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 297 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:882495 CAPLUS Full-text
DOCUMENT NUMBER: 159:68803
TITLE: Targeting microRNA's miR-409-5p, miR-379 and miR-154* to treat prostate cancer bone metastasis and drug resistant lung cancer
INVENTOR(S): Chung, Leland W. K.; Josson, Sajni; Gururajan, Murali; Jain, Anjali
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 79pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013082499	A1	20130606	WO 2012-US67403	20121130
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2012345666	A1	20140619	AU 2012-345666	20121130
CN 104080461	A	20141001	CN 2012-80067969	20121130
EP 2785355	A1	20141008	EP 2012-854115	20121130

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2015504847	T	20150216	JP 2014-544946		20121130
US 20140323551	A1	20141030	US 2014-14360489		20140523
US 20160017331	A1	20160121	US 2015-14863828		20150924
PRIORITY APPLN. INFO.:			US 2011-61565226	P	20111130
			WO 2012-US67403	W	20121130
			US 2014-14360489	A2	20140523
			US 2014-62055215	P	20140925

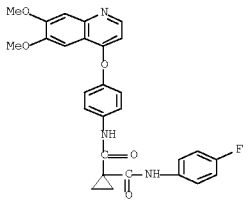
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention describes methods of treating cancer, cancer metastasis, and drug resistant cancers using miRNA inhibitors; for example, inhibitors of miR-409-5p. Also described are methods of using the miRNA as biomarkers; for example, to predict responsiveness to a cancer drug, to detect a disease state of cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting microRNA's to treat prostate cancer bone metastasis and drug resistant lung cancer and combination with other treatments and use of microRNA's as biomarkers)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 298 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:873882 CAPLUS Full-text

DOCUMENT NUMBER: 159:100783

TITLE: Medical combination containing hepatocyte growth factor receptor inhibitor and Bcl-2 inhibitor for treating cancer

INVENTOR(S): Zhao, Lei; Wang, Limei

PATENT ASSIGNEE(S): Beijing Tianhe Ruitong Technology Development Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 25pp.

CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

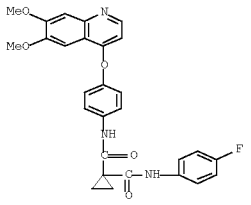
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103127510	A	20130605	CN 2011-10389330	20111130
CN 103127510	B	20150325		
PRIORITY APPLN. INFO.:			CN 2011-10389330	20111130

AB The title medical combination comprises a hepatocyte growth factor receptor (cMet) inhibitor and a Bcl-2 inhibitor. The medical combination can be used for preparing a drug for treating colon cancer, liver cancer, lung cancer, renal cancer, gastric cancer, brain tumor, sarcoma, neurospongioma, pancreas cancer, ovarian cancer or prostatic cancer. The medical combination has the advantages of good synergistic effects, high effects, low administration dosage and low side effects.

IT 849217-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical combination containing hepatocyte growth factor receptor inhibitor and Bcl-2 inhibitor for treating cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 299 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:869127 CAPLUS Full-text

DOCUMENT NUMBER: 159:436784

TITLE: A Dose-Ranging Study of Cabozantinib in Men with Castration-Resistant Prostate Cancer and Bone Metastases

AUTHOR(S): Lee, Richard J.; Saylor, Philip J.; Dror Michaelson, M.; Michael Rothenberg, S.; Smas, Malgorzata E.; Miyamoto, David T.; Gurski, Carol A.; Xie, Wanling; Maheswaran, Shyamala; Haber, Daniel A.; Goldin, Jonathan G.; Smith, Matthew R.

CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Boston, MA, USA

SOURCE: Clinical Cancer Research (2013), 19(11), 3088-3094
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-0319

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

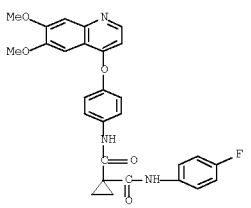
LANGUAGE: English

AB Background: Cabozantinib is an oral MET/VEGFR2 inhibitor. A recent phase II study of cabozantinib (100 mg daily) showed improved bone scans in subjects with metastatic castration-resistant prostate cancer (mCRPC), but adverse events (AE) caused frequent dose redns. This study was designed to determine the efficacy and tolerability of cabozantinib at lower starting doses. Exptl. Design: An adaptive design was used to determine the lowest active daily dose among 60, 40, and 20 mg. The primary endpoint was week 6 bone scan response, defined as ≥30% decrease in bone scan lesion area. The secondary endpoint was change in circulating tumor cells (CTC). Results: Among 11 evaluable subjects enrolled at 40 mg, there were 9 partial responses (PR), 1 complete response, and 1 stable disease (SD). Of 10 subjects subsequently enrolled at 20 mg, there were 1 PR, 5 SDs, and 4 with progressive disease. Among 13 subjects enrolled on the 40 mg expansion cohort, there were 6 PRs and 7 SDs. No subjects required dose reduction or treatment interruption at 6 or 12 wk; 3 subjects at dose level 0 discontinued due to AEs by 12 wk. At 40 mg, median treatment duration was 27 wk. 58% of subjects with ≥5 CTCs/7.5mL at baseline converted to <5. Conclusions: Cabozantinib 40 mg daily was associated with a high rate of bone scan response. Cabozantinib 40 mg daily was associated with better tolerability than previously reported for cabozantinib 100 mg daily. These observations informed the design of phase III studies of cabozantinib in mCRPC. Clin Cancer Res; 19(11); 3088-94. ©2013 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dose-ranging study of cabozantinib in men with castration-resistant prostate cancer and bone metastases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 300 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:847461 CAPLUS Full-text

DOCUMENT NUMBER: 159:357745

TITLE: The antiangiogenic ceiling in hepatocellular carcinoma: does it exist and has it been reached?

AUTHOR(S): Abou-Alfa, Ghassan K.; Venook, Alan P.

CORPORATE SOURCE: Section of Gastrointestinal Oncology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

SOURCE: Lancet Oncology (2013), 14(7), e283-e288
CODEN: LOANBN; ISSN: 1470-2045

DIGITAL OBJECT ID: 10.1016/S1470-2045(13)70161-X

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

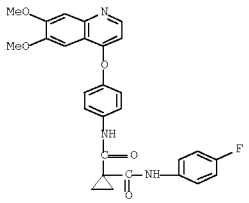
LANGUAGE: English

AB A review. The recommendation of sorafenib as std. of care in advanced hepatocellular carcinoma has lent support to the increased use of antiangiogenic therapies. However, in three phase 3 randomised trials that compared other antiangiogenics with sorafenib, results did not show superiority or non-inferiority of the new therapies. The 10-mo median overall survival shown in these studies for patients given sorafenib might be a ceiling for single-agent antiangiogenic therapy. Strategies to increase survival time include combination therapies that pair antiangiogenic treatment with biol. therapy or chemotherapy. The combination of sorafenib and erlotinib was not superior to sorafenib alone, which suggests no pos. interaction between antiangiogenics and tyrosine kinase inhibitors in the treatment of advanced hepatocellular carcinoma. A combination of sorafenib and doxorubicin is being assessed in a randomised phase 3 trial. Differences in patient outcome with sorafenib because of disease cause and the ethnic origin of patients suggest that sorafenib's multitarget capacity, including RAF kinase inhibition, might be important. MET inhibitors cabozantinib and tivantinib are drugs that might also bypass the so-called antiangiogenic ceiling and have led to selective treatment of patients that overexpress MET with these drugs. Although this intense period of research activity has not yet resulted in significant improvements in survival for patients with advanced hepatocellular carcinoma, we are certainly closer to a customised treatment, which should increase the antiangiogenic survival ceiling.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET inhibitors cabozantinib and tivantinib may be useful in treatment of patient with hepatocellular carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

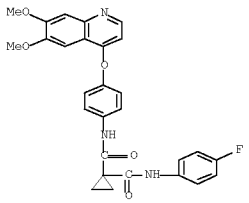


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 301 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:761990 CAPLUS Full-text
DOCUMENT NUMBER: 158:704608
TITLE: Method of quantifying cancer treatment
INVENTOR(S): Holland, Jaymes
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 50pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013070903	A1	20130516	WO 2012-US64134	20121108
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2854664	A1	20130516	CA 2012-2854664	20121108
AU 2012335750	A1	20140605	AU 2012-335750	20121108
AR 88813	A1	20140710	AR 2012-104223	20121108
CN 104039226	A	20140910	CN 2012-80066413	20121108
EP 2775921	A1	20140917	EP 2012-795939	20121108
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015505360	T	20150219	JP 2014-541261	20121108
IN 2014CN03674	A	20150703	IN 2014-CN3674	20140515

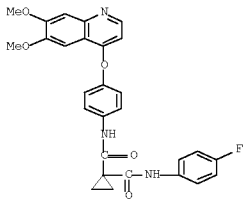
PRIORITY APPLN. INFO.: US 2011-61557362 P 20111108
WO 2012-US64134 W 20121108
OTHER SOURCE(S): CASREACT 158:704608
AB This invention is directed to a method for quantifying cancer treatment response in patients with bone metastases using computer aided bone scan assessment, comprising: (a) obtaining a bone scan image; (b) normalizing the obtained bone scan image to identify normalized bone scan lesions; and (c) quant. assessing the normalized bone scan lesions using bone scan lesion area, bone scan intensity, or bone scan lesion count.
IT 849217-68-1
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(quantifying cancer treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quantifying cancer treatment)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

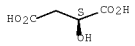
CRN 849217-68-1
CMF C28 H24 F N3 O5



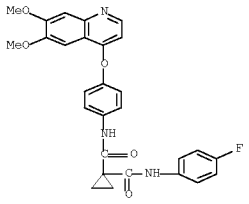
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quantifying cancer treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

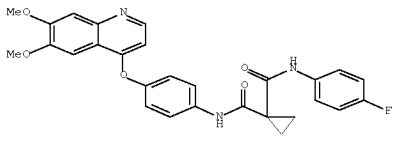


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 302 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:761969 CAPLUS Full-text
DOCUMENT NUMBER: 158:704607
TITLE: Dual inhibitor of Met and VEGF for treating cancer
INVENTOR(S): Aftab, Dana T.; Schimmoller, Frauke
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013070890	A1	20130516	WO 2012-US64116	20121108
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2854336	A1	20130516	CA 2012-2854336	20121108
AU 2012335737	A1	20140605	AU 2012-335737	20121108
IL 232421	A	20140630	IL 2012-232421	20121108
KR 2014088610	A	20140710	KR 2014-7015127	20121108
EP 2776033	A1	20140917	EP 2012-787328	20121108
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104159585	A	20141119	CN 2012-80066410	20121108
JP 2014532766	T	20141208	JP 2014-541256	20121108
MX 2014005458	A	20150416	MX 2014-5458	20140506
US 20140323522	A1	20141030	US 2014-14356927	20140508
ZA 2014003331	A	20151223	ZA 2014-3331	20140508
IN 2014CN04067	A	20151023	IN 2014-CN4067	20140530

PRIORITY APPLN. INFO.: US 2011-61557358 P 20111108
WO 2012-US64116 W 20121108
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:704607; MARPAT 158:704607
GI



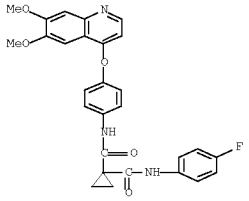
AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and bone metastases, with a dual inhibitor of MET and VEGF.

IT 849217-68-1

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3

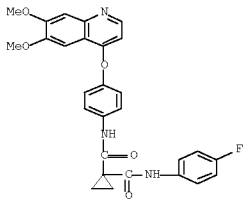
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1



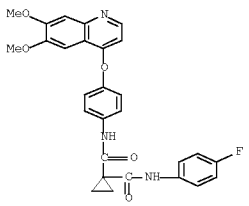
RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1

CMF C28 H24 F N3 O5

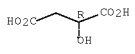


CM 2

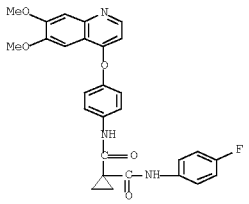
CRN 636-61-3

CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



CMF C28 H24 F N3 O5

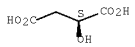


CM 2

CRN 97-67-6

CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib 1365530-43-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 303 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:729332 CAPLUS Full-text

DOCUMENT NUMBER: 158:676742

TITLE: Fusion proteins with a C-terminal domain of the gene ret receptor and their use in cancer diagnosis

INVENTOR(S): Ju, Young-Seok; Seo, Jeong-Sun; Kim, Kun-Hee

PATENT ASSIGNEE(S): Macrogen Inc., S. Korea

SOURCE: U.S. Pat. Appl. Publ., 61pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20130116280	A1	20130509	US 2012-13663565	20121030
WO 2013066047	A1	20130510	WO 2012-KR9056	20121031
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
KR 2014092846	A	20140724	KR 2014-7013826	20121031
EP 2773673	A1	20140910	EP 2012-845116	20121031
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2015504299	T	20150212	JP 2014-538724	20121031

PRIORITY APPLN. INFO.: US 2011-61553483 P 20111031
US 2012-13663565 A 20121030
WO 2012-KR9056 W 20121031

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A fusion protein including N-terminal domain of a fusion partner at N-terminal and C-terminal domain of RET protein at C-terminal and the gene encoding are identified as diagnostic markers for cancers, especially lung cancers. The somatic mutation forming the chimeric gene was identified in a poorly differentiated lung adenocarcinoma. The adenocarcinoma did not show any of the most common lung cancer-associated mutations, but several discordant reads, indicating transposition events, were identified. Expression of the chimeric KIF5B-RET gene in NIH-3T3 resulted in a neoplastic phenotype. Growth of these cells could be inhibited by the ret kinase inhibitor cabozantinib.

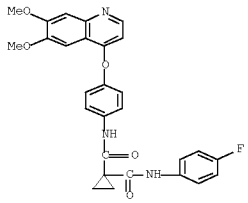
IT 849217-68-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(as inhibitor of ret receptor fusion protein in cancer therapy; fusion proteins with C-terminal domain of gene ret receptor and their use in cancer diagnosis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 304 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:728614 CAPLUS Full-text

DOCUMENT NUMBER: 158:672026

TITLE: Methods using heteroaryl compounds for treatment of disorders involving androgen-, estrogen- and progesterone-receptors

INVENTOR(S): Protter, Andrew A.; Hung, David T.; Chakravarty, Sarvajit; Bernales, Sebastian

PATENT ASSIGNEE(S): Medivation Technologies, Inc., USA

SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013067131	A1	20130510	WO 2012-US62980	20121101

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 305 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:725439 CAPLUS Full-text

DOCUMENT NUMBER: 158:676739

TITLE: Fusion proteins with a C-terminal domain of the gene ret receptor and their use in cancer diagnosis

INVENTOR(S): Ju, Young-Seok; Seo, Jeong-Sun; Kim, Eun-Hee

PATENT ASSIGNEE(S): Macrogen Inc., S. Korea

SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013066047	A1	20130510	WO 2012-KR9056	20121031

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20130116280	A1	20130509	US 2012-13663565	20121030
KR 2014092846	A	20140724	KR 2014-7013826	20121031
EP 2773673	A1	20140910	EP 2012-845116	20121031

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2015504299	T	20150212	JP 2014-538724	20121031

PRIORITY APPLN. INFO.:

US 2011-61553483	P	20111031
US 2012-13663565	A	20121030
WO 2012-KR9056	W	20121031

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A fusion protein including N-terminal domain of a fusion partner at N-terminal and C-terminal domain of RET protein at C-terminal and the gene encoding are identified as diagnostic markers for cancers, especially lung cancers. The somatic mutation forming the chimeric gene was identified in a poorly differentiated lung adenocarcinoma. The adenocarcinoma did not show any of the most common lung cancer-associated mutations, but several discordant reads, indicating transposition events, were identified. Expression of the chimeric KIF5B-RET gene in NIH-3T3 resulted in a neoplastic phenotype. Growth of these cells could be inhibited by the ret kinase inhibitor cabozantinib.

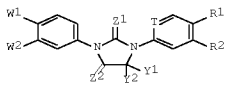
IT 849217-68-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as inhibitor of ret receptor fusion protein in cancer therapy; fusion proteins with C-terminal domain of gene ret receptor and their use in cancer diagnosis)

PRIORITY APPLN. INFO.: US 2011-61554919 P 20111102

OTHER SOURCE(S): MARPAT 158:672026

GI



I

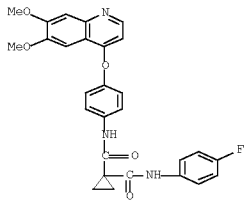
AB The disclosure describes compds. of formula I [W1 = CN, NO2, SO2R4; W2 = alkyl, alkenyl, alkynyl, halo; Z1 = S, O; Z2 = S, O, NR4; R4 = independently H, alkyl, aryl; Y1, Y2 = independently H, alkyl, alkenyl, aryl, arylalkyl, heterocyclic etc.; R1 = alkyl, cycloalkyl, heterocyclic etc.; R2 = independently H, halo, CN, alkyl etc.], or pharmaceutically acceptable salts thereof, useful for treating disorders involving androgen, estrogen, and/or progesterone receptors. In another embodiment of the invention the disorder is selected from the group consisting of neurodegenerative disorders, cancer, polyglutamate disease, rheumatoid arthritis, systemic hyperandrogenism, seborrhea, hirsutism, precocious puberty, polycystic ovary syndrome, acne, alopecia, benign prostatic hyperplasia, intrauterine fibroids, endometriosis, glaucoma, meningiomas, Kennedy's disease (KD) or X-linked spinal and bulbar muscular atrophy.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods using heteroaryl compds. for treatment of disorders involving androgen-, estrogen- and progesterone-receptors)

RN 849217-68-1 CAPLUS

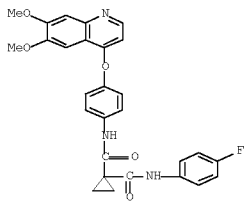
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 306 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:684015 CAPLUS Full-text

DOCUMENT NUMBER: 158:649640

TITLE: Free prostate specific antigen (PSA) antibodies as diagnostics, prognostics and therapeutics for prostate cancer

INVENTOR(S): Sawyers, Charles; Ulmert, David; Lewis, Jason; Evans, Michael; Lija, Hans

PATENT ASSIGNEE(S): Memorial Sloan-Kettering Cancer Center, USA

SOURCE: PCT Int. Appl., 103pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013063312	A1	20130502	WO 2012-US61982	20121025

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD,

SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2853705	A1	20130502	CA 2012-2853705		20121025
AU 2012328679	A1	20140612	AU 2012-328679		20121025
EP 2771688	A1	20140903	EP 2012-844178		20121025
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR					
CN 104040341	A	20140910	CN 2012-80063852		20121025
JP 2015502339	T	20150122	JP 2014-539018		20121025
US 20140308204	A1	20141016	US 2014-14353989		20140424
PRIORITY APPLN. INFO.:			US 2011-61551195	P	20111025
			WO 2012-US61982	W	20121025

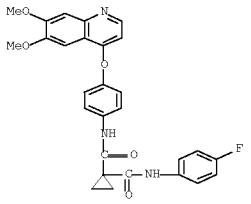
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The authors disclose the use of antibodies to free prostate-specific antigen (fPSA) in the diagnosis, prognosis, and therapeutic monitoring of prostate cancer. In one example, tumor localization of labeled anti-fPSA antibody is shown to be reduced by the antiandrogen MDV3100.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological activity); USES (Uses)
(antibodies to free PSA antigen therapy monitoring of)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 307 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:647172 CAPLUS Full-text
DOCUMENT NUMBER: 159:188392
TITLE: Emerging targeted therapies for castration-resistant prostate cancer
AUTHOR(S): Adamo, Vincenzo; Noto, Laura; Franchina, Tindara; Chiofalo, Giuseppe; Picciotto, Maria; Toscano, Giuseppe; Caristi, Nicola
CORPORATE SOURCE: Integrated Therapies in Oncology Unit, Department of Human Pathology, University of Messina, Messina, 98125, Italy
SOURCE: Frontiers in Cancer Endocrinology (2012), 3(May), 73

CODEN: FCERD9

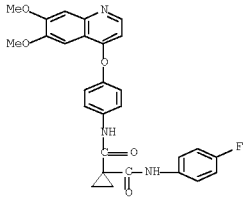
DIGITAL OBJECT ID:	10.3389/fendo.2012.00073
PUBLISHER:	Frontiers Media S.A.
DOCUMENT TYPE:	Journal; General Review; (online computer file)
LANGUAGE:	English

AB A review. Until recently, few therapeutic options were available for patients with castration-resistant prostate cancer (CRPC). Since 2010, four new mols. with a demonstrated benefit (sipuleucel-T, cabazitaxel, abiraterone and denosumab) have been approved in this setting and to-date several other agents are under investigation in clin. trials. The purpose of this review is to present an update of targeted therapies for CRPC. Presented data are obtained from literature and congress reports updated until Dec. 2011. Targeted therapies in advanced phases of clin. development include novel androgen signaling inhibitors, inhibitors of alternative signaling pathways, anti-angiogenic agents, inhibitors that target the bone microenvironment and immunotherapeutic agents. Radium-223 and MDV3100 demonstrated a survival advantage in phase III trials and the road for their introduction in clin. practice is rapidly ongoing. Results are also awaited for phase III studies currently underway or planned with new drugs given as monotherapy (TAK-700, cabozantinib, tasquinimod, PROSTVAC-VF, ipilimumab) or in combination with docetaxel (custirsen, aflibercept, dasatinib, zibotentan). The optimal timing, combination and sequencing of emerging therapies remain unknown and require further investigation. Addnl., the identification of novel markers of response and resistance to these therapies may better individualize treatment for patients with CRPC.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emerging targeted therapies for castration-resistance prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 308 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

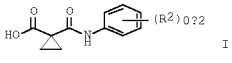
ACCESSION NUMBER: 2013:644308 CAPLUS Full-text
DOCUMENT NUMBER: 158:620790
TITLE: Process for preparing quinoline derivatives
INVENTOR(S): Wilson, Jo Ann; Naganathan, Sriram; Pfeiffer, Matthew; Andersen, Neil G.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2013059788	A1	20130425	WO 2012-US61320		20121022
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM					
CA 2852771	A1	20130425	CA 2012-2852771		20121022
AU 2012325768	A1	20140522	AU 2012-325768		20121022
IL 232139	A	20140528	IL 2012-232139		20121022
AR 88483	A1	20140611	AR 2012-103944		20121022
KR 2014088874	A	20140711	KR 2014-7012435		20121022
EP 2768796	A1	20140827	EP 2012-783763		20121022
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
JP 2014530880	T	20141120	JP 2014-537359		20121022
CN 104395284	A	20150304	CN 2012-80054241		20121022
ZA 2014002579	A	20150325	ZA 2014-2579		20140409
MX 2014004583	A	20141006	MX 2014-4583		20140415
US 20140256938	A1	20140911	US 2014-14353251		20140421
IN 2014CN02971	A	20150703	IN 2014-CN2971		20140421
PRIORITY APPLN. INFO.:			US 2011-61549312	P	20111020
			WO 2012-US61320	W	20121022

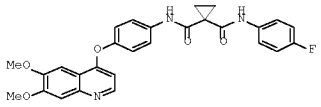
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 158:620790; MARPAT 158:620790

GI



I



II

AB The invention is directed to processes for prepg. compds. of formula I (R2 is H, F, Cl and Br) by activation of 1,1-cyclopropanedicarboxylic acid with thionyl chloride followed by amidation with substituted aniline derivative Example compound II L-malate was prepared by chlorination of 6,7-dimethoxyquinolin-4-ol followed by etherification of 4-chloro-6,7-dimethoxyquinoline with 4-aminophenol; the resulting 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine underwent acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropanecarbonyl chloride to give compound II, which underwent addition of L-malic acid to give the desired product.

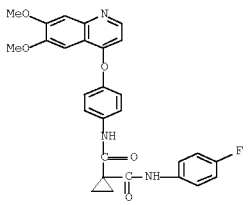
IT 1140909-48-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing quinoline derivs.)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

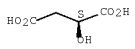
CRN 849217-68-1
CMF C28 H24 F N3 O5



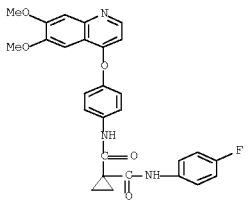
CM 2

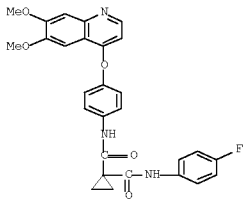
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



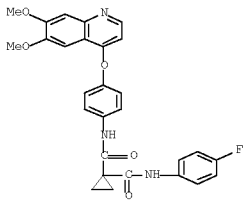
IT **849217-68-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing quinoline derivs.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 310 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:522453 CAPLUS Full-text
DOCUMENT NUMBER: 159:125821
TITLE: Emerging therapies in metastatic castration-sensitive and castration-resistant prostate cancer
AUTHOR(S): MacVicar, Gary R.; Hussain, Maha H.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Internal Medicine, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
SOURCE: Current Opinion in Oncology (2013), 25(3), 252-260
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e32835ff161
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Purpose of review: Therapeutic options for men with metastatic prostate cancer are expanding. Here we discuss the scientific progress in this disease that led to approval of several agents in the last decade and highlight ongoing clin. investigation. Recent findings: In androgen-sensitive disease, trials are evaluating the role of intermittent androgen-deprivation therapy, early chemotherapy, and novel targeted and hormonal therapies. For chemotherapy-naive, metastatic castration-resistant prostate cancer (mCRPC), abiraterone is effective. Trials with addnl. agents targeting androgen receptor (AR) signaling, such as TAK-700 and enzalutamide, are ongoing. Other agents in development target the endothelin pathway, angiogenesis, AR chaperones, and immune mechanisms. Docetaxel with prednisone remains the standard first-line chemotherapeutic regimen as trials incorporating novel agents with docetaxel have been neg. Postdocetaxel, enzalutamide improves survival. Early results with cabozantinib are encouraging, and phase III studies are ongoing. Denosumab and radium-223 reduce the risk of skeletal-related events (SREs), but only radium-223 improves survival. Summary: Progress in understanding the disease biol. and mechanisms of castration resistance led to significant therapeutic advancements, particularly in the setting of mCRPC in which several phase III trials, each incorporating agents with different mechanisms of action, have improved survival. As a result, new options exist, and the standard of care has changed significantly. Further advances are anticipated.
IT **849217-68-1**, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emerging therapies in metastatic castration-sensitive and castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



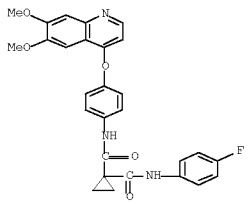
OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 311 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:522113 CAPLUS Full-text
DOCUMENT NUMBER: 159:125816
TITLE: From Bevacizumab to Tasquinimod: Angiogenesis as a Therapeutic Target in Prostate Cancer
AUTHOR(S): Schweizer, Michael T.; Carducci, Michael A.
CORPORATE SOURCE: Prostate Cancer Research Program, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins, Baltimore, MD, USA
SOURCE: Cancer Journal (Philadelphia, PA, United States) (2013), 19(1), 99-106
CODEN: CAJOCB; ISSN: 1528-9117
DIGITAL OBJECT ID: 10.1097/PPO.0b013e31827e0b86
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. It was first posited in the 1970s that angiogenesis may prove to be a useful target for anticancer therapies. Since then, a number of agents have been developed and tested across a range of tumor types; however, to date, there have unfortunately been more failures than successes. Prostate cancer (PCa) is no exception in this regard, and despite a strong preclin.

rationale for targeting angiogenesis in men with PCa, there has yet to be an antiangiogenic therapy proven to prolong survival in this group of patients. Drugs have been developed to target a host of angiogenesis mediators. These include vascular endothelial growth factor (VEGF), the VEGF receptors, antiangiogenic factors (e.g., thrombospondin-1), and downstream mediators of angiogenesis (e.g., hypoxia-inducible factor-1α and MET). At present, there are 2 drugs being tested in the phase III setting for men with PCa: cabozantinib and tasquinimod. Cabozantinib, a dual VEGF receptor-2/MET inhibitor, has shown dramatic beneficial effects on radiog. evident bone metastases and pain in the phase II setting. There are currently 2 large phase III trials underway to further investigate cabozantinib's role in treating men with PCa. Both trials randomize subjects to cabozantinib vs. mitoxantrone: one is designed to evaluate overall survival, and the other, pain response durability. The other drug, tasquinimod, has a somewhat poorly understood mechanism of action. It is thought to exert an antiangiogenic effect through the inhibition of myeloid-derived suppressor cells, key to the support of an angiogenic environment, and down-regulation of hypoxia-inducible factor-1α. A phase II trial randomizing men to tasquinimod vs. placebo revealed a median progression-free survival advantage in the exptl. arm (7.6 vs. 3.3 mo with placebo; P = 0.0042). Based on these encouraging phase II results, a randomized, double-blind, placebo-controlled trial in men with metastatic castration-resistant PCa was launched. That trial is powered for a primary endpoint of progression-free survival and is expected to enroll 1200 men.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiogenesis as therapeutic target in prostate cancer and the role of various angiogenesis targeting drugs including bevacizumab and tasquinimod)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



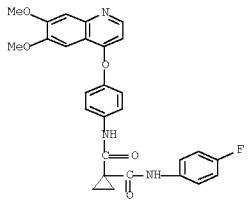
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 312 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:522110 CAPLUS Full-text
DOCUMENT NUMBER: 159:125815
TITLE: Targeting MET and Vascular Endothelial Growth Factor Receptor Signaling in Castration-Resistant Prostate Cancer
AUTHOR(S): Lee, Richard J.; Smith, Matthew R.
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA
SOURCE: Cancer Journal (Philadelphia, PA, United States) (2013), 19(1), 90-98
CODEN: CAJOCB; ISSN: 1528-9117
DIGITAL OBJECT ID: 10.1097/PPO.0b013e318281e280
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Effective management of bone metastases in men with castration-resistant prostate cancer (CRPC) remains an important unmet medical need. MET and vascular endothelial growth factor receptor (VEGFR) are rational targets for intervention in CRPC. Clin. trials involving agents that inhibit one but not both pathways have reported modest activity and no improvement in overall survival. Cabozantinib is an oral multitargeted tyrosine kinase inhibitor that inhibits both MET and VEGFR-2. A phase II randomized discontinuation study involving subjects with CRPC demonstrated that cabozantinib therapy is associated with improvement in bone scans, bone turnover markers, and pain response, but with significant adverse events leading to dose reduction and treatment discontinuation. Lower doses of cabozantinib retain high levels of activity with less toxicity. Ongoing phase III clin. trials will define the role of cabozantinib in CRPC. We summarize the rationale for targeting MET and VEGFR pathways in CRPC and the clin. data available to date.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting MET and vascular endothelial growth factor receptor signaling in castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 313 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:470327 CAPLUS Full-text
DOCUMENT NUMBER: 158:493976
TITLE: Combinations comprising c-Met antagonists and B-raf antagonists for treatment of cancer
INVENTOR(S): Wilson, Timothy R.; Koeppen, Hartmut; Merchant, Mark; Settleman, Jeffrey
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 148pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013043715	A1	20130328	WO 2012-US56106	20120919
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2846630	A1	20130328	CA 2012-2846630	20120919
US 20130078252	A1	20130328	US 2012-13622878	20120919
AU 2012312515	A1	20140313	AU 2012-312515	20120919
IL 231056	A	20140331	IL 2012-231056	20120919
AR 87918	A1	20140423	AR 2012-103446	20120919
KR 2014064971	A	20140528	KR 2014-7010162	20120919
CN 103930111	A	20140716	CN 2012-80055708	20120919
EP 2758055	A1	20140730	EP 2012-768982	20120919
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JP 2014534949	T	20141225	JP 2014-530956	20120919
ZA 2014001370	A	20150930	ZA 2014-1370	20120919
MX 2014002990	A	20140521	MX 2014-2990	20140313
US 20150125452	A1	20150507	US 2014-14535071	20141106

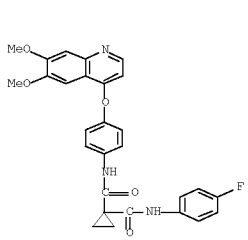
PRIORITY APPLN. INFO.:
US 2011-61536436 P 20110919
US 2011-61551328 P 20111025
US 2012-61598783 P 20120214
US 2012-61641139 P 20120501
US 2012-13622878 B1 20120919
WO 2012-US56106 W 20120919

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides combination therapies for treating a pathol. condition, such as cancer, wherein a c-met antagonist (e.g. crizotinib, tivantinib, anti-HGF antibody, onartuzumab) is combined with a B-raf antagonist (e.g. vemurafenib), thereby providing significant antitumor activity. C-met expression was inversely correlated with sensitivity to vemurafenib treatment. In one aspect, provided are methods for treating a cancer patient who has increased likelihood of developing resistance to B-raf antagonist comprising administering an effective amount (in combination) of B-raf antagonist and c-met antagonist. In addition, patients with B-raf mutant melanoma who had higher levels of circulating hepatocyte growth factor (HGF) showed substantially reduced progression free survival and overall survival when treated with B-raf antagonist, relative to patients with lower circulating HGF levels treated with B-raf antagonist.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations comprising c-Met antagonists and B-raf antagonists for treatment of cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

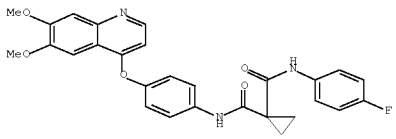
L4 ANSWER 314 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:466384 CAPLUS Full-text
DOCUMENT NUMBER: 158:494085
TITLE: Method for treating osteoporosis
INVENTOR(S): Aftab, Dana T.; Clary, Douglas
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 73pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013043840	A1	20130328	WO 2012-US56281	20120920
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
CA 2848512	A1	20130328	CA 2012-2848512	20120920
AU 2012312364	A1	20140410	AU 2012-312364	20120920
IL 231495	A	20140430	IL 2012-231495	20120920
KR 2014069133	A	20140609	KR 2014-7009534	20120920
CN 103957915	A	20140730	CN 2012-80051094	20120920
EP 2758057	A1	20140730	EP 2012-770368	20120920
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JP 2014527984	T	20141023	JP 2014-531955	20120920
AR 87995	A1	20140430	AR 2012-103501	20120921
ZA 2014001728	A	20160127	ZA 2014-1728	20140310
MX 2014003027	A	20141024	MX 2014-3027	20140313
IN 2014CN02093	A	20141010	IN 2014-CN2093	20140319
US 20140228401	A1	20140814	US 2014-14346570	20140321

PRIORITY APPLN. INFO.: US 2011-61538039 P 20110922
WO 2012-US56281 W 20120920

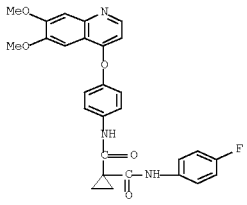
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:494085; MARPAT 158:494085
GI



cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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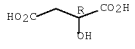
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CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

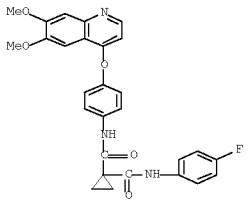


IT 849217-68-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for treating osteoporosis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

AB This invention is directed to the treatment of osteoporosis using N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide.
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for treating osteoporosis)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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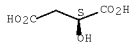
CRN 849217-68-1
CMF C28 H24 F N3 O5



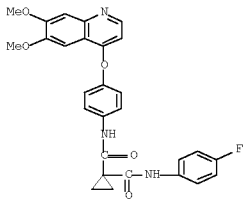
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treating osteoporosis)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-

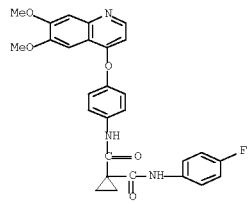


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 315 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:417299 CAPLUS Full-text
DOCUMENT NUMBER: 159:86304
TITLE: Pharmacokinetic evaluation of
AUTHOR(S): Karras, Spyridon; Pontikides, Nikolaos; Krassas, Gerasimos E.
CORPORATE SOURCE: Department of Endocrinology, Diabetes and Metabolism, Panagia General Hospital, Thessaloniki, Greece
SOURCE: Expert Opinion on Drug Metabolism & Toxicology (2013), 9(4), 507-515
CODEN: EODMAP; ISSN: 1742-5255
DIGITAL OBJECT ID: 10.1517/17425255.2013.780028
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Introduction: Conventional treatment modalities for thyroid cancer lead to complete remission in only one-third of patients with distant metastases. On the other hand, medullary thyroid cancer (MTC) and anaplastic thyroid cancer (ATC), although rare, are responsible for a significant percentage of thyroid cancer-related deaths. New treatments are needed to treat such patientsAreas covered: The aim of this review is to provide the latest information on , a new tyrosine kinase inhibitor (TKI) that is currently used mainly as a treatment of MTC. The authors collated data that were retrieved from a PubMed literature search.Expert opinion: CBZ targets multiple cell-signaling pathways involved in the mol. pathogenesis of thyroid cancer. These are namely VEGF receptor-2, hepatocyte growth factor receptor and rearranged during transfection receptor. Furthermore, it is a drug which may be used in cases where conventional therapies (mainly for MTC) are proved ineffective or have shown poor results with a good outcome. CBZ may also be administered alone or in combination with other drugs of the same family.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(understanding pharmacokinetics of cabozantinib may be useful in treatment of patient with medullary thyroid cancer)
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

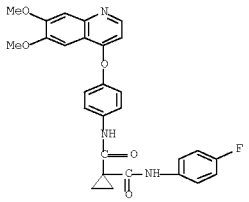


OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 316 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:414621 CAPLUS Full-text
DOCUMENT NUMBER: 159:53852
TITLE: Effects of dual targeting of tumor cells and stroma in human glioblastoma xenografts with a tyrosine kinase inhibitor against c-MET and VEGFR2
AUTHOR(S): Navis, Anna C.; Bourgonje, Annika; Wesseling, Pieter; Wright, Alan; Hendriks, Wiljan; Verrijp, Kiek; van der Laak, Jeroen A. W. M.; Heerschap, Arend; Leenders, William P. J.
CORPORATE SOURCE: Department of Pathology, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.
SOURCE: PLoS One (2013), 8(3), e58262
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0058262
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Anti-angiogenic treatment of glioblastoma with Vascular Endothelial Growth Factor (VEGF)- or VEGF Receptor 2 (VEGFR2) inhibitors normalizes tumor vessels, resulting in a profound radiol. response and improved quality of life. This approach however does not halt tumor progression by diffuse infiltration, as this phenotype is less angiogenesis dependent. Combined inhibition of angiogenesis and diffuse infiltrative growth would therefore be a more effective treatment approach in these tumors. The HGF/c-MET axis is important in both angiogenesis and cell migration in several tumor types including glioma. We therefore analyzed the effects of the c-MET- and VEGFR2 tyrosine kinase inhibitor cabozantinib (XL184, Exelixis) on c-MET pos. orthotopic E98 glioblastoma xenografts, which routinely present with angiogenesis-dependent areas of tumor growth, as well as diffuse infiltrative growth. In in vitro cultures of E98 cells, cabozantinib effectively inhibited c-MET phosphorylation, concomitant with inhibitory effects on AKT and ERK1/2 phosphorylation, and cell proliferation and migration. VEGFR2 activation in endothelial cells was also effectively inhibited in vitro. Treatment of BALB/c nu/nu mice carrying orthotopic E98 xenografts resulted in a significant increase in overall survival. Cabozantinib effectively inhibited angiogenesis, resulting in increased hypoxia in angiogenesis-dependent tumor areas, and induced vessel normalization. Yet, tumors ultimately escaped cabozantinib therapy by diffuse infiltrative outgrowth via vessel co-option. Of importance, in contrast to the results from in vitro expts., in vivo blockade of c-MET activation was incomplete, possibly due to multiple factors including restoration of the blood-brain barrier resulting from cabozantinib-induced VEGFR2 inhibition. In conclusion, cabozantinib is a promising therapy for c-MET pos. glioma, but improving delivery of the drug to the tumor and/or the surrounding tissue may be needed for full activity.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of dual targeting of tumor cells and stroma in human glioblastoma xenografts with tyrosine kinase inhibitor against c-MET and VEGFR2)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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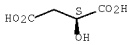
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CMF C28 H24 F N3 O5



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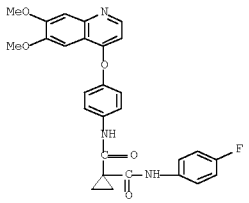
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

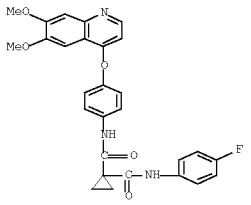
L4 ANSWER 317 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:378985 CAPLUS Full-text
DOCUMENT NUMBER: 159:193339
TITLE: Cellular signaling pathway alterations and potential targeted therapies for medullary thyroid carcinoma
AUTHOR(S): Giunti, Serena; Antonelli, Alessandro; Amorosi, Andrea; Santarpia, Libero
CORPORATE SOURCE: Department of Pathology, Centro Oncologico Fiorentino, Sesto Fiorentino, 50019, Italy
SOURCE: International Journal of Endocrinology (2013) 803171, 16 pp.
CODEN: IJENIG; ISSN: 1687-8345
DIGITAL OBJECT ID: 10.1155/2013/803171
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Parafollicular C-cell-derived medullary thyroid cancer (MTC) comprises 3% to 4% of all thyroid cancers. While cytotoxic treatments have been shown to have limited efficacy, targeted mol. therapies that inhibit rearranged during transfection (RET) and other tyrosine kinase receptors that are mainly involved in angiogenesis have shown great promise in the treatment of metastatic or locally advanced MTC. Multi-tyrosine kinase inhibitors such as vandetanib, which is already approved for the treatment of progressive MTC, and cabozantinib have shown distinct advantages with regard to rates of disease response and control. However, these types of tyrosine kinase inhibitor compds. are able to concurrently block several types of targets, which limits the understanding of RET as a specific target. Moreover, important resistances to tyrosine kinase inhibitors can occur, which limit the long-term efficacy of these treatments. Deregulated cellular signaling pathways and genetic alterations in MTC, particularly the activationof the RAS/mammalian target of rapamycin (mTOR) cascades and RET crosstalk signaling, are now emerging as novel and potentially promising therapeutic treatments for aggressive MTC.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cellular signaling pathway alterations and potential targeted therapies for medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 318 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:377358 CAPLUS Full-text
DOCUMENT NUMBER: 159:86211
TITLE: Cabozantinib as a Novel Therapy for Renal Cell Carcinoma
AUTHOR(S): Vaishampayan, Ulka
CORPORATE SOURCE: Wayne State University, Detroit, MI, 48201, USA
SOURCE: Current Oncology Reports (2013), 15(2), 76-82
CODEN: CORUAT; ISSN: 1534-6269
DIGITAL OBJECT ID: 10.1007/s11912-012-0289-x
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib/XL184 (Exelexis, Inc.) has demonstrated remarkable responses in kidney cancer. Preclin. results revealed VEGF, KIT and MET inhibition in a variety of solid tumors such as thyroid, ovarian, renal, lung, liver and prostate cancers. A phase II trial demonstrated efficacy in renal cancer with a 28 % objective response rate, stable disease rate of 62 % and median progression free survival of 14.7 mo. Predominant toxicities of fatigue and diarrhea were noted. Dramatic responses in bone metastases (three of four patients) make the agent especially valuable for palliation in a disease, where presence of bone metastases is a predictor of worse survival. Cabozantinib is an emerging novel agent with promising activity in advanced kidney cancer. Randomized trials are planned in comparison with standard VEGF inhibitor therapy. Defining the role of MET overexpression would help patient selection and enrich and enhance the future evaluation of this targeted novel agent.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as novel therapy may be useful for treatment of patient with renal cell carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-

quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

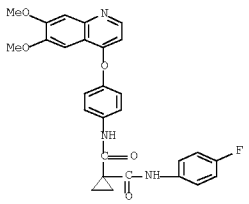


OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 319 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:359822 CAPLUS Full-text
DOCUMENT NUMBER: 159:33929
TITLE: Treatment directed to signalling molecules in patients with advanced differentiated thyroid cancer
AUTHOR(S): Saez, Jose M. G.
CORPORATE SOURCE: Endocrinology and Nutrition Service, L'Hospitalet of Llobregat, Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (CIBERDEM), University Hospital of Bellvitge, Barcelona, Spain
SOURCE: Anti-Cancer Agents in Medicinal Chemistry (2013), 13(3), 483-495
CODEN: AAMCE4; ISSN: 1871-5206
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Mutation detection in samples from thyroid cancer with the addition of BRAF mutation, and also the detection of RAS, RET/PTC, and PAX8/PPARγ mutations, may also contribute to cancer diagnosis. On the other hand, the MAPK/ERK (mitogen-activated protein kinase/extracellular signal-regulated kinase signaling pathway) and PI3K/Akt (lipid kinase phoshoinositid-3-kinase signaling pathway) play an important role in the transmission of cell signals. The genes, coding the signaling cascade proteins (RET, RAS, BRAF, PI3K, PTEN, AKT), are mutated or aberrantly expressed in thyroid cancer derived from follicular thyroid cells. Genetic and epigenetic alternations, concerning MAPK/ERK and PI3K/Akt signaling pathways, contribute to their activation and interaction as a consequence of malignant follicular cell transformation. The understanding of this mol. mechanism provides access to novel mol. prognostic and therapeutic strategies for inhibiting the oncogenic activity of the signaling pathways. This ability to investigate tumor biol. allows for the selection of different drugs. Nowadays the most relevant are treatments directed to tyrosine kinase receptors that bind for a wide variety of ligands and are frequently mutated and induce a constitutive activation such that a chimerical protein expression takes place in follicular cells in the domain of RET, as well as in other receptors. Many mols. such as: motesanib, sorafenib, vandetanib, sunitinib, XL-184, imatinib, axitinib, pazopanib, lenvatinib, combretastatin, gefitinib, cetuximab, bortezomib and thiazoldonedione have been developed. Some of them also can act in receptors of vascular endothelial growth factor and epidermal growth factor receptors. Information obtained through cytol. or biopsy samples permits the study of complex metabolic or genetic pathways, thus providing researchers with a high throughput tool for elucidating changes in the global expression patterns seen in tumor cells and allowing for different therapeutic strategies in thyroid cancer which take into account the predominant altered pathways observed in these samples.
IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment directed to signaling mols. in patients with advanced differentiated thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

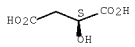
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

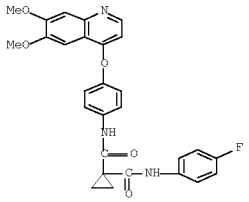
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 320 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:260769 CAPLUS Full-text
DOCUMENT NUMBER: 158:690611
TITLE: Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial
AUTHOR(S): Smith, David C.; Smith, Matthew R.; Sweeney, Christopher; Elfiky, Aymen A.; Logothetis, Christopher; Corn, Paul G.; Vogelzang, Nicholas J.; Small, Eric J.; Harzstark, Andrea L.; Gordon, Michael S.; Vaishampayan, Ulka N.; Haas, Naomi B.; Spira, Alexander I.; Lara, Primo N., Jr.; Lin, Chia-Chi; Srinivas, Sandy; Sella, Avishay; Schoffski, Patrick; Scheffold, Christian; Weitzman, Aaron L.; Hussain, Maha
CORPORATE SOURCE: University of Michigan, Ann Arbor, USA
SOURCE: Journal of Clinical Oncology (2013), 31(4), 412-419
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.45.0494
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Cabozantinib (XL 184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. Patients and Methods: Patients received 100 mg of cabozantinib daily. Those with stable disease per RECIST at 12 wk were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 wk and progression-free survival (PFS) after random assignment. Results: One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 wk was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 wk (95% CI, 10.7 to 62.4 wk) with cabozantinib and 5.9 wk (95% CI, 5.4 to 6.6 wk) with placebo (hazard ratio, 0.12; P < .001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by ≥ 50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot syndrome (8%). Conclusion: Cabozantinib has clin. activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and redns. in bone turnover markers, pain, and narcotic use.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib improved progression-free survival, reduced soft tissue lesions, bone turnover markers, pain and narcotic use in patient with castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 135 THERE ARE 135 CAPLUS RECORDS THAT CITE THIS RECORD (135 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

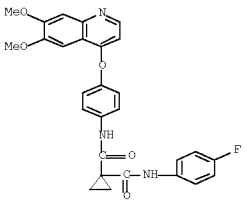
L4 ANSWER 321 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:260767 CAPLUS Full-text
DOCUMENT NUMBER: 160:42366
TITLE: Cabozantinib in prostate cancer: the beginning of a precision paradigm?
AUTHOR(S): Goodin, Susan; DiPaola, Robert S.
CORPORATE SOURCE: The Cancer Institute of New Jersey, University of Medicine and Dentistry of New Jersey Robert Wood Johnson Medical School, New Brunswick, NJ, USA
SOURCE: Journal of Clinical Oncology (2013), 31(4), 401-403
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.46.6185
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The research of Smith et al. (2013) entitled, 'Cabozantinib in patients with advanced prostate cancer: Results of a phase II randomized discontinuation trial' is reviewed with commentary and refs. The authors presented data on a novel orally bioavailable tyrosine kinase inhibitor (TKI), cabozantinib, with activity against multiple targets including

mesenchymal-epithelial transition factor (MET), also known as hepatocyte growth factor receptor, and the vascular endothelial growth factor receptor 2 (VEGFR2). They reported a reduction in uptake on bone scan with improvement in 68% of men (79 of 116) with bone metastasis and complete resolution in 14 patients.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 322 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:187940 CAPLUS Full-text

DOCUMENT NUMBER: 159:33573

TITLE: Profile of cabozantinib and its potential in the treatment of advanced medullary thyroid cancer

AUTHOR(S): Hart, Christopher D.; De Boer, Richard H.

CORPORATE SOURCE: Department of Oncology, Royal Melbourne Hospital, Parkville, Victoria, 3050, Australia

SOURCE: OncoTargets and Therapy (2013), 6, 1-7
CODEN: OTNHAZ; ISSN: 1178-6930

DIGITAL OBJECT ID: 10.2147/OTT.S27671

PUBLISHER: Dove Medical Press Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

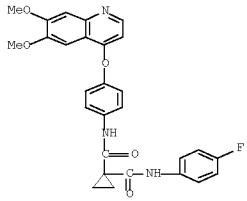
LANGUAGE: English

AB A review. Medullary thyroid cancer is an uncommon malignancy for which until recently little effective treatment existed. It is often characterized by mutation and overexpression of the receptor tyrosine kinases RET (rearranged during transfection), VEGFR2 (vascular endothelial growth factor receptor 2) and MET (mesenchymal-epithelial transition factor), which make attractive targets for drug development. Cabozantinib is an orally bioavailable tyrosine kinase inhibitor which blocks MET, VEGRF2 and RET, and has shown considerable activity in medullary thyroid cancer in a Phase III trial, including in heavily pretreated patients. Its novel combination of vascular endothelial growth factor and MET inhibition is believed to address the MET escape pathway, which is thought to be the cause of nonsustained tumor responses resulting from inhibition of vascular endothelial growth factor alone.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(profile of cabozantinib and potential in treatment of advanced medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 323 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1893113 CAPLUS Full-text

DOCUMENT NUMBER: 158:123654

TITLE: Methods of treating cancer using a chemotherapeutic agent with an agent that blocks the activity of hepatocyte growth factor or its cognate receptor c-MET.

INVENTOR(S): Golub, Todd; Straussman, Ravid

PATENT ASSIGNEE(S): The Broad Institute, Inc., USA; Dana-Farber Cancer Institute, Inc.

SOURCE: PCT Int. Appl., 104pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012178038	A1	20121227	WO 2012-US43788	20120622

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140348819	A1	20141127	US 2014-14128916	20140819
PRIORITY APPLN. INFO.:			US 2011-61501091	P1 20110624
			WO 2012-US43788	W 20120622

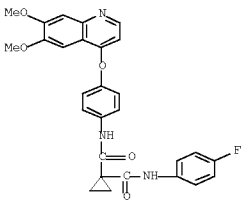
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods of treating cancer by preventing or reducing chemoresistance in a tumor by administering a chemotherapeutic agent together with another agent that blocks the activity of hepatocyte growth factor or its cognate receptor c-MET.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer treatment using a chemotherapeutic agent with an agent that blocks the activity of HGF or its cognate receptor c-MET)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

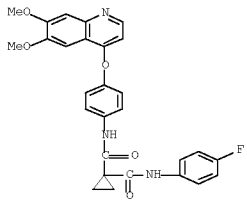


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

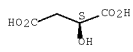
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 324 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1845709 CAPLUS Full-text

DOCUMENT NUMBER: 158:644003

TITLE: New agents in metastatic prostate cancer

AUTHOR(S): Choudhury, Atish D.; Kantoff, Philip W.

CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA, USA

SOURCE: Journal of the National Comprehensive Cancer Network (2012), 10(11), 1403-1409
CODEN: JNCCA4; ISSN: 1540-1405

PUBLISHER: Harborside Press

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

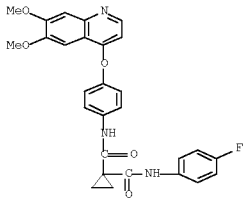
AB A review. Discoveries of mol. mechanisms and therapeutic targets in metastatic castration-resistant prostate cancer (CRPC) have led to significant advancements in the development of effective agents in this setting, with diverse mechanisms of action. Within the past 2 years, 5 agents have been approved for the treatment of patients with metastatic CRPC (cabazitaxel, abiraterone, sipuleucel-T, denosumab, and enzalutamide), and another (Alpharadin) has shown overall survival benefit in a phase III trial.

This article summarizes the phase III data showing clin. benefit from these agents, highlights other promising therapies in phase III studies as single agents (PROSTVAC-VF, ipilimumab, cabozantinib), discusses important unanswered questions regarding these therapies, and provides a schema for their use based on current regulatory approval and how this is likely to evolve as data from ongoing studies are reported. Although curative interventions in metastatic CRPC still do not exist, the hope is that optimization of therapeutic strategies can reduce the morbidity and mortality associated with this disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new agents in metastatic prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 325 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1765841 CAPLUS Full-text

DOCUMENT NUMBER: 158:670189

TITLE: Cabozantinib for the Treatment of Advanced Medullary Thyroid Cancer

AUTHOR(S): Nagilla, Madhavi; Brown, Rebecca L.; Cohen, Ezra E. W.

CORPORATE SOURCE: Section of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Chicago, Chicago, IL, 60645, USA

SOURCE: Advances in Therapy (2012), 29(11), 925-934
CODEN: ADTHE7; ISSN: 0741-238X

DIGITAL OBJECT ID: 10.1007/s12325-012-0060-6

PUBLISHER: Springer Healthcare Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

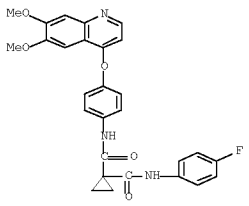
LANGUAGE: English

AB A review. Introduction Patients with advanced medullary thyroid cancer (MTC) have poor prognoses and limited treatment options. Improved knowledge about mol. aberrations associated with MTC and the availability of novel targeted tyrosine kinase inhibitors (TKIs) have led to new potential treatment modalities. Cabozantinib is an oral multitargeted TKI with activity against multiple receptors including RET, vascular endothelial growth factor receptor type 2 (VEGFR2), and MET that has been evaluated in MTC in the preclin. and clin. arenas. Methods This article reviews unmet clin. needs in advanced MTC. The authors consider novel agents that have been studied in MTC, with a focus on the investigational agent cabozantinib. Up-to-date clin. data of cabozantinib in MTC are discussed. Results Recent clin. evaluation suggests that cabozantinib is the first agent to prolong progression-free survival in patients with progressive MTC. These findings indicate that cabozantinib may be an effective therapy in advanced MTC. No improvement in overall survival has been demonstrated but data are not mature. Conclusion Cabozantinib may be an effective treatment option for patients with advanced MTC and is worthy of further evaluation.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for the treatment of advanced medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 326 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1630842 CAPLUS Full-text

DOCUMENT NUMBER: 157:699601

TITLE: Method of treating cancer and bone cancer pain

INVENTOR(S): Schwab, Gisela; Aftab, Dana T.

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

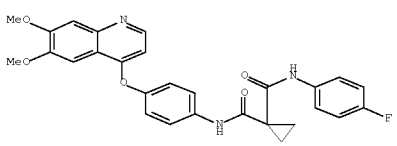
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012151326	A1	20121108	WO 2012-US36191	20120502
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2834778	A1	20121108	CA 2012-2834778	20120502
AR 86242	A1	20131127	AR 2012-101544	20120502
AU 2012250759	A1	20131128	AU 2012-250759	20120502
IL 229094	A	20131231	IL 2012-229094	20120502
KR 2014025496	A	20140304	KR 2013-7031635	20120502
EP 2704717	A1	20140312	EP 2012-720754	20120502
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CN 103717221	A	20140409	CN 2012-80026424	20120502
JP 2014513129	T	20140529	JP 2014-509417	20120502
BR 112013028314	U2	20151103	BR 2013-212013028314	20120502
MX 2013012695	A	20140327	MX 2013-12695	20131030
ZA 2013008206	A	20140730	ZA 2013-8206	20131101
IN 2013KN03259	A	20140221	IN 2013-KN3259	20131105
US 20140179736	A1	20140626	US 2014-14115236	20140228
PRIORITY APPLN. INFO.:			US 2011-61481682 P	20110502
			US 2011-61557366 P	20111108
			WO 2012-US36191 W	20120502

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 157:699601; MARPAT 157:699601

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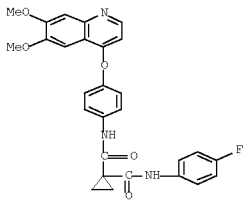


AB This invention is directed to the treatment of cancer, particularly lung cancer, breast cancer, melanoma, renal cell carcinoma, thyroid cancer that has metastasized to the bone. The invention is also directed to a method for treating bone cancer pain in an individual in need of such treatment comprising administering to the individual an effective amount of a compound of Formula I.

IT 849217-68-1
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(method of treating cancer and bone cancer pain)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



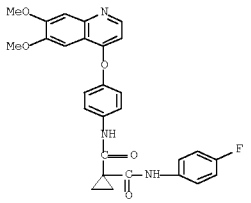
IT 1140909-48-3
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cancer and bone cancer pain)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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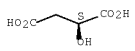
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

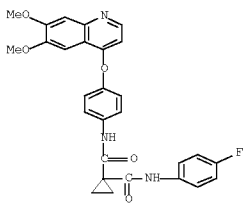
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cancer and bone cancer pain)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

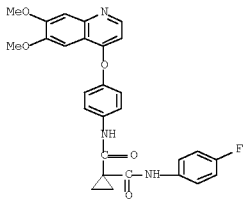
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

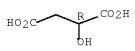
L4 ANSWER 328 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1483426 CAPLUS Full-text
DOCUMENT NUMBER: 157:573884
TITLE: Methods for predicting and improving the survival of gastric cancer patients
INVENTOR(S): Kim, Phillip; Singh, Sharat
PATENT ASSIGNEE(S): Nestec SA, Switz.
SOURCE: PCT Int. Appl., 147pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 327 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1563334 CAPLUS Full-text
DOCUMENT NUMBER: 158:492390
TITLE: New developments in castrate-resistant prostate cancer
AUTHOR(S): Shore, N.; Mason, M.; de Reijke, Th. M.
CORPORATE SOURCE: Carolina Urologic Research Center, Atlantic Urology Clinics, Myrtle Beach, SC, USA
SOURCE: BJU International (2012), 109(Suppl. 6), 22-32
CODEN: BJINFO; ISSN: 1464-4096
DIGITAL OBJECT ID: 10.1111/j.1464-410X.2012.11217.x
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Castrate-resistant prostate cancer (CRPC) occurs when disease progresses in the presence of castrate levels of androgens and remains sensitive to further hormonal manipulation. For many years the treatment of CRPC was limited to the use of docetaxel for metastatic disease. However, this has recently changed with the approval of several new agents. Sipuleucel-T, an immunotherapeutic vaccine, is now available in the US for patients with non-metastatic CRPC and abiraterone, an oral enzyme inhibitor of androgen biosynthesis, as well as cabazitaxel, a cytotoxic chemotherapeutic, have been approved for the treatment of metastatic CRPC. Also, denosumab, a s.c. antibody, is now an option for the treatment of patients with CRPC with bone metastases, in addition to zoledronic acid, an i.v. bisphosphonate. Further treatment advances for metastatic CRPC therapeutics are in late stage phase III development. These include therapies affecting the androgen receptor (MDV3100) as well as addnl. immune-based therapeutics, PROSTVAC and ipilimumab. A broad range of agents is also emerging under the term targeted therapies. The endothelin-A receptor antagonist zibotentan, the tyrosine kinase inhibitors dasatinib, sorafenib and cabozantinib, the anti-angiogenic agent aflibercept, and the clusterin inhibitor custirsen, are all currently being tested for efficacy in metastatic CRPC. The mechanism of action of these and other promising agents are discussed alongside current therapeutic options and their potential place in the treatment landscape for CRPC is considered.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new developments in castrate-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

PATENT INFORMATION:

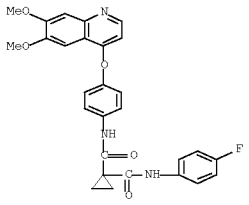
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012138785	A1	20121011	WO 2012-US32206	20120404
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RW:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
CA 2831468	A1	20121011	CA 2012-2831468	20120404
AU 2012240242	A1	20131010	AU 2012-240242	20120404
IL 228579	A	20131128	IL 2012-228579	20120404
EP 2694972	A1	20140212	EP 2012-716858	20120404
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KR 2014020318	A	20140218	KR 2013-7029113	20120404
CN 103597354	A	20140219	CN 2012-80027365	20120404
CN 103597354	B	20160420		
JP 2014517259	T	20140717	JP 2014-503964	20120404
NZ 615738	A	20151127	NZ 2012-615738	20120404
SG 10201601301	A1	20160330	SG 2016-10201601301	20120404
MX 2013011431	A	20140606	MX 2013-11431	20130930
US 20140099300	A1	20140410	US 2013-14044792	20131002
PRIORITY APPLN. INFO.:			US 2011-61471678 P	20110404
			US 2012-61590787 P	20120125
			WO 2012-US32206 W	20120404

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention provides assays and methods for predicting the post-operative survival of a subject having an early stage gastric cancer after tumor surgery. The present invention also provides methods for treating a subject having an early stage gastric cancer by administering a combination therapy tailored to the signal transduction biomarkers that are activated in the cancer. In particular embodiments, the methods of the invention rely on the detection of the activation state or level of a specific combination of signal transducer analytes in a cancer cell obtained from the subject. Thus, the methods of the invention are particularly useful for predicting the survival or prognosis of a subject having an early stage gastric cancer and for guiding both pre- and post-operative treatment decisions by identifying subjects who would benefit from combination therapy as opposed to monotherapy.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cMET and HER as markers and drug targets for predicting survival of a subject having type I or II gastric cancer after tumor surgery)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-

cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

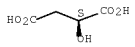
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

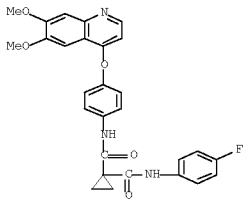


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 329 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1450760 CAPLUS Full-text
DOCUMENT NUMBER: 157:567006
TITLE: Method of treating cancer
INVENTOR(S): Aftab, Dana T.; Schimmoller, Frauke
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 17pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120252840	A1	20121004	US 2012-13438964	20120404
US 20150196545	A1	20150716	US 2015-14668312	20150325
US 20160051532	A1	20160225	US 2015-14933801	20151105

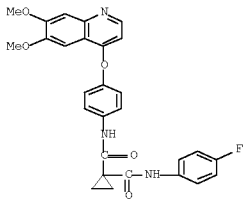
PRIORITY APPLN. INFO.: US 2011-61471367 P 20110404
US 2012-13438964 A1 20120404
US 2015-14668312 A1 20150325
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:567006
AB This invention is directed to the treatment of cancer, particularly ocular melanoma, with a dual inhibitor of MET and VEGF such as Compound 1.
IT 849217-68-1
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(method of treating cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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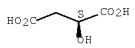
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CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
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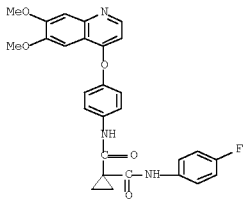
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IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cancer)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

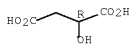
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



L4 ANSWER 330 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1270117 CAPLUS Full-text
DOCUMENT NUMBER: 157:438359
TITLE: Preparation of substituted quinoline compounds as protein tyrosine kinase modulators
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., USA; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120219522	A1	20120830	US 2012-13400586	20120221
US 9133162	B2	20150915		
CA 2820709	A1	20120907	CA 2012-2820709	20120221
CA 2820709	C	20160216		
WO 2012118632	A1	20120907	WO 2012-US25834	20120221

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MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

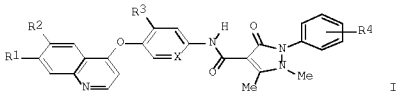
KR 2013095806	A	20130828	KR 2013-7015842		20120221
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JP 5707518	B2	20150430			
ZA 2013003793	A	20140730	ZA 2013-3793		20120221
AU 2012223639	B2	20150319	AU 2012-223639		20120221
RU 2568258	C2	20151120	RU 2013-135662		20120221
MX 2013007278	A	20130913	MX 2013-7278		20130621
US 20150342945	A1	20151203	US 2015-14824096		20150812

PRIORITY APPLN. INFO.:
US 2011-61447104 P 20110228
US 2012-13400586 A3 20120221
WO 2012-US25834 W 20120221

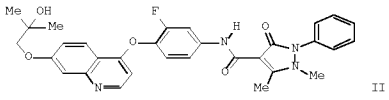
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 157:438359; MARPAT 157:438359

GI



I



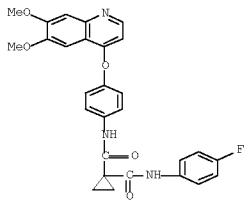
II

AB The present invention provides novel substituted quinoline compds. I [R1, R2 = H, alkoxy, hydroxyalkoxy; R3 = H, F; R4 = H, F, Cl, Br, I, etc.; X = CH or N, wherein at least one of R1 and R2 = hydroxyalkoxy], pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. Syntheses of exemplified compds. I were described. E.g., a multi-step synthesis of the pyrazolecarboxamide II, starting from 3-benzyloxybenzenamine, was provided. Exemplified compds. I were tested for their efficacy as inhibitors of receptor tyrosine kinases such as c-Met, VEGFR and Axl, and as antitumor agents (data given). The invention also provides pharmaceutically acceptable compns. comprising compds. I and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted quinoline compds. as protein tyrosine kinase modulators)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 331 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1269771 CAPLUS Full-text

DOCUMENT NUMBER: 157:431629

TITLE: Methods for detecting cancer and/or determining response to therapeutic agent, and numerous circulating markers (including proteins, nucleic acids and vesicles) used in said methods

INVENTOR(S): Spetzler, David; Holterman, Daniel A.; Pawlowski, Traci; Tasinato, Andrea

PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, S.A.R.L., Luxembourg

SOURCE: PCT Int. Appl., 695pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012115885	A1	20120830	WO 2012-US25741	20120217
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG,				

ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2827894	A1	20120830	CA 2012-2827894	20120217
AU 2012220872	A1	20130912	AU 2012-220872	20120217
CN 103492590	A	20140101	CN 2012-80019718	20120217
EP 2678448	A1	20140101	EP 2012-749642	20120217
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2014507160	T	20140327	JP 2013-555467	20120217
US 20140141986	A1	20140522	US 2014-14001016	20140207
AU 2015268602	A1	20160107	AU 2015-268602	20151209

PRIORITY APPLN. INFO.:
US 2011-61445273 P 20110222
US 2011-61446313 P 20110224
US 2011-61471417 P 20110404
US 2011-61501680 P 20110627
US 2011-61523763 P 20110815
AU 2011-291599 A3 20110818
WO 2012-US25741 W 20120217

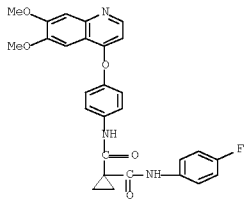
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods for detecting cancer, for detg. whether a cancer is responding to treatment, and /or for determining whether a cancer is likely to respond to treatment that involve detecting of circulating biomarkers. The invention relates that said circulating biomarkers can includie nucleic acids, proteins, vesicles and/or microRNAs. The invention also relates that said biol. samples used in the disclosed methods include isolated extracellular microvesicle populations. The invention also provides kits comprising all reagents used in the disclosed methods. In the examples, the invention disclosed that specific biomarkers are elevated in specific types of cancer, which can used in diagnosis and in determining treatments.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for detecting cancer and/or determining response to therapeutic agent, and numerous circulating markers (including proteins, nucleic acids and vesicles) used in said methods)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 332 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1201570 CAPLUS Full-text

DOCUMENT NUMBER: 157:382704

TITLE: Processes for preparing quinoline compounds and pharmaceutical compositions containing such compounds

INVENTOR(S): Wilson, Jo Ann

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

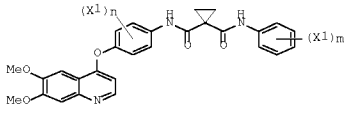
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012109510	A1	20120816	WO 2012-US24591	20120210
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2826751	A1	20120816	CA 2012-2826751	20120210
AU 2012214322	A1	20130829	AU 2012-214322	20120210
AR 85155	A1	20130911	AR 2012-100446	20120210
IL 227848	A	20130930	IL 2012-227848	20120210
CN 103459373	A	20131218	CN 2012-80017723	20120210
EP 2673262	A1	20131218	EP 2012-704492	20120210

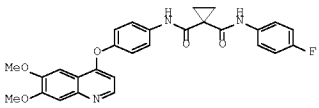
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JP 2014505109	T	20140227	JP 2013-553580		20120210
KR 2014044782	A	20140415	KR 2013-7023174		20120210
NZ 614130	A	20151030	NZ 2012-614130		20120210
MX 2013009116	A	20140131	MX 2013-9116		20130807
ZA 2013006072	A	20140430	ZA 2013-6072		20130813
IN 2013KN02666	A	20140103	IN 2013-KN2666		20130903
US 20140200242	A1	20140717	US 2014-13984559		20140320
PRIORITY APPLN. INFO.:			US 2011-61441520	P	20110210
			US 2011-61441527	P	20110210
			WO 2012-US24591	W	20120210

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:382704; MARPAT 157:382704
GI



I

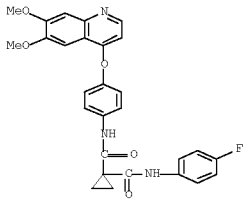


II

AB The invention is directed to processes for prepg. quinoline compds. of formula I wherein X1 is H, Br, Cl and F; X2 is H, Br, Cl and F; n is 1-2 and m is 1-2; and pharmaceutically acceptable salts thereof. Example compound II L-malate was prepared by chlorination of 6,7-dimethoxyquinolin-4-ol followed by etherification of 4-chloro-6,7-dimethoxyquinoline with 4-aminophenol; the resulting 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine underwent acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropanecarbonyl chloride to give compound II, which underwent addition of L-malic acid to give the desired product.

IT 849217-68-1P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for preparing quinoline derivs. and pharmaceutical compns. thereof)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

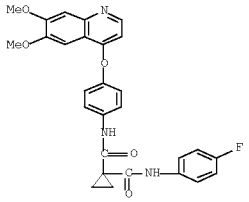


IT 1140909-48-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparing quinoline derivs. and pharmaceutical compns. thereof)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

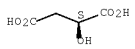
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

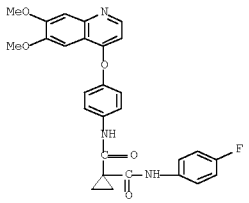


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 333 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1051547 CAPLUS Full-text
DOCUMENT NUMBER: 157:218520
TITLE: Molecular diagnostic methods for predicting brain metastasis of breast cancer
INVENTOR(S): Wong, Stephen T. C.; Zhao, Hong
PATENT ASSIGNEE(S): The Methodist Hospital Research Institute, USA
SOURCE: U.S. Pat. Appl. Publ., 53pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120184560	A1	20120719	US 2011-13245706	20110926
PRIORITY APPLN. INFO.:			US 2010-61386186 P	20100924

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Disclosed are mol. diagnostic compns. and methods for predicting brain metastasis of breast cancer, as well as methods for drug repositioning to identify existing and new therapeutics for use in developing individualized, patient-specific treatment regimens for improving diagnoses and patient outcomes in individuals at risk for brain metastasis of breast cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. diagnostic methods for predicting brain metastasis of breast cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 334 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1042874 CAPLUS Full-text
DOCUMENT NUMBER: 157:221701
TITLE: Bcl-2-like protein 11 (BIM) SRM/MRM assay
INVENTOR(S): Krizman, David B.; Hembrough, Todd; Thyparambil, Sheeno; Liao, Wei-Li
PATENT ASSIGNEE(S): Expression Pathology, Inc., USA
SOURCE: PCT Int. Appl., 28pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

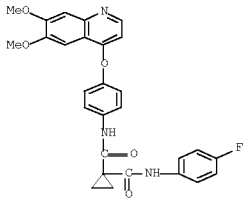
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012097276	A2	20120719	WO 2012-US21283	20120113
WO 2012097276	A3	20121129		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2824752	A1	20120719	CA 2012-2824752	20120113
AU 2012205337	A1	20130801	AU 2012-205337	20120113
IL 227471	A	20130829	IL 2012-227471	20120113
EP 2663863	A2	20131120	EP 2012-734572	20120113
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JP 2014505251	T	20140227	JP 2013-549580		20120113
US 20130302334	A1	20131114	US 2013-13942574		20130715
PRIORITY APPLN. INFO.:			US 2011-61432462	P	20110113
			WO 2012-US21283	W	20120113

AB Specific peptides, and derived ionization characteristics of those peptides, from the Bcl-2-like protein 11 (BIM) are provided that are particularly advantageous for quantifying the BIM protein directly in biol. samples that have been fixed in formalin by the method of Selected Reaction Monitoring (SRM) mass spectrometry, or what can also be termed as Multiple Reaction Monitoring (MRM). Such biol. samples are chemical preserved and fixed where the biol. sample is selected from tissues and cells treated with formaldehyde containing agents/fixatives including formalin-fixed tissue/cells, formalin- fixed/paraffin embedded (FFPE) tissue/cells, FFPE tissue blocks and cells from those blocks, and tissue culture cells that have been formalin fixed and or paraffin embedded. A protein sample is prepared from the biol. sample using the Liquid Tissue reagents and protocol, and the BIM protein is quantitated in the Liquid Tissue sample by the method of SRM/MRM mass spectrometry by quantitating in the protein sample at least one or more of the peptides described. These peptides can be quantitated if they reside in a modified or an unmodified form. An example of a modified form of a BIM peptide is phosphorylation of a tyrosine, threonine, serine, and/or other amino acid residues within the peptide sequence. Samples were prepared with Liquid Tissue and digested with trypsin. Three peptides from BIM were found to be suitable for SRM/MRM assay.

IT [redacted], Cabozantinib
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(determination of cancer resistance to; BIM protein determination by determining BIM peptides by SRM/MRM mass spectrometry)

RN [redacted]
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



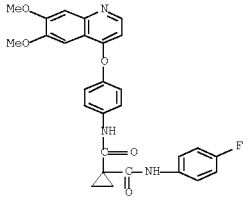
L4 ANSWER 335 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:924299 CAPLUS Full-text
DOCUMENT NUMBER: 157:122897
TITLE: Drug selection for therapy for malignancies involving between the expression and/or activation levels of cMet protein and/or HER3 protein in the sample compared to the control protein and/or control sample.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for therapy for malignancies involving aberrant c-Met signaling using antibody-based arrays)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

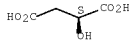
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 336 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:706472 CAPLUS Full-text
DOCUMENT NUMBER: 156:628365
TITLE: c-Met signaling using antibody-based arrays
INVENTOR(S): Singh, Sharat; Hoe, Nicholas; Princen, Fred; Liu, Xinjun
PATENT ASSIGNEE(S): Prometheus Laboratories Inc., USA
SOURCE: PCT Int. Appl., 140pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012088337	A1	20120628	WO 2011-US66624	20111221
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2822283	A1	20120628	CA 2011-2822283	20111221
AU 2011348256	A1	20130711	AU 2011-348256	20111221
IL 227009	A	20130829	IL 2011-227009	20111221
EP 2656077	A1	20131030	EP 2011-805738	20111221
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CN 103384828	A	20131106	CN 2011-80068269	20111221
KR 2014002711	A	20140108	KR 2013-7019356	20111221
JP 2014503821	T	20140213	JP 2013-546392	20111221
NZ 612483	A	20150327	NZ 2011-612483	20111221
SG 10201510086	A1	20160128	SG 2015-10201510086	20111221
US 20140024548	A1	20140123	US 2013-13923316	20130620
MX 2013007429	A	20140131	MX 2013-7429	20130621
PRIORITY APPLN. INFO.:			US 2010-61426948 P	20101223
			US 2011-61438904 P	20110202
			WO 2011-US66624 W	20111221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods for selecting a suitable anticancer drug therapy, and for identifying and predicting response, for the treatment of a malignant cancer involving aberrant c-Met signaling. The present invention also provides methods for monitoring the status of a malignant cancer involving aberrant c-Met signaling and monitoring how a patient with the malignant cancer is responding to anticancer drug therapy. Information on the expression and/or activation states of components of signal transduction pathways (e.g., HER3 and/or c-Met signal transduction pathway components) derived from practice of the present invention can be used for malignant cancer diagnosis, prognosis, and in the design of cancer treatments for malignancies involving aberrant c-Met signaling. Certain embodiments comprise administering a cMet inhibitor alone or a cMet inhibitor in combination with a pathway-directed therapy based upon the differences

TITLE: Cancer cell-derived receptor activator of the NF-KB ligand drives bone and soft tissue metastases
INVENTOR(S): Chu, Gina C. Y.; Chung, Leland W. K.; Zhau, Haiyen E.; Wang, Ruoxiang
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012064967	A2	20120518	WO 2011-US60204	20111110
WO 2012064967	A3	20120705		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20130263297	A1	20131003	US 2013-13889135	20130507
PRIORITY APPLN. INFO.:			US 2010-61412360 P	20101110
			US 2011-61442679 P	20110214
			WO 2011-US60204 A2	20111110
			US 2012-61718626 P	20121025

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

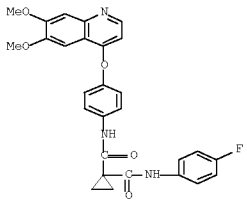
AB The present invention relates to metastases. More specifically, the invention relates to compns. and methods for the inhibition of metastases of cancer cells, such as prostate cancer cells, to bones and soft tissue. The present invention also relates to the treatment of cancer, including but not limited to prostate cancer. Also provided are animal models for studying cancer metastasis; particularly, prostate cancer metastasis.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer cell-derived receptor activator of the NF-KB ligand drives bone and soft tissue metastases)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

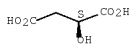
CRN 849217-68-1
CMF C28 H24 F N3 O5



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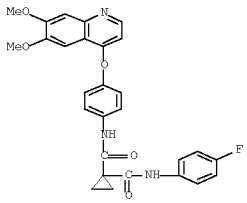
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



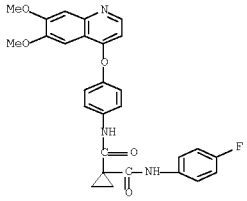
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 337 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:560657 CAPLUS Full-text
DOCUMENT NUMBER: 158:122090
TITLE: Recent advances in the molecular pathogenesis and targeted therapies of medullary thyroid carcinoma
AUTHOR(S): Almeida, Madson Q.; Hoff, Ana O.
CORPORATE SOURCE: Instituto do Cancer da Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil
SOURCE: Current Opinion in Oncology (2012), 24(3), 229-234
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e328351c71a
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: This review will focus on the recent advances in mol. pathogenesis and targeted therapies for medullary thyroid carcinoma (MTC). Unlike hereditary MTC in which rearranged during transfection (RET) mutations are the most important precipitating events, in sporadic MTC the genetic or mol. biomarkers are yet to be established. Recent findings: Targeted mol. therapies that inhibit RET and other tyrosine kinase receptors involved in angiogenesis have shown great promise in the treatment of metastatic or locally advanced MTC and are under investigation. In addition, the recent findings of H-RAS mutations in 56% of RET-neg. sporadic MTC and the activation of the mammalian target of rapamycin (mTOR) intracellular signaling pathway in hereditary MTC suggests that addnl. or alternative genetic events are important for MTC pathogenesis. Summary: Recently, vandetanib (ZD6474), an inhibitor of vascular endothelial growth factor receptor (VEGFR) 2 and VEGFR 3, RET, and epidermal growth factor receptor (EGFR), was approved for the treatment of adults with symptomatic or progressive MTC. Significant advantages for vandetanib over placebo were seen in terms of response rate, disease control rate, and biochem. response in a phase III study. Furthermore, cabozantinib (XL184), an inhibitor of VEGFR 1 and VEGFR 2, hepatocyte growth factor receptor (MET), and RET, was associated with partial response and stable disease in 29 and 41%, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vandetanib and cabozantinib was effective in treatment of patient with medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 338 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:508891 CAPLUS full-text
DOCUMENT NUMBER: 158:93453
TITLE: Novel Molecular Targets for the Therapy of Castration-Resistant Prostate Cancer
AUTHOR(S): Agarwal, Neeraj; Sonpavde, Guru; Sternberg, Cora N.
CORPORATE SOURCE: Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA
SOURCE: European Urology (2012), 61(5), 950-960
CODEN: EUURAV; ISSN: 0302-2838
DIGITAL OBJECT ID: 10.1016/j.eururo.2011.12.028
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Improved understanding of mechanisms underlying metastatic castration-resistant prostate cancer (mCRPC) progression has led to the recognition of multiple mol. targets and advances in the therapeutic landscape. The addition of abiraterone acetate, sipuleucel-T, cabazitaxel, and denosumab to the therapeutic armamentarium and the impending addition of MDV-3100 and radium-223 underscore the importance of androgen pathway inhibition, immunotherapy, tubulin antagonism, and pathophysiol. of bone metastasis. Review the next generation of mol. targets in mCRPC. Medline databases were searched for >100 original articles published as of Oct. 18, 2011, with the search terms metastatic castration-resistant prostate cancer, targeted therapy, biol. agents, and immunotherapy. Proceedings from the last 5 yr of conferences of the American Society of Clin. Oncol., American Urol. Association, European Society of Medical Oncol., and the European Association of Urol. were also searched. We included novel and promising drugs that have reached clin. trial evaluation. The major findings were addressed in an evidence-based fashion. Prospective trials and important preclin. data were analyzed.mCRPC is a disease with multiple mol. drivers. Mol. pathways being targeted in ongoing phase 3 trials are androgen signaling (MDV3100, TAK700), immunoregulatory pathways (ipilimumab, Prostvac-VF-TRICOM), Src (dasatinib), Met (cabozantinib), clusterin (custirsen), and angiogenesis (aflibercept, tasquinimod). The strides made in identifying multiple other novel mol. targets offer potential opportunities for further improving outcomes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(knowledge on novel mol. targets like Met signaling pathway using drugs like cabozantinib could be more beneficial in patient with metastatic castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

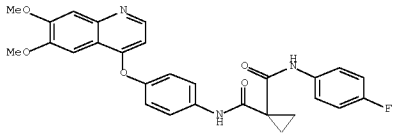


OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (25 CITINGS)
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 339 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:495814 CAPLUS full-text
DOCUMENT NUMBER: 156:469436
TITLE: Dual inhibitors of Met and VEGF for the treatment of castration- resistant prostate cancer and osteoblastic bone metastases
INVENTOR(S): Smith, David; Hussain, Maha
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012044572	A1	20120405	WO 2011-US53233	20110926
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2812750	A1	20120405	CA 2011-2812750	20110926
AU 2011307304	A1	20130502	AU 2011-307304	20110926
IL 225507	A	20130530	IL 2011-225507	20110926
EP 2621481	A1	20130807	EP 2011-764655	20110926
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2013537916	T	20131007	JP 2013-530386	20110926
CN 103402505	A	20131120	CN 2011-80056580	20110926
KR 2014025304	A	20140304	KR 2013-7010372	20110926
MX 2013003594	A	20130801	MX 2013-3594	20130327
ZA 2013002422	A	20131223	ZA 2013-2422	20130404
IN 2013KN00998	A	20130906	IN 2013-KN998	20130409
US 20140057943	A1	20140227	US 2013-13876290	20131105

PRIORITY APPLN. INFO.: US 2010-61386959 P 20100927
US 2011-61481671 P 20110502
WO 2011-US53233 W 20110926
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:469436; MARPAT 156:469436
GI

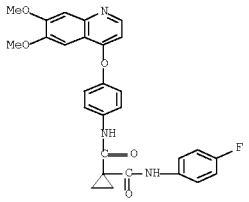


AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and osteoblastic bone metastases, with a dual inhibitor of MET and VEGF.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

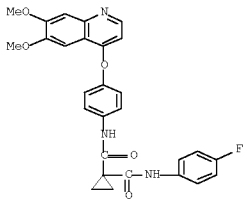


IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

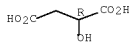
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CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 340 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:495788 CAPLUS Full-text

DOCUMENT NUMBER: 156:469435

TITLE: Dual inhibitors of Met and VEGF for the treatment of castration resistant prostate cancer and osteoblastic bone metastases

INVENTOR(S): Smith, David; Hussain, Maha

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

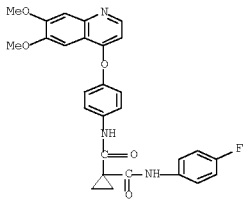
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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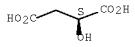
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2812744	A1	20120405	CA 2011-2812744	20110926
AU 2011307309	A1	20130502	AU 2011-307309	20110926
EP 2621483	A1	20130807	EP 2011-764657	20110926

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2013537918	T	20131007	JP 2013-530392	20110926
CN 103391773	A	20131113	CN 2011-80056999	20110926
US 20140057908	A1	20140227	US 2013-13876306	20131108

PRIORITY APPLN. INFO.:
US 2010-61386971 P 20100927
US 2010-61386983 P 20100927
US 2010-61386993 P 20100927
WO 2011-US53245 W 20110926

OTHER SOURCE(S): CASREACT 156:469435; MARPAT 156:469435

AB This invention discloses compds. directed at the treatment of cancer, particularly castration- resistant prostate cancer and osteoblastic bone metastases, with a dual inhibitor of MET and VEGF.

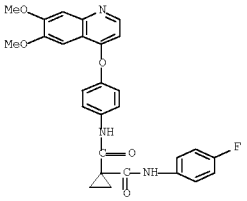
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

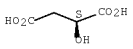
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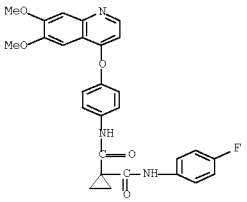
CM 2

CRN 97-67-6
CMF C4 H6 O5

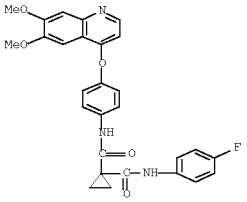
Absolute stereochemistry. Rotation (-).



IT [illegible]
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



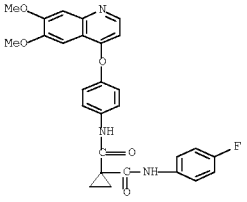
quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT [illegible]
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(c-met modulators as antitumor agents)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

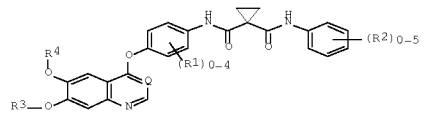
CRN 636-61-3

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 341 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:425741 CAPLUS Full-text
DOCUMENT NUMBER: 156:412018
TITLE: Methods of using C-met modulators as Anticancer agents
INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-Ming; Forsyth, Timothy Patrick; Khoury, Richard George; Leahy, James William; Mac, Morrison B.; Mann, Larry W.; Nuss, John M.; Parks, Jason Jevious; Wang, Yong; Xu, Wei; Simeone, Diane
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 25pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20120070368	A1	20120322	US 2011-13087094		20110414
US 20150202196	A1	20150723	US 2014-14518733		20141020
PRIORITY APPLN. INFO.:			US 2010-61325095	P	20100416
			US 2011-13087094	B1	20110414

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:412018; MARPAT 156:412018
GI

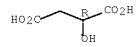


I

AB Disclosed are methods of treating cancer by administering a compd. of Formula I (wherein R1, R2 = independently, halo; R3, R4 = independently, (C1-C6)-alkyl; Q = CH, N) in combination with gemcitabine (GEM).
IT [illegible]
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(c-met modulators as antitumor agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-

CMF C4 H6 O5

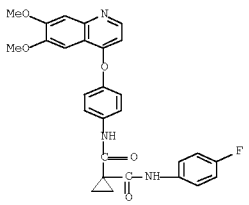
Absolute stereochemistry. Rotation (+).



L4 ANSWER 342 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:373163 CAPLUS Full-text
DOCUMENT NUMBER: 157:622817
TITLE: Multi-targeted tyrosine kinase inhibitors in clinical development: focus on XL-184 (cabozantinib)
AUTHOR(S): Bowles, D. W.; Kessler, E. R.; Jimeno, A.
CORPORATE SOURCE: Division of Medical Oncology, University of Colorado Denver, Aurora, CO, USA
SOURCE: Drugs of Today (2011), 47(11), 857-868
CODEN: MDACAP; ISSN: 1699-3993
DIGITAL OBJECT ID: 10.1358/dot.2011.47.11.1688487
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. XL-184 (cabozantinib) is a novel, small-mol., multi-targeted receptor tyrosine kinase inhibitor with particular activity against hepatocyte growth factor receptor (tyrosine-protein kinase Met), vascular endothelial growth factor receptor 2 (VEGFR-2) and proto-oncogene tyrosine-protein kinase receptor Ret. There is ample evidence of Met, VEGFR-2 and Ret signaling in several tumor types. Preclin. data suggest that XL-184 has activity in tumors derived from both epithelial and mesenchymal origins. Phase I and II clin. studies support significant antitumor activity, particularly in medullary thyroid cancer and cancers metastatic to the bone. This review will evaluate XL-184's preclin. pharmacol., pharmacokinetics, drug interactions and clin. activity in phase I through phase III studies.
IT [illegible], XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(focus on XL-184 (cabozantinib) is a novel multi-targeted tyrosine kinase inhibitors in clin. development)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

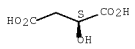
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 343 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:345887 CAPLUS Full-text
DOCUMENT NUMBER: 156:388076
TITLE: C-met biomarker in treatment efficacy and prognosis
INVENTOR(S): Patel, Premal; Peterson, Amy C.; Yauch, Robert L.; Zha, Jiping
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 134pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012031027	A1	20120308	WO 2011-US50069	20110831

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2808236	A1	20120308	CA 2011-2808236	20110831
US 20120089541	A1	20120412	US 2011-13223173	20110831
AU 2011295919	A1	20130307	AU 2011-295919	20110831
IL 224962	A	20130430	IL 2011-224962	20110831
EP 2612151	A1	20130710	EP 2011-754597	20110831

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

CN 103221825	A	20130724	CN 2011-80051781	20110831
KR 2013103734	A	20130924	KR 2013-7008025	20110831
JP 2013537966	T	20131007	JP 2013-526209	20110831
ZA 2013001175	A	20140430	ZA 2013-1175	20110831
SG 10201408229	A1	20150227	SG 2014-10201408229	20110831
MX 2013002084	A	20130509	MX 2013-2084	20130221
IN 2013DN01711	A	20141024	IN 2013-DN1711	20130225
AU 2013202759	A1	20130502	AU 2013-202759	20130406
US 20140037625	A1	20140206	US 2013-14046867	20131004
AU 2016200630	A1	20160218	AU 2016-200630	20160202

PRIORITY APPLN. INFO.:

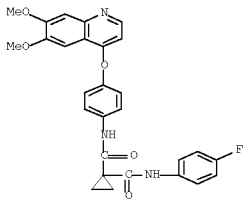
US 2010-61378911	P	20100831
US 2010-61389922	P	20101005
US 2010-61390995	P	20101007
US 2010-61420703	P	20101207
US 2011-61487527	P	20110518
US 2011-61492338	P	20110601
US 2011-61503489	P	20110630
AU 2011-295919	A3	20110831
US 2011-13223173	B1	20110831
WO 2011-US50069	W	20110831
AU 2013-202759	A3	20130406

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The authors disclose the use of c-met as a biomarker for patient selection and patient prognosis in cancer. In a clin. trial, combination treatment with MetMAb (onartuzumab) and erlotinib provided a clin. meaningful benefit to patients with non-small cell lung cancer (NSCLC) that expressed high levels of c-met biomarker. The results showed that the efficacy, as evaluated by progression free survival (PFS) and overall survival (OS), was pos. especially when compared to PFS and OS data for erlotinib treatment alone. The addition of MetMAb to erlotinib nearly doubled the progression free and overall survival in patients with NSCLC that expressed high levels of c-met biomarker. The clin. trial data also showed that treatment with MetMAb in combination with erlotinib increased the risk of progression and death in patients with NSCLC that expressed low levels of c-met biomarker.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Met receptor as biomarker for combination therapy efficacy and cancer prognosis)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 344 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:340365 CAPLUS Full-text
DOCUMENT NUMBER: 156:380310
TITLE: Synergistic drug combination for the treatment of cancer
INVENTOR(S): Gusenbauer, Simone; Ullrich, Axel
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 111pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2425830	A1	20120307	EP 2010-75382	20100903

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BA, ME, RS

PRIORITY APPLN. INFO.: EP 2010-75382 20100903

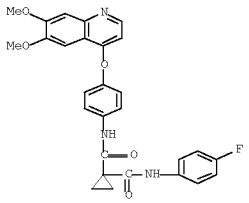
AB The invention relates to synergistic drug combinations and the use of said drug combinations for the treatment of proliferative diseases such as cancer. Combination of drugs include e.g. chlorethamine, cyclophosphamide, trofosfamide, daunorubicin, doxorubicin, mitomycin C.

IT 1140909-48-3, X1184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic drug combination for treatment of cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

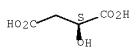
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 345 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:265414 CAPLUS Full-text
DOCUMENT NUMBER: 156:357951
TITLE: Circulating biomarkers for disease
INVENTOR(S): Spetzler, David; Holterman, Daniel; Pawlowski, Traci; Kuslich, Christine
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, Luxembourg
SOURCE: PCT Int. Appl., 639pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012024543	A1	20120223	WO 2011-US48327	20110818

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2808417	A1	20120223	CA 2011-2808417		20110818
AU 2011291599	A1	20130307	AU 2011-291599		20110818
AU 2011291599	B2	20150910			
EP 2606353	A1	20130626	EP 2011-818814		20110818
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR					
JP 2013540995	T	20131107	JP 2013-526012		20110818
US 20140148350	A1	20140529	US 2013-13817383		20130520
US 20150301055	A1	20151022	US 2015-14789729		20150701
AU 2015268602	A1	20160107	AU 2015-268602		20151209
PRIORITY APPLN. INFO.:			US 2010-61374951	P	20100818
			US 2010-61379670	P	20100902
			US 2010-61381305	P	20100909
			US 2010-61383305	P	20100915
			US 2010-61391504	P	20101008
			US 2010-61393823	P	20101015
			US 2010-61411890	P	20101109
			US 2010-61413377	P	20101112
			US 2010-61414870	P	20101117
			US 2010-61416560	P	20101123
			US 2010-61421851	P	20101210
			US 2010-61423557	P	20101215
			US 2010-61428196	P	20101229
			US 2011-61471417	P	20110404
			US 2010-61321392	P	20100406
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			US 2010-61322690	P	20100409
			US 2010-61332174	P	20100506
			US 2010-61334547	P	20100513
			US 2010-61348214	P	20100525
			US 2010-61348685	P	20100526
			US 2010-61354125	P	20100611
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			US 2010-61356974	P	20100621
			US 2010-61357517	P	20100622
			US 2010-61362674	P	20100708
			US 2010-61364785	P	20100715
			US 2010-61370088	P	20100802
			WO 2011-US31479	A	20110406
			AU 2011-291599	A3	20110818
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			US 2013-13817383	A1	20130520

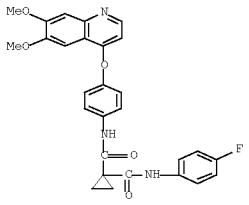
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Biomarkers can be assessed for diagnostic, therapy-related or prognostic methods to identify phenotypes, such as a condition or disease, or the stage or progression of a disease. Circulating biomarkers from a bodily fluid can be used in profiling of physiol. states or determining phenotypes. These include nucleic acids, protein, and circulating structures such as vesicles. Biomarkers can be used for theranostic purposes to select candidate treatment regimens for diseases, conditions, disease stages, and stages of a condition, and can also be used to determine treatment efficacy. The biomarkers can be circulating biomarkers, including vesicles and microRNA. Various anti-DLL4 antibodies were tethered to beads and used to capture vesicles in blood samples from subjects with breast cancer, colorectal cancer or normal subjects. The bead captured vesicles were detected with fluorescently-labeled antibodies against the tetraspanins CD9, CD63, and CD81. The median fluorescence intensity of the captured and labeled vesicles was measured using laser detection. There were noticeable differences both among normals and breast cancer plasma as well as between the avs. of normals and cancer patients.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DLL4, vesicle, and microRNA circulating biomarkers for disease diagnosis, therapy, prognosis, or theranostics)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 346 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:155432 CAPLUS Full-text

DOCUMENT NUMBER: 157:565304

TITLE: Drug development to overcome resistance to EGFR inhibitors in lung and colorectal cancer

AUTHOR(S): Dienstmann, Rodrigo; De Dosso, Sara; Felip, Enriqueta; Tabernero, Josep

CORPORATE SOURCE: Medical Oncology Department, Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, 08035, Spain

SOURCE: Molecular Oncology (2012), 6(1), 15-26
CODEN: MOONC3; ISSN: 1574-7891

DIGITAL OBJECT ID: 10.1016/j.molonc.2011.11.009

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; General Review; (online computer file)

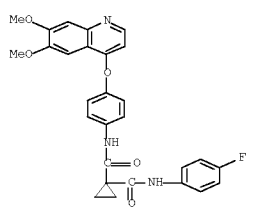
LANGUAGE: English

AB A review. Epidermal growth factor receptor (EGFR) is a validated target in different human malignancies. EGFR tyrosine kinase inhibitors (TKIs) are known to contribute considerably to the extension of progression-free survival in EGFR-mutant non-small cell lung cancer and monoclonal antibodies (mAbs) targeting EGFR have also improved the efficacy outcomes in KRAS wild-type colorectal cancer. Nevertheless, a significant percentage of lung and colorectal cancer patients do not respond to anti-EGFR agents and secondary resistance after initial benefit is a challenging reality faced by clinicians. Extensive preclin. work on the potential mechanisms of resistance to EGFR inhibitors in different disease settings has guided the development of second-generation irreversible EGFR TKIs, more efficient anti-EGFR mAbs, and combination strategies with agents targeting other receptors and downstream effectors. In order to elucidate the role of the multiple therapeutic strategies under investigation to overcome EGFR inhibitors-resistance, rational drug development based on stringent preclin. data, biomarker validation and proper selection of patients in the ongoing clin. trials are of paramount importance. Preliminary results of clin. trials evaluating these approaches will be discussed in this manuscript, with emphasis on TKIs in lung cancer and mAbs in advanced colorectal cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug development to overcome resistance to EGFR inhibitors in lung and colorectal cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 347 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:99813 CAPLUS Full-text

DOCUMENT NUMBER: 157:249246

TITLE: HGF/c-MET targeted therapeutics: novel strategies for cancer medicine

AUTHOR(S): Yap, Timothy A.; Sandhu, Shahneen K.; Alam, Salma M.; de Bono, Johann S.

CORPORATE SOURCE: The Royal Marsden NHS Foundation Trust, Sutton, Surrey, SM2 5PT, UK

SOURCE: Current Drug Targets (2011), 12(14), 2045-2058
CODEN: CDTUAU; ISSN: 1389-4501

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The hepatocyte growth factor/mesenchymal-epithelial transition factor (HGF/c-MET) receptor tyrosine kinase (RTK) pathway plays a pleotropic role in cell proliferation, migration, invasion, angiogenesis and survival. Although it has critical physiol. functions in embryonic development and tissue repair, this signaling cascade is frequently deregulated in a wide range of tumors. Aberrant HGF/c-MET signaling, driven by various mechanisms, including constitutive activation and over-expression, has multifunctional effects in oncogenesis and is implicated in the acquisition of an aggressive phenotype with metastatic potential. The central role of c-MET activity in cancer progression, as well as disparities between quiescent HGF/c-MET signaling in normal tissue and overexpression in tumor may provide a degree of tumor selectivity for therapeutic intervention, making HGF or c-MET inhibition an attractive proposition in oncol. This review focuses on the underlying oncogenic role of aberrant HGF/c-MET signaling in malignant progression, as well as recent preclin. and clin. data on the different strategies employed in inhibiting HGF/c-MET function.

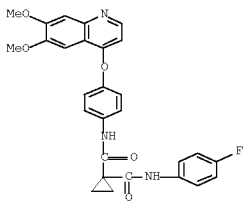
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapies targeting hepatocyte growth factor/mesenchymal-epithelial transition factor signaling involved in cell proliferation, migration, invasion, angiogenesis and survival may be useful for treatment of patient with cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

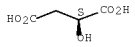
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 134 THERE ARE 134 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 348 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:94602 CAPLUS Full-text
DOCUMENT NUMBER: 156:167648
TITLE: Administration of hypoxia activated prodrugs and antiangiogenic agents for the treatment of cancer
INVENTOR(S): Hart, Charles; Curd, John; Kroll, Stewart; Sun, Jessica
PATENT ASSIGNEE(S): Threshold Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012009288	A2	20120119	WO 2011-US43594	20110711
WO 2012009288	A9	20120419		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2803675	A1	20120119	CA 2011-2803675	20110711
KR 2013045341	A	20130503	KR 2013-7002206	20110711
EP 2593139	A2	20130522	EP 2011-807356	20110711

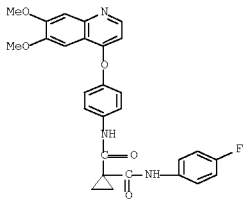
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JP 2013531038	T	20130801	JP 2013-519747	20110711
MX 2012014428	A	20130305	MX 2012-14428	20121210
ZA 2013000692	A	20130925	ZA 2013-692	20130125
US 20140010805	A1	20140109	US 2013-13809135	20130724
PRIORITY APPLN. INFO.:			US 2010-61363610 P	20100712
			US 2011-61470412 P	20110331
			US 2011-61470812 P	20110401
			WO 2011-US43594 W	20110711

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Administration of a hypoxia activated prodrug in combination with an antiangiogenic agent is useful for treating cancer. Hypoxia activated prodrug is selected from the group consisting of TH-281, TH-302, and TH-308. The antiangiogenic agent is selected from the group consisting of an anti-VEGF antibody, a VEGF-trap, an anti-VEGFR antibody, a VEGFR inhibitor, thalidomide etc.
IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of hypoxia activated prodrugs and antiangiogenic agents for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

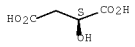
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L4 ANSWER 349 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:90800 CAPLUS Full-text
DOCUMENT NUMBER: 156:186804
TITLE: C-met modulator pharmaceutical compositions comprising N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide
INVENTOR(S): Wilson, Jo Ann
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 40pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012009722	A1	20120119	WO 2011-US44378	20110718

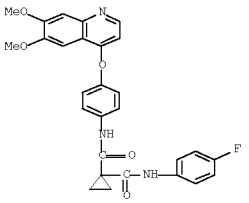
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2805645	A1	20120119	CA 2011-2805645	20110718
AR 82252	A1	20121121	AR 2011-102584	20110718
AU 2011278950	A1	20130307	AU 2011-278950	20110718
IL 224189	A	20130324	IL 2011-224189	20110718
EP 2593090	A1	20130522	EP 2011-740764	20110718

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

CN 103221035	A	20130724	CN 2011-80044602	20110718
JP 2013531045	T	20130801	JP 2013-519870	20110718
KR 2013137586	A	20131217	KR 2013-7003043	20110718
NZ 607118	A	20150529	NZ 2011-607118	20110718
IN 2013KN00112	A	20130705	IN 2013-KN112	20130114
MX 2013000567	A	20130501	MX 2013-567	20130115
ZA 2013000458	A	20130925	ZA 2013-458	20130117
US 20130337015	A1	20131219	US 2013-13810537	20130826
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			WO 2011-US44378 W	20110718

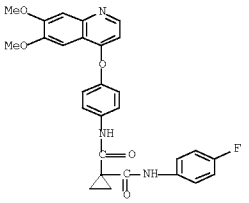
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:186804
AB Pharmaceutical compns. and unit dosage forms comprising N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (I) are disclosed. Thus, 6,7-dimethoxyquinolin-4-ol was converted to 4-chloro-6.7-dimethoxyquinoline followed by reaction with 4-aminphenol to give 4-(6,7-dimethoxy-quinolin-4-yloxy)-phenylamine. This was further allowed to react with 1-(4-fluorophenylcarbamoyl)cyclopropanecarbonyl chloride to give I. A tablet composition comprised 31.68% along with excipients such as microcryst. cellulose 38.85, lactose, HPC, and Croscarmellose sodium.
IT 849217-68-1, 1140909-48-3, Cabozantinib S-malate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-met modulator pharmaceutical comps. comprising dimethoxyquinolinyloxyphenyl(fluorophenyl)cyclopropanedicarboxamide)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

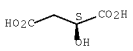
CRN 849217-68-1
CMF C28 H24 F N3 O5

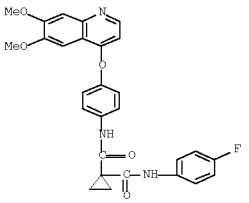


CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

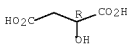




CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

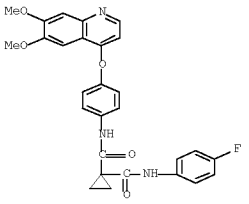


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 350 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:10093 CAPLUS Full-text
DOCUMENT NUMBER: 157:152076
TITLE: In the clinic: ongoing clinical trials evaluating c-MET-inhibiting drugs
AUTHOR(S): Sharma, Neelesh; Adjei, Alex A.
CORPORATE SOURCE: Department of Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA
SOURCE: Therapeutic Advances in Medical Oncology (2011), 3(Suppl. 1), S37-S50
CODEN: TAMOB8; ISSN: 1758-8340
DIGITAL OBJECT ID: 10.1177/1758834011423403
PUBLISHER: Sage Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The c-MET (mesenchymal-epithelial transition factor) pathway is dysregulated in many human cancers and promotes tumor growth, invasion and dissemination. The c-MET receptor tyrosine kinase can be activated via gene mutation, gene amplification, protein overexpression and/or a Ligand-dependent autocrine/paracrine loop. Abnormalities in c-MET signaling have been reported to correlate with poor clin. outcomes and drug resistance in patients with cancer. Significant progress has been made in advancement of c-MET pathway inhibitors through to clin. trials. A robust pipeline of high-quality inhibitors targeting different aspects of c-MET activation is currently being explored in phase I, II and III clin. trials across multiple tumor types. Preliminary data demonstrate promising clin. activity with these agents, along with an acceptable toxicity profile. In this manuscript, the pharmacol. profile of drugs targeting the c-MET pathway and available data from ongoing clin. trials of these drugs are discussed.
IT 1140909-48-3, X1184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ongoing clin. trials evaluating mesenchymal-epithelial transition factor-inhibiting drugs)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

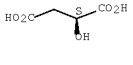
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

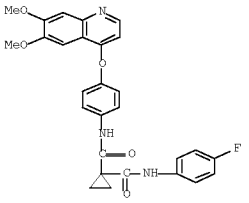


OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

IT 1235470-36-6 1235670-38-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C-met modulator pharmaceutical compns. comprising dimethoxyquinolinyloxyphenyl(fluorophenyl)cyclopropanedicarboxamide)
RN 1235470-36-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

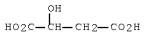
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 6915-15-7
CMF C4 H6 O5



RN 1235470-38-8 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

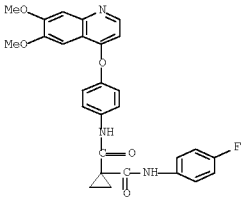
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 351 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:1586879 CAPLUS Full-text
DOCUMENT NUMBER: 156:655505
TITLE: Cabozantinib (XL184), a Novel MET and VEGFR2 Inhibitor, Simultaneously Suppresses Metastasis, Angiogenesis, and Tumor Growth
AUTHOR(S): Yakes, F. Michael; Chen, Jason; Tan, Jenny; Yamaguchi, Kyoko; Shi, Yongchang; Yu, Peiwen; Qian, Fawn; Chu, Felix; Bentzien, Frauke; Cancilla, Belinda; Orf, Jessica; You, Andrew; Laird, A. Douglas; Engst, Stefan; Lee, Lillian; Lesch, Justin; Chou, Yu-Chien; Joly, Alison H.
CORPORATE SOURCE: Exelixis, Inc., South San Francisco, CA, 94083, USA
SOURCE: Molecular Cancer Therapeutics (2011), 10(12), 2298-2308
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-11-0264
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The signaling pathway of the receptor tyrosine kinase MET and its ligand hepatocyte growth factor (HGF) is important for cell growth, survival, and motility and is functionally linked to the signaling pathway of VEGF, which is widely recognized as a key effector in angiogenesis and cancer progression. Dysregulation of the MET/VEGF axis is found in a number of human malignancies and has been associated with tumorigenesis. Cabozantinib (XL184) is a small-mol. kinase inhibitor with potent activity toward MET and VEGF receptor 2 (VEGFR2), as well as a number of other receptor tyrosine kinases that have also been implicated in tumor pathobiol., including RET, KIT, AXL, and FLT3. Treatment with cabozantinib inhibited MET and VEGFR2 phosphorylation in vitro and in tumor models in vivo and led to significant redns. in cell invasion in vitro. In mouse models, cabozantinib dramatically altered tumor pathol., resulting in decreased tumor and endothelial cell proliferation coupled with increased apoptosis and dose-dependent inhibition of tumor growth in breast, lung, and glioma tumor models. Importantly, treatment with cabozantinib did not increase lung tumor burden in an exptl. model of metastasis, which has been observed with inhibitors of VEGF signaling that do not target MET. Collectively, these data suggest that cabozantinib is a promising agent for inhibiting tumor angiogenesis and metastasis in cancers with dysregulated MET and VEGFR signaling. Mol Cancer Ther; 10(12); 2298-308.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib inhibited proliferation of human, mouse and rat cancer cell and suppressed metastasis, angiogenesis, tumor growth via inhibiting MET and VEGFR2 protein phosphorylation in mouse and rat xenografted with cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 216 THERE ARE 216 CAPLUS RECORDS THAT CITE THIS RECORD (217 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 352 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:1503311 CAPLUS Full-text
DOCUMENT NUMBER: 155:694113
TITLE: Replication-competent retroviral vectors carrying expression cassettes for cytosine deaminase variants
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Perez, Omar D.; Logg, Christopher R.
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 207pp., Cont.-in-part of Appl. No. PCT/US2009/058512.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20110287020	A1	20111124	US 2011-13072704	20110326
US 8829173	B2	20140909		
WO 2010036986	A2	20100401	WO 2009-US58512	20090926
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CN 105274125	A	20160127	CN 2015-10505943	20090926
WO 2011126864	A2	20111013	WO 2011-US30402	20110329
WO 2011126864	A3	20120419		
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JP 2013523754	T	20130617	JP 2013-502771	20110329
US 20130130986	A1	20130523	US 2013-13638490	20130116
AU 2013205006	A1	20130516	AU 2013-205006	20130413
AU 2013205006	B2	20160218		
US 20160053232	A1	20160225	US 2014-14477741	20140904
JP 2015119712	A	20150702	JP 2015-4923	20150114
JP 2015186479	A	20151029	JP 2015-97980	20150513

PRIORITY APPLN. INFO.:
US 2008-61100666 P 20080926
US 2008-61120618 P 20081208
US 2009-61186823 P 20090613
WO 2009-US58512 A2 20090926
US 2010-61318728 P 20100329
AU 2009-303690 A3 20090926
CN 2009-80147509 A3 20090926
JP 2011-529291 A3 20090926
JP 2011-529292 A3 20090926
US 2011-13072704 A1 20110326
WO 2011-US30402 W 20110329

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

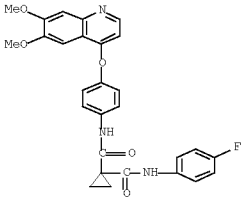
AB Methods of delivering cytosine deaminase variants for prodrug activation using retroviral expression vectors are described. The vector includes the viral gag, pol, and env genes with the cytosine deaminase gene being coexpressed using an internal ribosome entry site. Vectors were derived from the prior art pACE-GFPemd vector. The envelope protein of the virus is amphotropic and excess viral sequences outside the long terminal repeats were removed. The resulting vector was named pACE-emdGFP. The vector was stable in storage and replicated efficiently in mammalian cells and could be used to deliver a range of therapeutic genes. The Saccharomyces cerevisiae cytosine deaminase gene was modified to give a codon usage suitable for mammalian cells and to improve thermostability of the enzyme. Use of these vectors results in high intracellular copy nos. for the therapeutic gene and these cells can be superinfected by the vector.

IT 1140909-48-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in cancer therapy with retroviral gene therapy vectors; replication-competent retroviral vectors carrying expression cassettes for cytosine deaminase variants)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

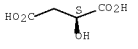
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

L4 ANSWER 353 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:1304241 CAPLUS Full-text
DOCUMENT NUMBER: 155:559702
TITLE: Detection of circulating mRNA, microRNA, protein and vesicle markers in disease diagnosis and selection of therapies
INVENTOR(S): Kuslich, Christine; Poste, George; Klass, Michael; Spetzler, David; Pawlowski, Traci
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, Luxembourg
SOURCE: PCT Int. Appl., 584pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011127219	A1	20111013	WO 2011-US31479	20110406
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
CA 2795776	A1	20111013	CA 2011-2795776	20110406
AU 2011237669	A1	20121101	AU 2011-237669	20110406
IL 222232	A	20121129	IL 2011-222232	20110406
EP 2556172	A1	20130213	EP 2011-766687	20110406
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
CN 103025890	A	20130403	CN 2011-80027541	20110406
KR 2013043104	A	20130429	KR 2012-7028831	20110406
JP 2013526852	T	20130627	JP 2013-503934	20110406
IN 2012DN09454	A	20160101	IN 2012-DN9454	20121101
US 20140162888	A1	20140612	US 2013-13639756	20130424
US 20150301055	A1	20151022	US 2015-14789729	20150701
JP 2016028584	A	20160303	JP 2015-176236	20150908
AU 2015268602	A1	20160107	AU 2015-268602	20151209

PRIORITY APPLN. INFO.:

US 2010-61321392	P	20100406
US 2010-61321407	P	20100406
US 2010-61322690	P	20100409
US 2010-61332174	P	20100506
US 2010-61334547	P	20100513
US 2010-61348214	P	20100525
US 2010-61348685	P	20100526
US 2010-61354125	P	20100611
US 2010-61355387	P	20100616
US 2010-61356974	P	20100621
US 2010-61357517	P	20100622
US 2010-61362674	P	20100708
US 2010-61364785	P	20100715
US 2010-61370088	P	20100802
US 2010-61379670	P	20100902
US 2010-61381305	P	20100909
US 2010-61383305	P	20100915
US 2010-61391504	P	20101008
US 2010-61393823	P	20101015
US 2010-61411890	P	20101109
US 2010-61413377	P	20101112
US 2010-61416560	P	20101123
US 2010-61274124	P	20100301
US 2010-61374951	P	20100818
US 2010-61414870	P	20101117
US 2010-61421851	P	20101210
US 2010-61423557	P	20101215
US 2010-61428196	P	20101229
JP 2012-556185	A3	20110301
US 2011-61471417	P	20110404
WO 2011-US31479	W	20110406
AU 2011-291599	A3	20110818
WO 2011-US48327	A	20110818
US 2013-13639756	A2	20130424
US 2013-13817383	A1	20130520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Biomarkers can be assessed for diagnostic, therapy-related or prognostic methods to identify phenotypes, such as a condition or disease, or the stage or progression of a disease. Circulating biomarkers from a bodily fluid can be used in profiling of physiol. states or determining phenotypes. These include nucleic acids, protein, and circulating structures such as vesicles. Biomarkers can be used for theranostic purposes to select candidate treatment regimens for diseases, conditions, disease stages, and stages of a condition, and can also be used to determine treatment efficacy. The biomarkers can be circulating biomarkers, including microvesicles and their protein content and microRNAs.

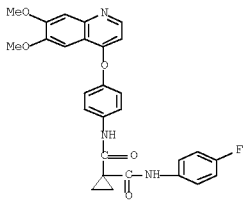
IT 1140909-48-3, XL184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (selection for cancer therapy; detection of circulating mRNA, microRNA, protein and vesicle markers in disease diagnosis)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

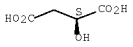
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5



Absolute stereochemistry. Rotation (-).

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 354 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:1016190 CAPLUS full-text

DOCUMENT NUMBER: 156:353197

TITLE: Biologically targeted therapies for thyroid cancers

AUTHOR(S): Sherman, Steven I.

CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders Division of Internal Medicine, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

SOURCE: Thyroid Cancer (2011), 329-349. Editor(s): Carpi, Angelo; Mechanick, Jeffrey I. CRC Press: Boca Raton, Fla.
CODEN: 69OKVM; ISBN: 978-1-4398-6221-6

DIGITAL OBJECT ID: 10.1201/b10945-21

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review. Systemic chemotherapies for advanced or metastatic thyroid carcinomas have been of only limited effectiveness. For patients with differentiated thyroid epithelial or medullary thyroid carcinomas unresponsive to conventional treatments, novel therapies are needed to improve disease outcomes. Multiple novel therapies primarily targeting angiogenesis have entered clin. trials for metastatic thyroid carcinoma. Partial response rates up to 30% have been reported in single agent studies, but prolonged disease stabilization is more commonly seen. The most successful agents target the vascular endothelial growth factor receptors, with potential targets including the mutant kinases associated with papillary and medullary oncogenesis. Two drugs approved for other malignancies, sorafenib and sunitinib, have had promising preliminary results reported, and are being used selectively for patients who do not qualify for clin. trials. Addnl. agents targeting tumor vasculature, nuclear receptors, epigenetic abnormalities, and the immune response to neoplasia have also been investigated. Randomized trials for several agents are under way that may lead to eventual drug approval for thyroid cancer. Treatment for patients with metastatic or advanced thyroid carcinoma now emphasizes clin. trial opportunities for novel agents with considerable promise. Alternative options now exist for use of these mol. targeted therapies, especially tyrosine kinase inhibitors, which are well tolerated and may prove worthy of regulatory approval for this disease.

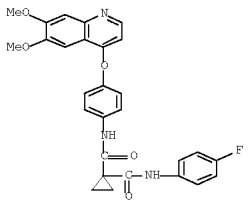
IT 1140909-48-3, XL 184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biol. targeted therapies for thyroid cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 355 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:991678 CAPLUS full-text

DOCUMENT NUMBER: 156:440657

TITLE: Activity of XL184 (cabozantinib), an oral tyrosine kinase inhibitor, in patients with medullary thyroid cancer

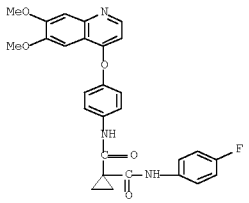
AUTHOR(S): Kurzrock, Razelle; Sherman, Steven I.; Ball, Douglas W.; Forastiere, Arlene A.; Cohen, Roger B.; Mehra, Ranee; Pfister, David G.; Cohen, Ezra E. W.; Janisch, Linda; Nauling, Forlisa; Hong, David S.; Ng, Chaan S.; Ye, Lei; Gagel, Robert F.; Frye, John; Muller, Thomas; Ratain, Mark J.; Salgia, Ravi

CORPORATE SOURCE: The University of Texas MD Anderson Cancer Center,

Houston, USA
SOURCE: Journal of Clinical Oncology (2011), 29(19), 2660-2666
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2010.32.4145
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: XL184 (cabozantinib) is a potent inhibitor of MET, vascular endothelial growth factor receptor 2 (VEGFR2), and RET, with robust antiangiogenic, antitumor, and anti-invasive effects in preclin. models. Early observations of clin. benefit in a phase I study of cabozantinib, which included patients with medullary thyroid cancer (MTC), led to expansion of an MTC-enriched cohort, which is the focus of this article. Patients and Methods: A phase I dose-escalation study of oral cabozantinib was conducted in patients with advanced solid tumors. Primary end points included evaluation of safety, pharmacokinetics, and maximum-tolerated dose (MTD) determination Addnl. end points included RECIST (Response Evaluation Criteria in Solid Tumors) response, pharmacodynamics, RET mutational status, and biomarker analyses. Results: Eighty-five patients were enrolled, including 37 with MTC. The MTD was 175 mg daily. Dose-limiting toxicities were grade 3 palmar plantar erythrodysesthesia (PPE), mucositis, and AST, ALT, and lipase elevations and grade 2 mucositis that resulted in dose interruption and reduction Ten (29%) of 35 patients with MTC with measurable disease had a confirmed partial response. Overall, 18 patients experienced tumor shrinkage of 30% or more, including 17 (49%) of 35 patients with MTC with measurable disease. Addnl., 15 (41%) of 37 patients with MTC had stable disease (SD) for at least 6 mo, resulting in SD for 6 mo or longer or confirmed partial response in 68% of patients with MTC. Conclusion: Cabozantinib has an acceptable safety profile and is active in MTC. Cabozantinib may provide clin. benefit by simultaneously targeting multiple pathways of importance in MTC, including MET, VEGFR2, and RET. A global phase III pivotal study in MTC is ongoing (ClinicalTrials.gov number NCT00215605).
IT 1140909-48-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activity of cabozantinib, an oral tyrosine kinase inhibitor, in patients with medullary thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

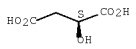
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

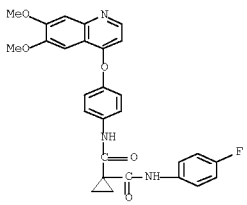


OS.CITING REF COUNT: 162 THERE ARE 162 CAPLUS RECORDS THAT CITE THIS RECORD (163 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 356 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:945715 CAPLUS Full-text
DOCUMENT NUMBER: 156:301829
TITLE: Current status of molecularly targeted drugs for the treatment of advanced thyroid cancer
AUTHOR(S): Takami, Hiroshi E.
CORPORATE SOURCE: Department of Surgery, Teikyo University School of Medicine, Tokyo, 173-8605, Japan
SOURCE: Endocrine Journal (Kyoto, Japan) (2011), 58(3), 151-153
CODEN: ENJOEO; ISSN: 0918-8959
DIGITAL OBJECT ID: 10.1507/endocrj.K11E-076
PUBLISHER: Japan Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The prognosis of almost all thyroid cancers is good, but some patients have indications for these molecularly targeted drugs. Some of these drugs, i.e., vandetanib, XL-184, sorafenib, motesanib, axitinib, and pazopanib, are clearly useful clin.
IT 1140909-48-3, XL-184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(current status of molecularly targeted drugs for the treatment of advanced thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

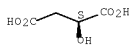
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

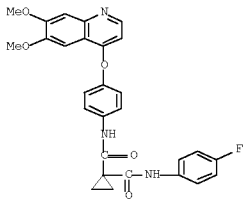


OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 357 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:724271 CAPLUS Full-text
DOCUMENT NUMBER: 155:290943
TITLE: The effects of four different tyrosine kinase inhibitors on medullary and papillary thyroid cancer cells
AUTHOR(S): Verbeek, Hans H. G.; Alves, Maria M.; de Groot, Jan-Willem B.; Osinga, Jan; Plukker, John T. M.; Links, Thera P.; Hofstra, Robert M. W.
CORPORATE SOURCE: Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, 9700 RB, Neth.
SOURCE: Journal of Clinical Endocrinology and Metabolism (2011), 96(6), E991-E995
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2010-2381
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Medullary and papillary thyroid carcinoma (MTC and PTC) are 2 types of thyroid cancer that can originate from activating mutations or rearrangements in the RET gene. Therapeutic options are limited in recurrent disease, but because RET is a tyrosine kinase (TK) receptor involved in cellular growth and proliferation, treatment with a TK inhibitor might be promising. Several TK inhibitors were tested in clin. trials, but it is unknown which inhibitor is most effective and whether there is any specificity for particular RET mutations. We aimed to compare the effect of 4 TK inhibitors (axitinib, sunitinib, vandetanib, and XL184) on cell proliferation, RET expression and autophosphorylation, and ERK activation in cell lines expressing a MEN2A (MTC-TT), a MEN2B (MZ-CRC-1) mutation, and a RET/PTC (TPC-1) rearrangement. The 3 cell lines were cultured and treated with the 4 TK inhibitors. Effects on cell proliferation and RET and ERK expression and activation were determined XL184 and vandetanib most effectively inhibited cell proliferation, RET autophosphorylation in combination with a reduction of RET expression, and ERK phosphorylation in MTC-TT and MZ-CRC-1, resp. TPC-1 cells showed a decrease in RET autophosphorylation after treatment with XL184, but no effect was observed on ERK activation. There is indeed specificity for different RET mutations, with XL184 being the most potent inhibitor in MEN2A and PTC and vandetanib the most effective in MEN2B in vitro. No TK inhibitor was superior for all the cell lines tested, indicating that mutation-specific therapies could be beneficial in treating MTC and PTC.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Tyr kinase inhibitors effect on medullary and papillary thyroid cancer related to RET mutation, rearrangement, and ERK)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

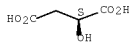
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

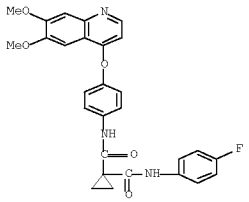


OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 358 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:461207 CAPLUS Full-text
DOCUMENT NUMBER: 156:46100
TITLE: Novel agents and new therapeutics in castration-resistant prostate cancer
AUTHOR(S): Wu, Yichao; Rosenberg, Jonathan E.; Taplin, Mary-Ellen
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SOURCE: Current Opinion in Oncology (2011), 23(3), 290-296
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e3283449400
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: This review highlights recent therapeutic advances in systemic therapies for prostate cancer (PCa). Recent findings: Progress in PCa therapeutics has been made during the past year with the approval of a vaccine therapy, second-line chemotherapy, and reported survival advantage for a CYP (17,20) lyase inhibitor in castration-resistant prostate cancer (CRPC). This report will summarize the recently reported and expected data for PCa trials including an evaluation of intermittent vs. continuous androgen deprivation therapy. Denosumab is shown to support bone mineral d. in hormonal sensitive PCa patients. Targeting of androgen-dependent pathways in CRPC postchemotherapy has been shown to improve survival with the lyase inhibitor abiraterone, and lead to prostate-specific antigen and objective responses with an androgen receptor antagonist (MDV3100). However, the addition of bevacizumab to docetaxel/prednisone in treating metastatic CRPC failed to provide a survival benefit. Cabazitaxel in metastatic CRPC postdocetaxel did demonstrate a survival benefit. Provenge, an autologous dendritic cell-based vaccine, demonstrated a reduction in the risk of death in metastatic CRPC. Other immunotherapy agents, including Prostvac and ipilimumab are under investigation. We also discuss the receptor tyrosine kinase inhibitor XL184 and poly (ADP-ribose) polymerase inhibitors which are in early clin. trials. Summary: Recent advances in androgen targeting, chemotherapy, immunotherapy, and other targeted therapies have led to significant improvements in the care of CRPC patients.
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel agents and new therapeutics in castration-resistant prostate cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

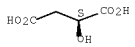
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

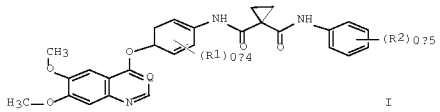
L4 ANSWER 359 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:174316 CAPLUS Full-text
DOCUMENT NUMBER: 154:225400
TITLE: C-met modulators as antitumor agents
INVENTOR(S): Aftab, Dana T.; Mueller, Thomas; Weitzman, Aaron; Holland, Jaymes
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011017639	A1	20110210	WO 2010-US44749	20100806
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2770100	A1	20110210	CA 2010-2770100	20100806
AU 2010279234	A1	20120301	AU 2010-279234	20100806
KR 2012059540	A	20120608	KR 2012-7006111	20100806
EP 2461810	A1	20120613	EP 2010-742985	20100806
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR				
CN 102647985	A	20120822	CN 2010-80045677	20100806
JP 2013501731	T	20130117	JP 2012-523982	20100806
IL 217889	A	20130228	IL 2010-217889	20100806
NZ 598055	A	20140530	NZ 2010-598055	20100806
IL 238849	A	20150630	IL 2010-238849	20100806
NZ 624643	A	20151127	NZ 2010-624643	20100806
IN 2012MN00278	A	20120824	IN 2012-MN278	20120203
ZA 2012000842	A	20121128	ZA 2012-842	20120203
MX 2012001654	A	20120314	MX 2012-1654	20120207
US 20120282179	A1	20121108	US 2012-13389266	20120712
US 20160000772	A1	20160107	US 2015-14699683	20150429

PRIORITY APPLN. INFO.:

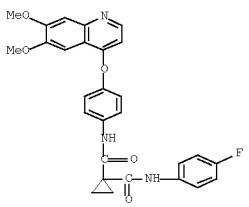
US 2009-61232382	P	20090807
IL 2010-217889	A3	20100806
NZ 2010-598055	A3	20100806
WO 2010-US44749	W	20100806
US 2012-13389266	B1	20120712

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 154:225400; MARPAT 154:225400
GI



I

AB Methods of treating cancer by administering a compd. of Formula I (wherein R1 = halo; R2 = halo; Q = CH, N; n = 0-4; m = 0-5) or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments are described.
IT 849217-68-1
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(methods of using c-met modulators)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

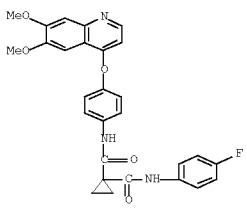


IT 1140909-48-3
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(methods of using c-met modulators)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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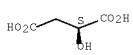
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



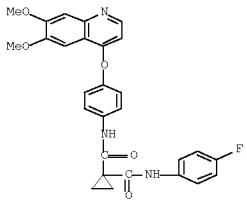
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 360 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:111410 CAPLUS Full-text
DOCUMENT NUMBER: 155:346258
TITLE: Antiangiogenic agents in the treatment of recurrent or newly diagnosed glioblastoma: analysis of single-agent and combined modality approaches
AUTHOR(S): Beal, Kathryn; Abrey, Lauren E.; Gutin, Philip H.
CORPORATE SOURCE: Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Radiation Oncology (2011), 6, 2
CODEN: ROANCM; ISSN: 1748-717X
URL: http://www.ro-journal.com/content/pdf/1748-717X-6-2.pdf

DIGITAL OBJECT ID: 10.1186/1748-717X-6-2
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Surgical resection followed by radiotherapy and temozolomide in newly diagnosed glioblastoma can prolong survival, but it is not curative. For patients with disease progression after frontline therapy, there is no standard of care, although further surgery, chemotherapy, and radiotherapy may be used. Antiangiogenic therapies may be appropriate for treating glioblastomas because angiogenesis is critical to tumor growth. In a large, noncomparative phase II trial, bevacizumab was evaluated alone and with irinotecan in patients with recurrent glioblastoma; combination treatment was associated with an estimated 6-mo progression-free survival (PFS) rate of 50.3%, a median overall survival of 8.9 mo, and a response rate of 37.8%. Single-agent bevacizumab also exceeded the predetd. threshold of activity for salvage chemotherapy (6-mo PFS rate, 15%), achieving a 6-mo PFS rate of 42.6% (p<0.0001). On the basis of these results and those from another phase II trial, the US Food and Drug Administration granted accelerated approval of single-agent bevacizumab for the treatment of glioblastoma that has progressed following prior therapy. Potential antiangiogenic agents - such as cilengitide and XL184 - also show evidence of single-agent activity in recurrent glioblastoma. Moreover, the use of antiangiogenic agents with radiation at disease progression may improve the therapeutic ratio of single-modality approaches. Overall, these agents appear to be well tolerated, with adverse event profiles similar to those reported in studies of other solid tumors. Further research is needed to determine the role of antiangiogenic therapy in frontline treatment and to identify the optimal schedule and partnering agents for use in combination therapy.
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiangiogenic agents in the treatment of recurrent or newly diagnosed glioblastoma)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

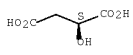
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 361 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:80577 CAPLUS Full-text
DOCUMENT NUMBER: 154:174225
TITLE: Drug selection for gastric cancer therapy using antibody-based arrays
INVENTOR(S): Singh, Sharat; Kim, Phillip; Liu, Xinjun; Ybarrondo, Belen
PATENT ASSIGNEE(S): Prometheus Laboratories Inc., USA
SOURCE: PCT Int. Appl., 189pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011008990	A1	20110120	WO 2010-US42182	20100715

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2768013	A1	20110120	CA 2010-2768013	20100715
AU 2010273319	A1	20120223	AU 2010-273319	20100715
AU 2010273319	B2	20150122		
EP 2454598	A1	20120523	EP 2010-800567	20100715

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BA, ME, RS

JP 2012533738	T	20121227	JP 2012-520794	20100715
JP 5795311	B2	20151014		
US 20110281748	A1	20111117	US 2011-13014674	20110126
US 20130237436	A9	20130912		
US 20120270745	A1	20121025	US 2012-13354257	20120119
AU 2013202682	A1	20130502	AU 2013-202682	20130405
AU 2013202682	B2	20150716		
JP 2016001187	A	20160107	JP 2015-159663	20150812

PRIORITY APPLN. INFO.:

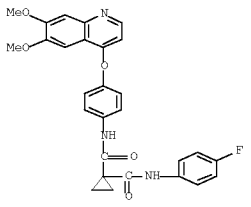
US 2009-61225866	P	20090715
US 2009-61265218	P	20091130
US 2010-61325000	P	20100416
US 2006-61007527	P	20060921
US 2007-60913087	P	20070420
AU 2007-299774	A3	20070920
WO 2007-US79002	A1	20070920
US 2008-46381	A2	20080311
JP 2012-520794	A3	20100715
WO 2010-US42182	W	20100715
US 2011-13014674	A2	20110126
US 2011-61436945	P	20110127
US 2011-61467950	P	20110325

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention provides methods for selecting a suitable anticancer therapy, and for identifying and predicting response for the treatment of a gastric cancer. The present invention provides compns. and methods for detecting the status (e.g., expression and/or activation levels) of components of signal transduction pathways in tumor cells (e.g., gastric tumor cells). Information on the expression and/or activation states of components of signal transduction pathways (e.g., HER2 and/or c-Met signal transduction pathway components) derived from practice of the present invention can be used for gastric cancer diagnosis, prognosis, and in the design of gastric cancer treatments. The compns. and methods of the present invention advantageously provide accurate prediction, selection, and monitoring of cancer patients (e.g., gastric cancer patients) most likely to benefit from targeted therapy by performing pathway profiling on easily accessible tumor cells using multiplexed, antibody-based proximity assays.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for gastric cancer therapy using antibody-based arrays for detecting the status of signal transduction pathways)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

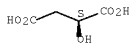
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

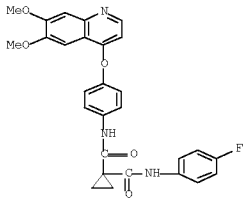


OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 362 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:1570396 CAPLUS Full-text
DOCUMENT NUMBER: 155:177406
TITLE: Targeting RET Receptor Tyrosine Kinase Activation in Cancer
AUTHOR(S): Phay, John E.; Shah, Manisha H.
CORPORATE SOURCE: Department of Surgery, Division of Surgical Oncology, Department of Internal Medicine, and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA
SOURCE: Clinical Cancer Research (2010), 16(24), 5936-5941
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-09-0786
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. After ligand binding induces dimerization, the RET receptor tyrosine kinase activates multiple signal transduction pathways. Constitutively activating mutations and chromosomal rearrangements are the primary oncogenic event in a significant number of medullary thyroid cancers (MTC) and papillary thyroid cancers (PTC), resp. When specific germline mutations in RET are identified early, prophylactic thyroidectomy can be timed to remove at-risk tissue in patients with multiple endocrine neoplasia 2 (MEN2) syndromes who would otherwise develop MTC. Conventional therapy for progressive metastatic MTC is limited. Small-mol. tyrosine kinase inhibitors can target multiple kinases at nanomolar concns., including RET, and have shown efficacy against a variety of malignancies. Initial clin. evidence suggests that several of these inhibitors, including sorafenib, vandetanib, motesanib, sunitinib, and XL-184, may have some benefit in treating progressive MTC. Although initial success seen in these trials seems to be modest, it represents a major breakthrough in the treatment of patients with widespread metastatic MTC. Clin Cancer Res; 16(24); 5936-41.
IT 1140909-48-3, XL-184,
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(role of RET receptor tyrosine kinase activation in cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

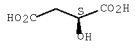
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

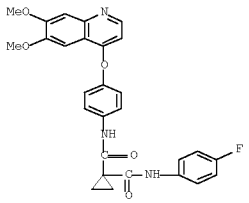


OS.CITING REF COUNT: 50 THERE ARE 50 CAPLUS RECORDS THAT CITE THIS RECORD (50 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 363 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:1240526 CAPLUS Full-text
DOCUMENT NUMBER: 153:595314
TITLE: Tyrosine kinase inhibitors in thyroid cancer
AUTHOR(S): Illouz, Frederic
CORPORATE SOURCE: Service EDN, Centre de reference des pathologies de la receptivite hormonale, CHU d'Angers, Fr.
SOURCE: Correspondances en Metabolismes, Hormones, Diabetes et Nutrition (2010), 14(7), 210-214
CODEN: CMHDBH; ISSN: 2100-9619
PUBLISHER: Edimark SAS
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French
AB A review.
IT 1140909-48-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitors in thyroid cancer therapy)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

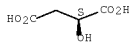
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 364 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:1003327 CAPLUS Full-text
DOCUMENT NUMBER: 153:278035
TITLE: Treatment of lung cancer with a PARP inhibitor in combination with a growth factor inhibitor
INVENTOR(S): Sherman, Barry M.; Bradley, Charles; Ossovskaya, Valeria S.
PATENT ASSIGNEE(S): BiPar Sciences, Inc., USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

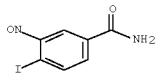
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010091140	A1	20100812	WO 2010-US23137	20100204

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV,

SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2751397	A1	20100812	CA 2010-2751397		20100204
AR 75239	A1	20110316	AR 2010-100305		20100204
AU 2010210636	A1	20110922	AU 2010-210636		20100204
KR 2011113648	A	20111017	KR 2011-7020246		20100204
EP 2393364	A1	20111214	EP 2010-739097		20100204
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CN 102307475	A	20120104	CN 2010-80006536		20100204
JP 2012516895	T	20120726	JP 2011-549246		20100204
IL 214366	A	20130131	IL 2010-214366		20100204
MX 2011008221	A	20110817	MX 2011-8221		20110804
IN 2011CN06195	A	20121012	IN 2011-CN6195		20110829
US 20120130144	A1	20120524	US 2011-13146865		20111222
PRIORITY APPLN. INFO.:			US 2009-61149977	P	20090204
			WO 2010-US23137	W	20100204

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 153:278035
GI



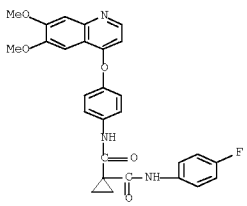
AB In one aspect, the present invention provides a method of treating lung cancer, comprising administering to a subject at least one PARP inhibitor in combination with at least one growth factor inhibitor. In another aspect, the present invention provides a method of treating non-small cell lung cancer comprising administering to a subject at least one PARP inhibitor in combination with at least one growth factor inhibitor.

IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of lung cancer with a PARP inhibitor in combination with a growth factor inhibitor)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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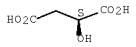
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

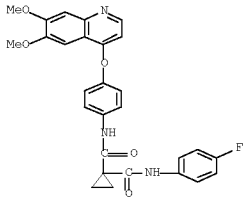
L4 ANSWER 365 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:944155 CAPLUS Full-text
DOCUMENT NUMBER: 155:230334
TITLE: Patients with advanced head and neck cancers have similar progression-free survival on phase I trials and their last food and drug administration-approved treatment
AUTHOR(S): Garrido-Laguna, Ignacio; Janku, Filip; Falchook, Gerald S.; Fu, Siqing; Hong, David S.; Naing, Aung; Aaron, Joanne; Wang, Xuemei; Kies, Merrill; Kurzrock, Razelle
CORPORATE SOURCE: Departments of Investigational Cancer Therapeutics (Phase I Clinical Trials Program), The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Clinical Cancer Research (2010), 16(15), 4031-4037
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-10-0672
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: To compare clin. outcomes of metastatic head and neck cancer patients treated in phase I clin. trials with clin. outcomes of those patients who had their last Food and Drug Administration (FDA)-approved therapy in the setting of metastatic disease. Exptl. Design: We retrospectively reviewed the outcomes of 61 consecutive patients with head and neck tumors treated in 36 phase I trials at The University of Texas M.D. Anderson Cancer Center between July 2004 and Sept. 2009. Results: The most common histol. was head and neck squamous cell carcinoma (62%). Median age was 55 years (range, 26-80). Eastern Cooperative Oncol. Group performance status was 0 to 1 for 95% of patients. Fifty-nine patients had received FDA-approved drugs as the backbone of their last systemic therapy before inclusion in phase I trials (median, 2 systemic therapies). Progression-free survival (PFS) on phase I trials was not inferior to PFS on their last FDA-approved therapies (12 vs. 10.7 wk, log-rank P = 0.87). Fifty-three patients were evaluable for response by Response Evaluation Criteria in Solid Tumors criteria. Four (7%) had partial responses and 16 (26%) had stable disease for ≥4 mo. In univariate anal., number of metastatic sites, lactate dehydrogenase (LDH) levels at baseline, and Royal Marsden Hospital prognosis scores were significant predictors of survival. Only LDH was significant in multivariate anal. (hazard ratio, 6.35; P ≤ 0.0001). Conclusions: For patients with heavily pretreated advanced head and neck tumors, PFS on phase I trials is not inferior to PFS with their last FDA-approved therapy. The only significant predictor of survival in the multivariate anal. was baseline LDH.

IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(patients with advanced head and neck cancers have similar progression-free survival on phase I trials and their last food and drug administration-approved treatment)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

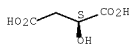
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



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REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 366 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:928655 CAPLUS Full-text
DOCUMENT NUMBER: 154:425137
TITLE: XL-184, a MET, VEGFR-2 and RET kinase inhibitor for the treatment of thyroid cancer, glioblastoma multiforme and NSCLC
AUTHOR(S): Zhang, Ying; Guessous, Fadila; Kofman, Alex; Schiff, David; Abounader, Roger
CORPORATE SOURCE: Department of Microbiology, University of Virginia, Charlottesville, VA, 22903, USA
SOURCE: IDrugs (2010), 13(2), 112-121
CODEN: IDRUFN; ISSN: 2040-3410
URL: http://www.biomedcentral.com/content/pdf/cd-1071541.pdf

PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. XL-184 (BMS-907351), under development by Exelixis Inc and Bristol-Myers Squibb Co, is a pan-tyrosine kinase inhibitor for the potential oral treatment of medullary thyroid cancer, glioblastoma multiforme and NSCLC. The prinicipal targets of XL-184 are MET, VEGFR-2 and RET, but the drug is also reported to display inhibitory activity against KIT, FLT3 and TEK. Preclin. studies demonstrated that XL-184 potently inhibited multiple receptor tyrosine kinases in various cancer cell lines and animal xenograft models, and that the drug exhibited significant oral bioavailability and blood-brain barrier penetration. A phase I clin. trial in patients with advanced solid malignancies indicated that XL-184 accumulated dose-dependently in the plasma and had a long terminal half-life. A phase II trial in patients with progressive or recurrent glioblastoma revealed modest but promising median progression-free survival. Toxicity and side effects for the drug have generally been of low-to-moderate severity. At the time of publication, three addnl. trials of XL-184 were recruiting patients, including a phase I trial in combination with standard of care in patients with glioblastoma, a phase I/II trial in combination with erlotinib

in patients with NSCLC, and a phase III trial in patients with medullary thyroid cancer.

IT 1140909-48-3

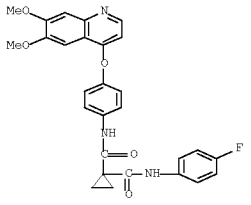
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL-184, a MET, VEGFR-2 and RET kinase inhibitor for the treatment of thyroid cancer, glioblastoma multiforme and NSCLC)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

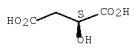
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 48 THERE ARE 48 CAPLUS RECORDS THAT CITE THIS RECORD (48 CITINGS)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 367 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2010:912816 CAPLUS Full-text

DOCUMENT NUMBER: 153:204211

TITLE: Preparation of malate salts of N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide and crystalline forms thereof for the treatment of cancer.

INVENTOR(S): St Clair Brown, Adrian; Lamb, Peter; Gallagher, William P.

PATENT ASSIGNEE(S): Exelixis, Inc., USA; Bristol-Meyers Squibb Company

SOURCE: PCT Int. Appl., 72pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010083414	A1	20100722	WO 2010-US21194	20100115
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AR 75025	A1	20110302	AR 2010-100098	20100115
AU 2010204619	A1	20110901	AU 2010-204619	20100115
EP 2387563	A1	20111123	EP 2010-701175	20100115
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KR 2012013301	A	20120214	KR 2011-7018924	20100115
CN 102388024	A	20120321	CN 2010-80012656	20100115
JP 2012515220	T	20120705	JP 2011-546390	20100115
JP 5677318	B2	20150225		
IL 214086	A	20130131	IL 2010-214086	20100115
PT 2387563	E	20130325	PT 2010-701175	20100115
ES 2402524	T3	20130506	ES 2010-701175	20100115
NZ 594594	A	20131129	NZ 2010-594594	20100115
EA 19959	B1	20140730	EA 2011-70941	20100115
TW 1447108	B	20140801	TW 2010-101140	20100115
IL 234097	A	20140930	IL 2010-234097	20100115
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ZA 2011005167	A	20120328	ZA 2011-5167	20110713
MX 2011007620	A	20111104	MX 2011-7620	20110715
IN 2011KN03402	A	20121102	IN 2011-KN3402	20110811
US 20120035212	A1	20120209	US 2011-13145054	20111020
US 8877776	B2	20141104		
HK 1164305	A1	20131108	HK 2012-104893	20120518
AU 2013203780	A1	20130502	AU 2013-203780	20130411
US 20150057310	A1	20150226	US 2014-14340871	20140725
JP 2015096543	A	20150521	JP 2014-264071	20141226

PRIORITY APPLN. INFO.:

US 2009-61145421	P	20090116
AU 2010-204619	A3	20100115
IL 2010-214086	A3	20100115
JP 2011-546390	A3	20100115
NZ 2010-594594	A3	20100115
WO 2010-US21194	W	20100115
US 2011-13145054	A3	20111020

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 153:204211

AB N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide malate salts were prepared Thus, 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid (preparation given) was stirred with (COCl)2 in THF/DMF at ≤30° and the mixture was added to 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine (preparation given) and K2CO3 in THF/H2O followed by addition of H2O and stirring for 10 h to give N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide. The latter in EtOH was treated with malic acid in H2O followed by addition of C, thiol silica, heating to 78°, and addition of H2O followed by filtration, addition of Me2CHOH, cooling, and filtration to give N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide malate.

IT 1235470-36-6

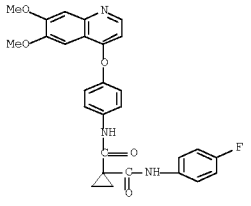
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)

RN 1235470-36-6 CAPLUS

CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

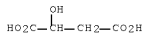
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CM 2

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IT 1235470-37-7P 1235470-38-8P

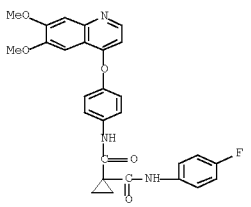
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)

RN 1235470-37-7 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

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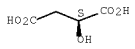
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CM 2

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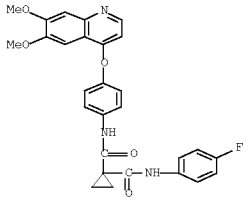
Absolute stereochemistry. Rotation (-).



RN 1235470-38-8 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

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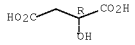
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CMF C28 H24 F N3 O5



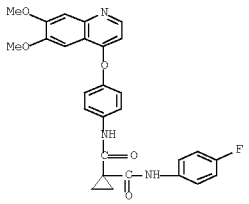
CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



IT 849217-68-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



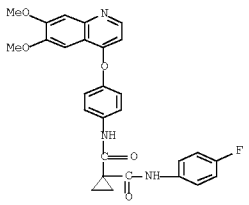
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 368 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:726266 CAPLUS full-text
DOCUMENT NUMBER: 153:633557
TITLE: Targeted therapy for thyroid cancer: an updated review of investigational agents
AUTHOR(S): Deshpande, Hari A.; Gettinger, Scott N.; Sosa, Julie A.
CORPORATE SOURCE: Yale Cancer Center, New Haven, CT, 06520, USA
SOURCE: Current Opinion in Investigational Drugs (BioMed Central) (2010), 11(6), 661-668
CODEN: COIDAZ; ISSN: 2040-3429
URL: http://www.biomedcentral.com/content/pdf/cd-1102161.pdf

PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The treatment of thyroid cancer is evolving. The mol. mechanisms of carcinogenesis for many thyroid cancers have been investigated, and have yielded targets for potential therapies. These targets include VEGFR in the treatment of all thyroid cancers, BRAF in the treatment of papillary thyroid cancer, and RET in the treatment of medullary thyroid cancer (MTC). Many promising drugs that target one or more of these proteins are currently being evaluated, including sorafenib and sunitinib, both of which are still under development for the treatment of thyroid cancer but which have been approved for use in other malignancies. In addition, compds. such as vandetanib (AstraZeneca plc) and XL-184 (Bristol-Myers Squibb Co/Exelixis Inc) have demonstrated activity in early-phase clin. trials of MTC and are being tested further in randomized trials.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL-184 targeting vascular endothelial growth factor receptor, RET and BRAF protein may be effective in patient with thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

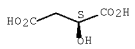
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



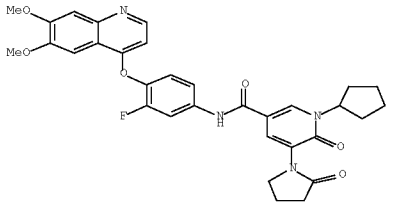
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 369 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:439254 CAPLUS Full-text
DOCUMENT NUMBER: 152:422278
TITLE: Methods for the treatment of cancer
INVENTOR(S): Johns, Terrance
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 139pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010039248	A1	20100408	WO 2009-US5421	20090930
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2009300328	A1	20100408	AU 2009-300328	20090930
CA 2738583	A1	20100408	CA 2009-2738583	20090930
EP 2349328	A1	20110803	EP 2009-740207	20090930
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
JP 2012504606	T	20120223	JP 2011-530051	20090930
MX 2011003363	A	20110427	MX 2011-3363	20110329
US 20110229469	A1	20110922	US 2011-13122106	20110613
JP 2015107974	A	20150611	JP 2014-256872	20141219
AU 2015201812	A1	20150430	AU 2015-201812	20150410

PRIORITY APPLN. INFO.: US 2008-61101971 P 20081001
AU 2009-300328 A3 20090930
JP 2011-530051 A3 20090930
WO 2009-US5421 W 20090930
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 152:422278
GI



AB Methods for treating cancer with at least one HGF-Met inhibitor and at least one EGFR inhibitor are provided.

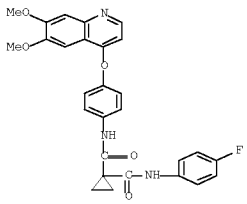
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treatment of cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

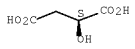
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 370 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:402977 CAPLUS Full-text
DOCUMENT NUMBER: 152:423197
TITLE: Recombinant replication-competent retroviral vectors expressing therapeutic products for treatment of proliferative disorders
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas; Perez, Omar
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010036986	A2	20100401	WO 2009-US58512	20090926
WO 2010036986	A3	20100701		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2344648	A2	20110720	EP 2009-816967	20090926
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
CN 102227503	A	20111026	CN 2009-80147515	20090926
CN 102227503	B	20151021		
JP 2012503987	T	20120216	JP 2011-529292	20090926
JP 5684130	B2	20150311		
ZA 2011002115	A	20120725	ZA 2011-2115	20090926
CN 105274125	A	20160127	CN 2015-10505943	20090926
PH 12011500630	B1	20151211	PH 2011-12011500630	20110325
US 20110287020	A1	20111124	US 2011-13072704	20110326
US 8829173	B2	20140909		
AU 2013205006	A1	20130516	AU 2013-205006	20130413
AU 2013205006	B2	20160218		
US 20160053232	A1	20160225	US 2014-14477741	20140904
JP 2015119712	A	20150702	JP 2015-4923	20150114
JP 2015186479	A	20151029	JP 2015-97980	20150513

PRIORITY APPLN. INFO.:

US 2008-61100666	P	20080926
US 2008-61120618	P	20081208
US 2009-61186823	P	20090613
AU 2009-303690	A3	20090926
CN 2009-80147509	A3	20090926
JP 2011-529291	A3	20090926
JP 2011-529292	A3	20090926
WO 2009-US58512	W	20090926
US 2010-61318728	P	20100329
US 2011-13072704	A1	20110326

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Recombinant replication-competent retroviral (RCR) vectors are provided comprising: a retroviral gag protein; a retroviral pol protein; a retroviral envelop, a retroviral polynucleotide comprising long terminal repeat (LTR) sequence at the 3' end of the retroviral polynucleotide sequence; a mammalian-suitable promoter sequence at the 5' end of the retroviral polynucleotide, a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous polynucleotide; and cis-acting sequences necessary for reverse transcription, packaging and integration in a target cell. The RCR maintains higher replication competency after 6 passages compared to a pACE vector. The heterologous polynucleotide may encode modified cytosine deaminase (thermostabilized and codon optimized), single-chain antibody to CTLA-4, microRNAs miR-128-1 and miR-128-2, γ-interferon, interleukin 2, or other therapeutic proteins of interest. The disclosure further relates to cells and vector expressing or comprising such modified CDs and methods of using such modified CDs in the treatment of disease and disorders, and in particular cell proliferative disorders such as cancer.

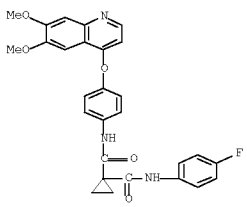
IT 1140909-48-3, XL 184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy with; recombinant replication-competent retroviral vectors expressing therapeutic products for treatment of proliferative disorders)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

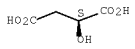
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 371 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:55413 CAPLUS Full-text
DOCUMENT NUMBER: 152:163651
TITLE: Methods for diagnosis, prognosis and treatment
INVENTOR(S): Fantl, Wendy J.; Rosen, David B.; Cesano, Alessandra; Putta, Santosh K.; Nolan, Garry P.; Cohen, Aileen C.; Evenson, Erik
PATENT ASSIGNEE(S): Nodality, Inc., USA
SOURCE: PCT Int. Appl., 201pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010006291	A1	20100114	WO 2009-US50295	20090710
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2304436	A1	20110406	EP 2009-790295	20090710
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
US 20150017119	A1	20150115	US 2014-14279905	20140516

PRIORITY APPLN. INFO.:

US 2008-61079766	P	20080710
US 2008-61085789	P	20080801
US 2008-61104666	P	20081010
US 2008-61120320	P	20081205
US 2009-460029	A3	20090710
WO 2009-US50295	W	20090710
US 2012-13473829	A1	20120517

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides an approach for the detn. of the activation states of a plurality of proteins in single cells. This approach permits the rapid detection of heterogeneity in a complex cell population based on activation states, expression markers and other criteria, and the identification of cellular subsets that exhibit correlated changes in activation within the cell population. Moreover, this approach allows the correlation of cellular activities or properties. In addition, the use of

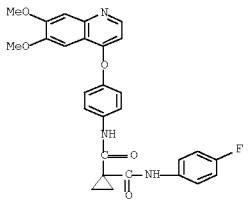
modulators of cellular activation allows for characterization of pathways and cell populations. Several exemplary diseases that can be analyzed using the invention include AML, MDS, and MPN.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hematopoietic cell flow cytometry anal. and pathway stimulation for diagnosing, prognosing, therapy and progression of acute leukemia, myelodysplastic syndrome and myeloproliferative syndrome)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

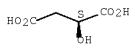
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

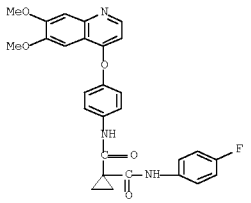
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

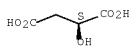
L4 ANSWER 372 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

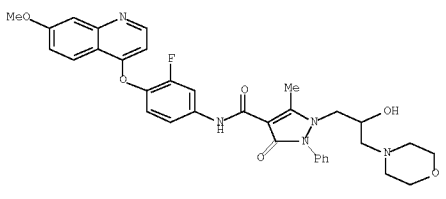
L4 ANSWER 373 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:1435911 CAPLUS Full-text
DOCUMENT NUMBER: 151:565112
TITLE: Combinations VEGF(R) inhibitors and hepatocyte growth factor (c-met) inhibitors for the treatment of cancer
INVENTOR(S): Burgess, Theresa L.; Coxon, Angela; Dussault, Isabelle; Kaplan-Lefko, Paula; Polverino, Anthony J.; Beaupre, Darrin
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009140549	A1	20091119	WO 2009-US44034	20090514

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2009246263	A1	20091119	AU 2009-246263	20090514
AU 2009246263	B2	20140821		
CA 2723617	A1	20091119	CA 2009-2723617	20090514
EP 2288383	A1	20110302	EP 2009-747630	20090514
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, RS				
JP 2011520908	T	20110721	JP 2011-509721	20090514
JP 5699075	B2	20150408		
MX 2010012290	A	20110221	MX 2010-12290	20101110
US 20110104161	A1	20110505	US 2011-992359	20110111
US 20140243339	A1	20140828	US 2014-14194431	20140228
PRIORITY APPLN. INFO.:			US 2008-61127753 P	20080514
			WO 2009-US44034 W	20090514
			US 2011-992359 B3	20110111

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 151:565112
GI



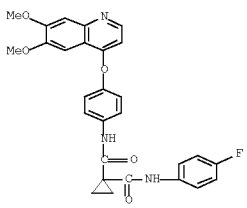
AB This invention is in the field of pharmaceutical agents and specifically relates to compds., compns., uses and methods for treating cancer, by combining VEGF(R) inhibitors and inhibitors of HGF/SF:c-Met. E.g., enhanced activity was observed when AMG 706 (Motesanib) was combined with Amgen Compound 3 [N-[4-[4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)-2-fluorophenoxy]pyridin-2-yl]morpholine-4-carboxamide] compared to either single agent alone when tested on human gastric adenocarcinoma cancer cells.

IT 1140909-48-3, XL 184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combinations VEGF(R) inhibitors and hepatocyte growth factor inhibitors for cancer treatment)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

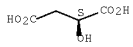
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

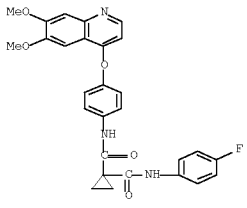


OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 374 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:1001773 CAPLUS Full-text
DOCUMENT NUMBER: 152:349858
TITLE: Novel treatment of medullary thyroid cancer
AUTHOR(S): Sugawara, Masahiro; Geffner, David L.; Martinez, Dorothy; Hershman, Jerome M.
CORPORATE SOURCE: aEndocrinology and Diabetes Division, Veterans Affairs Greater Los Angeles Medical Center, Department of Medicine, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA
SOURCE: Current Opinion in Endocrinology, Diabetes and Obesity (2009), 16(5), 367-372
CODEN: COEDFK; ISSN: 1752-296X
DIGITAL OBJECT ID: 10.1097/MED.0b013e3283304f0c
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: Metastatic medullary thyroid cancer (MTC) is an incurable disease once metastasis becomes unresectable. Many therapeutic drugs and methods have been tried to circumvent this difficulty. We review currently published treatments and hope for future developments of more effective treatment methods. Recent findings: Motesanib, vandetanib, axitinib (tyrosine kinase inhibitors), and XL184 (multikinase inhibitor) have been shown to achieve partial response or stable disease state of metastatic MTC. Sunitinib and sorafenib, currently available tyrosine kinase inhibitors, can also be tried for patients with MTC. However, these medications are not curative and do not improve survival rate. Only carcinoembryonic antigen-I-iodine-based radioimmunotherapy improved survival of a subset of patients with a very aggressive type of MTC. Drugs currently available for possible use of MTC treatment include bortezomib (proteasome inhibitor), valproic acid (histone deacetylase inhibitor), capecitabine (5-fluorouracil prodrug), and indomethacin (NSAID), although clin. studies have yet to be done. Cardiac natriuretic hormones and an extract of the plant Cautleya gracilis are new agents to be studied for MTC. Summary: Kinase inhibitors are the first drugs showing some efficacy in MTC. To improve survival, unconventional drugs or other therapies with or without kinase inhibitors need to be considered.
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multikinase inhibitors like XL184 was effective in patient with metastatic thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

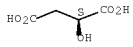
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

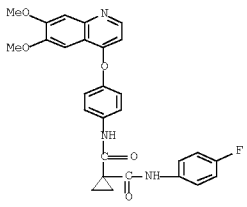


OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 375 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:378374 CAPLUS Full-text
DOCUMENT NUMBER: 153:495871
TITLE: EGFR agonist: irreversible EGFR-TKI and c-Met inhibitors combination
AUTHOR(S): Yadoya, Takehito; Takahashi, Toshiaki; Yamamoto, Nobuyuki
CORPORATE SOURCE: Dep. of Respiratory Diseases, Shizuoka Cancer Center, Shizuoka, Japan
SOURCE: Mebio Oncology (2009), 6(1), 23-31
CODEN: MOENAJ; ISSN: 1349-2179
PUBLISHER: Mejikarubyusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review discussing (1) resistant mechanism to reversible epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), (2) irreversible EGFR-TKIs HKI-272, BIBW-2992, PF-299804 and CI-1033 and (3) c-Met inhibitors AMG-102, XL-184, XL-880 and ARQ-197.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epidermal growth factor receptor agonist and the combination of irreversible EGFR-TKI and c-Met inhibitors)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

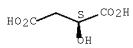
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 376 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:239386 CAPLUS Full-text
DOCUMENT NUMBER: 150:275539
TITLE: Methods for diagnosis, prognosis and methods of treatment
INVENTOR(S): Fantl, Wendy J.; Putta, Santosh K.; Perez, Omar D.; Francis-Lang, Helen L.; Cohen, Aileen C.
PATENT ASSIGNEE(S): Nodality, Inc., USA
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009025847	A2	20090226	WO 2008-US9975	20080821
WO 2009025847	A3	20090611		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2008289442	A1	20090226	AU 2008-289442	20080821
CA 2696402	A1	20090226	CA 2008-2696402	20080821
US 20090098594	A1	20090416	US 2008-229476	20080821
EP 2179037	A2	20100428	EP 2008-795509	20080821
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CN 101802182	A	20100811	CN 2008-80107737	20080821
JP 2010536371	T	20101202	JP 2010-521884	20080821
EP 2860247	A1	20150415	EP 2014-189449	20080821
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IN 2010DN01966	A	20100820	IN 2010-DN1966	20100319
US 20120309029	A1	20121206	US 2012-13493857	20120611
US 9182385	B2	20151110		
US 20160097770	A1	20160407	US 2015-14825486	20150813

PRIORITY APPLN. INFO.: US 2007-60957160 P 20070821
US 2008-61048920 P 20080429
EP 2008-795509 A3 20080821
US 2008-229476 A1 20080821
WO 2008-US9975 W 20080821
US 2012-13493857 A1 20120611

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

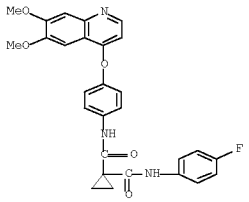
AB This invention is directed to methods and compns. for diagnosis, prognosis and for determining methods of treatment. The physiol. status of cells present in a sample (e.g. clin. sample) can be used in diagnosis or prognosis of a condition (e.g. chronic lymphocytic leukemia), in patient selection for therapy, to monitor treatment and to modify or optimize therapeutic regimens. The physiol. status of a cell can be determined by comparing the intracellular status of one or more activation elements (e.g. the phosphorylation status of a signaling mol.) in a cell (e.g. a cancer cell) to that of another cell (e.g. a normal cell). The physiol. status of a cell can be further classified by adding one or more modulators (e.g. an inhibitor or activator) to the cell in question. In some embodiments, the invention is directed to methods of determining a phenotypic profile of a population of cells.

IT 1140909-48-3, XL 184
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(methods for diagnosis, prognosis and treatment of diseases)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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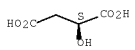
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

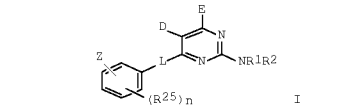


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

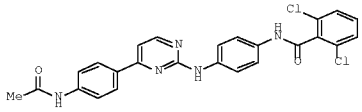
L4 ANSWER 377 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:140345 CAPLUS Full-text
DOCUMENT NUMBER: 150:214411
TITLE: Pyrimidine derivatives as JAK-2 inhibitors in combination with other agents and their preparation and use in the treatment of diseases
INVENTOR(S): Lamb, Peter
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 854pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009017838	A2	20090205	WO 2008-US9360	20080731
WO 2009017838	A3	20090702		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				

PRIORITY APPLN. INFO.: US 2007-60962776 P 20070801
OTHER SOURCE(S): CASREACT 150:214411; MARPAT 150:214411
GI



I

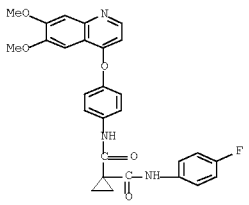


II

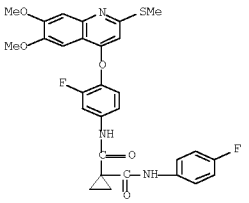
AB A method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a JAK-2 compound of formula I, or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of formula I and a pharmaceutically acceptable carrier, in combination with an active agent selected from of a Raf inhibitor, an EGFR inhibitor, a VEGFR inhibitor, a ErbB2 inhibitor, a BCR-Abl, inhibitor, a Flt3 inhibitor, a Src inhibitor, a c Kit inhibitor, an Akt inhibitor, a Ret inhibitor, an IFG1R inhibitor, an m-Tor inhibitor, a PI3K inhibitor, a PI3Kalpha inhibitor, wherein the mammal is in need of the treatment. Compds. of formula I wherein D and E are independently H, halo, CF3, heterocycloalkyl and alkyl; D and E taken together to form a 5- to 7-membered heteroaryl, and 5- to 7-membered heterocycloalkyl; L is a bond, O and NH; Z is alkoxy, cycloalkyl, and (un)substituted heteroaryl; Z and R25 taken together for form a 5- to 6-membered heterocycloalkyl, 5- to 6-membered heteroaryl, 5- to 6-membered cycloalkyl, etc.; each R25 is independently alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, etc.; R1 is H; R2 is (un)substituted aryl, (un)substituted heteroaryl, alkyl, etc.; n is 0 - 4; and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by acylation of 2-(4-aminophenylamino)-5-(4-acetylaminophenyl)pyrimidine with 2,6-dichlorobenzoyl chloride. All the invention compds. were evaluated for their JAK-2 inhibitory activity (some data given).

IT 849217-68-1P 849217-85-2P 849217-90-9P
849217-94-3P 849221-39-2P 849221-43-6P
849221-44-9P 849221-45-0P 849221-47-2P
849221-48-3P 849221-49-4P 849221-55-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as JAK-2 inhibitors in combination with other agents useful in treatment of diseases)

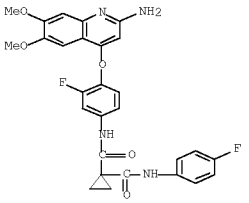
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



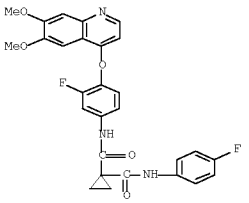
RN 849217-85-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-dimethoxy-2-(methylthio)-4-quinolinyl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



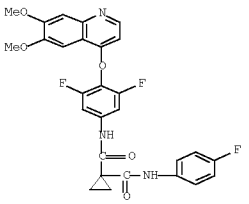
RN 849217-90-9 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(2-amino-6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



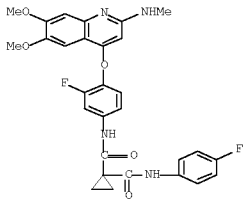
RN 849217-94-3 CAPLUS
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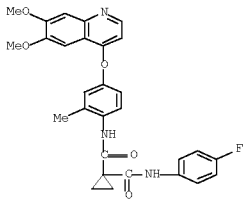
RN 849221-44-9 CAPLUS
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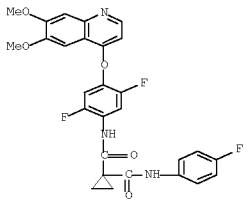
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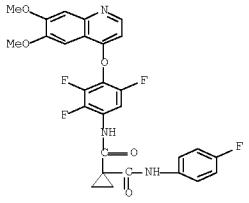
RN 849221-39-2 CAPLUS
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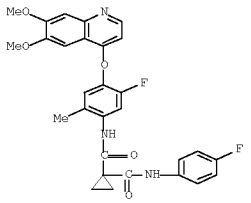
RN 849221-41-6 CAPLUS
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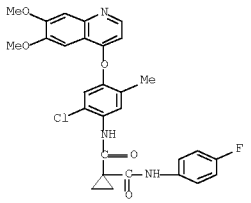
RN 849221-47-2 CAPLUS
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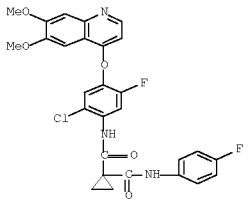
RN 849221-48-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-5-fluoro-2-methylphenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 849221-49-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]-5-methylphenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 849221-55-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]-5-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L4 ANSWER 378 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2008:1282443 CAPLUS Full-text
DOCUMENT NUMBER: 149:486836
TITLE: Methods for treating cancer resistant to ErbB therapeutics
INVENTOR(S): Janne, Pasi A.; Engelman, Jeffrey; Cantley, Lewis C.
PATENT ASSIGNEE(S): Dana Farber Cancer Institute, USA; Beth Israel Deaconess Medical Center; Massachusetts General Hospital
SOURCE: PCT Int. Appl., 96pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008127710	A2	20081023	WO 2008-US4804	20080411
WO 2008127710	A3	20081204		
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AU 2008239594	B2	20131024		
CA 2683559	A1	20081023	CA 2008-2683559	20080411
EP 2076289	A2	20090708	EP 2008-742861	20080411
EP 2076289	B1	20141112		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
JP 2010523680	T	20100715	JP 2010-503084	20080411
ES 2529790	T3	20150225	ES 2008-742861	20080411
EP 2851091	A1	20150325	EP 2014-189064	20080411
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR				
US 20120225870	A1	20120906	US 2010-450826	20100318
US 8715665	B2	20140506		
AU 2013203111	A1	20130502	AU 2013-203111	20130409
AU 2013203111	B2	20151008		
US 20140296100	A1	20141002	US 2014-14256418	20140418
JP 2014141530	A	20140807	JP 2014-97474	20140509

PRIORITY APPLN. INFO.:

US 2007-60923384	P	20070413
AU 2008-239594	A3	20080411
EP 2008-742861	A3	20080411
JP 2010-503084	A3	20080411
WO 2008-US4804	W	20080411
US 2010-450826	A1	20100318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

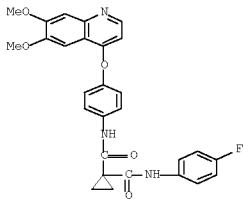
AB Provided herein are methods for treating cancer that is resistant to treatment with an anti- ErbB therapeutic agent and which is associated with an activating MET gene mutation or a MET gene amplification. The methods involve administering to a subject a combination of an anti- ErbB therapeutic and an anti-MET therapeutic. Also provided are methods for reducing ErbB mediated signaling or PI3 kinase mediated signaling in a cancer cell.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treating cancer resistant to ErbB therapeutics using combination of anti-Met receptor agent and anti-ErbB receptor agent in relation to activation mutation or gene amplification)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

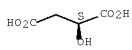
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

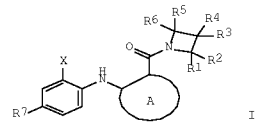
L4 ANSWER 379 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2008:771167 CAPLUS Full-text
DOCUMENT NUMBER: 149:104583
TITLE: N-Acylazetidine derivatives as MEK inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer
INVENTOR(S): Lamb, Peter
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 534pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008076415	A1	20080626	WO 2007-US25751	20071214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,				

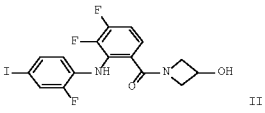
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2007334402	A1	20080626	AU 2007-334402		20071214
AU 2007334402	B2	20140213			
CA 2671982	A1	20080626	CA 2007-2671982		20071214
CA 2671982	C	20160126			
US 20080166359	A1	20080710	US 2007-2340		20071214
US 7999006	B2	20110816			
EP 2101759	A1	20090923	EP 2007-853418		20071214
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS					
CN 101605540	A	20091216	CN 2007-80051355		20071214
JP 2010513288	T	20100430	JP 2009-541420		20071214
JP 5311673	B2	20131009			
CN 105106199	A	20151202	CN 2015-10422958		20071214
AU 2013204026	A1	20130516	AU 2013-204026		20130411
JP 2013151569	A	20130808	JP 2013-102016		20130514
PRIORITY APPLN. INFO.:			US 2006-60875412	P	20061214
			AU 2007-334402	A3	20071214
			CN 2007-80051355	A3	20071214
			JP 2009-541420	A3	20071214
			WO 2007-US25751	W	20071214

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 149:104583; MARPAT 149:104583
GI



I



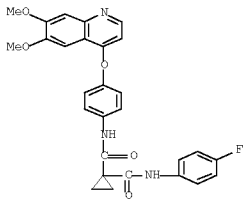
II

AB The invention provides methods of treating cancer by administering a compound of formula I, or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments. Compds. of formula I wherein ring A is (un)substituted (hetero)arylene; X is (halo)alkyl, halo and haloalkoxy; R1, R2, R3, R4, R5 and R6 are independently H, halo, NO2, NH2 and derivs., OH and derivs., NHSO2H and derivs., CN, SH and derivs., etc.; R7 is H, halo and alkyl; and their pharmaceutically acceptable salts and solvates thereof are claimed. Example compound II was prepared by amidation of 3,4-difluoro-2-[(2-fluoro-4- iodophenyl)amino]benzoic acid with azetidin-3-ol hydrochloride. All the invention compds. were evaluated for their MEK inhibitory activity (some data given).

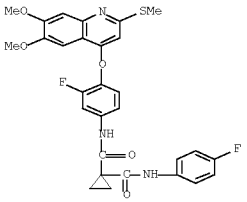
IT 849217-68-1 849217-85-2P 849217-90-9,

N-[4-[[2-Amino-6,7-bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-94-3,
N-[3-Fluoro-4-[[2-(methylamino)-6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849221-39-2, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2-methylphenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849221-41-6, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849221-44-9, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3,5-difluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849221-45-0, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2,5-difluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849221-47-2, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2,3,5-trifluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849221-48-3, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-2-methylphenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849221-49-4, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2-chloro-5-methylphenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
849221-55-2, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2-chloro-5-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-acylazetidine derivs. as MEK inhibitors useful in the mono- and combination therapy of cancer)

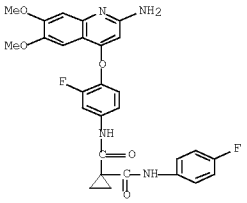
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



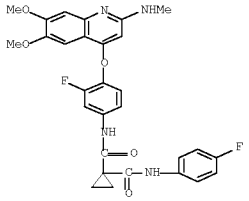
RN 849217-85-2 CAPLUS
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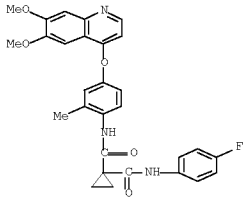
RN 849217-90-9 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(2-amino-6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



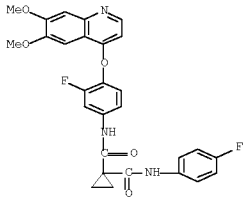
RN 849217-94-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-dimethoxy-2-(methylamino)-4-quinolinyl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



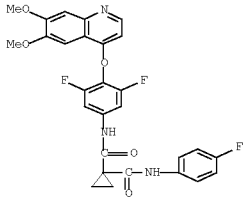
RN 849221-39-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-2-methylphenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



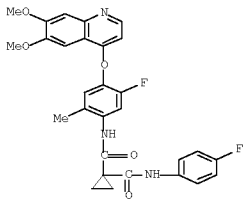
RN 849221-41-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



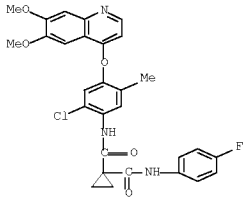
RN 849221-44-9 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-3,5-difluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



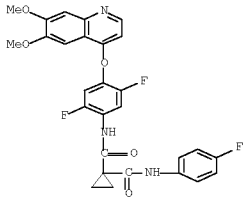
RN 849221-45-0 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-2,5-difluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



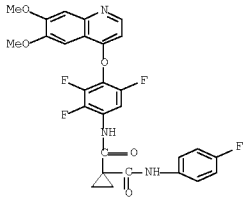
RN 849221-49-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]-5-methylphenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



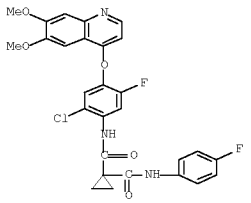
RN 849221-55-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]-5-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 849221-47-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-2,3,5-trifluorophenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 849221-48-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-5-fluoro-2-methylphenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 380 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2008:699999 CAPLUS Full-text
DOCUMENT NUMBER: 149:30417
TITLE: Antibodies and inhibitory nucleic acids for targeing HIF-1α and for diagnosing/treating tumor or metastasis
INVENTOR(S): Huang, L. Eric
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 157pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008070616	A2	20080612	WO 2007-US86264	20071203
WO 2008070616	A3	20090430		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20100074897	A1	20100325	US 2009-517132	20090710

PRIORITY APPLN. INFO.: US 2006-60868188 P 20061201
WO 2007-US86264 W 20071203
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed are compns. and methods related to HIF-1α (hypoxia-inducible factor 1α). The compns. and methods comprise use of HIF-1α inhibitors for reducing tumor growth or metastatic tumor growth. The HIF-1α inhibitor is an antibody (including monoclonal, human and humanized antibody), small mol., siRNA, shRNA, or antisense polynucleotide.

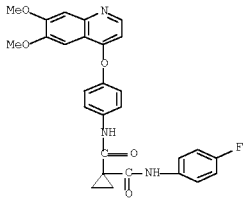
IT 1140909-48-3, XL 184
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibodies and inhibitory nucleic acids for targeing HIF-1α and for diagnosing/treating tumor or metastasis)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

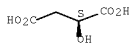
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 381 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN

AU 2011201326	A1	20110414	AU 2011-201326	20110323
AU 2011201326	B2	20120112		
AU 2012202120	A1	20120503	AU 2012-202120	20120412
US 20120288497	A1	20121115	US 2012-13472862	20120516
JP 2012211155	A	20121101	JP 2012-131988	20120611
US 20140023654	A1	20140123	US 2013-13952997	20130729

PRIORITY APPLN. INFO.:

US 2005-60750551	P	20051215
AU 2006-324477	A3	20061212
CN 2006-80052740	A3	20061212
EP 2006-820476	A3	20061212
JP 2008-545075	A3	20061212
WO 2006-GB4611	W	20061212
US 2008-97384	B1	20080613
US 2010-890101	A1	20100924
AU 2011-201326	A3	20110323
US 2012-13472862	A1	20120516

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to agents which possess anti-angiogenic activity and are accordingly useful in methods of treatment of disease states associated with angiogenesis in the animal or human body. More specifically the invention concerns a combination of a monoclonal antibody against human angiopoietin 2 (anti-Ang-2) and an antagonist of the biol. activity of VEGF-A, and/or KDR receptor, and/or FLT1, and uses of such antagonists. The nucleotide sequences and the encoded amino acid sequences of anti-Ang-2 monoclonal antibodies are disclosed.

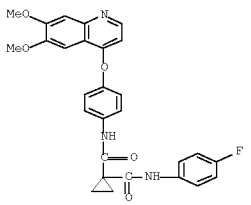
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); BIOL (Biological study)
(combination of anti-angiopoietin 2 human monoclonal antibody and of VEGF-A, KDR and/or FLT1 antagonist for treating cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



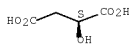
ACCESSION NUMBER: 2007:671771 CAPLUS Full-text
DOCUMENT NUMBER: 147:93969
TITLE: Combination of anti-angiopoietin 2 human monoclonal antibody and of VEGF-A, KDR and/or FLT1 antagonist for treating cancer
INVENTOR(S): Brown, Jeffrey Lester; Emery, Stephen Charles; Blakey, David Charles
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007068895	A1	20070621	WO 2006-GB4611	20061212
WO 2007068895	A9	20080612		
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AU 2006324477	A1	20070621	AU 2006-324477	20061212
CA 2633211	A1	20070621	CA 2006-2633211	20061212
KR 2008073766	A	20080811	KR 2008-7015745	20061212
KR 1371773	B1	20140307		
EP 1962903	A1	20080903	EP 2006-820476	20061212
EP 1962903	B1	20130313		
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CN 101370519	A	20090218	CN 2006-80052740	20061212
CN 101370519	B	20130724		
JP 2009521412	T	20090604	JP 2008-545075	20061212
JP 5179373	B2	20130410		
NZ 569787	A	20110729	NZ 2006-569787	20061212
EP 2518083	A2	20121031	EP 2011-167374	20061212
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ES 2411505	T3	20130705	ES 2006-820476	20061212
CN 103341168	A	20131009	CN 2013-10251494	20061212
AR 58359	A1	20080130	AR 2006-105550	20061215
NO 2008002448	A	20080710	NO 2008-2448	20080528
IN 2008DN04540	A	20090320	IN 2008-DN4540	20080528
MX 2008007686	A	20080627	MX 2008-7686	20080613
US 20090123474	A1	20090514	US 2008-97384	20080613
HK 1121674	A1	20131011	HK 2008-112903	20081125
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

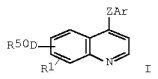


OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 382 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2006:1066309 CAPLUS Full-text
DOCUMENT NUMBER: 145:418960
TITLE: Preparation of quinolines as modulators of c-Met, KDR, c-Kit, flt-3, and flt-4 kinases.
INVENTOR(S): Forsyth, Timothy Patrick; Mac, Morrison B.; Leahy, James William; Nuss, John M.; Xu, Wei
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 147pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006108059	A1	20061012	WO 2006-US12709	20060406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006231646	A2	20061012	AU 2006-231646	20060406
AU 2006231646	A1	20061012		
CA 2603748	A1	20061012	CA 2006-2603748	20060406
EP 1874759	A1	20080109	EP 2006-749361	20060406
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008537748	T	20080925	JP 2008-505496	20060406
US 20080161305	A1	20080703	US 2007-910720	20071121

PRIORITY APPLN. INFO.: US 2005-60669207 P 20050406
WO 2006-US12709 W 20060406
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 145:418960; MARPAT 145:418960
GI



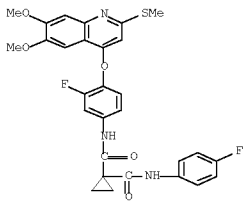
AB Title compds. [I; R1 = H, halo, OR3, NO2, NH2, NR3R4; R3 = H, R4; R4 = (substituted) alkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl; NR3R4 = 5-7 membered (substituted) heterocyclyl; Z = S, SO, SO2, O, NR5; R5 = H, (substituted) alkyl; Ar = (substituted) Ph, pyridyl, pyridazinyl, benzothienyl, benzoxazolyl, benzimidazolyl; D = O, S, SO, SO2, NR15; R15 = M1M2; M1 = null, CSNR13, CO, SO2, SO2NR13, etc.; M2 = H, alkyl, alkoxy, (substituted) cyclyl(alkyl)carbonyl, cyclyl(alkyl), etc.; R50 = R3, specified (substituted) (bicyclic) ring; with provisos], were prepared Thus, N-[3-fluoro-4-[[6-(methoxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl]oxy]phenyl]-N'-[2-(4-fluorophenyl)ethyl]ethanediamide (preparation given) inhibited c-Met, KDR, c-Kit, flt-3, and flt-4 kinases with IC50 <50 nM.

IT 849217-85-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinolines as modulators of c-Met, KDR, c-Kit, flt-3, and flt-4 kinases)

RN 849217-85-2 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-dimethoxy-2-(methylthio)-4-quinolinyl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

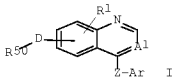
L4 ANSWER 383 OF 383 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2005:300201 CAPLUS Full-text
DOCUMENT NUMBER: 142:373856
TITLE: Preparation of quinolines and quinazolines as inhibitors of c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases
INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-ming; Chen, Jeff; Dalrymple, Lisa Esther; Forsyth, Timothy Patrick; Huynh, Tai Phat; Jammalamadaka, Vasu; Khoury, Richard George; Leahy, James William; Mac, Morrison B.; Mann, Grace; Mann, Larry W.; Nuss, John M.; Parks, Jason Jevious; Takeuchi, Craig Stacy; Wang, Yong; Xu, Wei
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 428 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030140	A2	20050407	WO 2004-US31523	20040924
WO 2005030140	A3	20050519		
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AU 2004275842	A1	20050407	AU 2004-275842	20040924
AU 2004275842	B2	20100902		
CA 2537812	A1	20050407	CA 2004-2537812	20040924
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CA 2744997	A1	20050407	CA 2004-2744997	20040924
EP 1673085	A2	20060628	EP 2004-789057	20040924
EP 1673085	B1	20111109		
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JP 2007506777	T	20070322	JP 2006-528265	20040924
JP 4638436	B2	20110223		
EP 2210607	A1	20100728	EP 2010-160517	20040924
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EP 2213661	B1	20110720		
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AT 532782	T	20111115	AT 2004-789057	20040924
ES 2369652	T3	20111202	ES 2010-160518	20040924
EP 2392564	A1	20111207	EP 2011-179941	20040924
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EP 2392565	A1	20111207	EP 2011-179942	20040924
EP 2392565	B1	20140319		
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EP 2609919	A2	20130703	EP 2013-151957	20040924
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EP 2612853	A1	20130710	EP 2013-151945	20040924
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ES 2436888	T3	20140107	ES 2011-179941	20040924
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US 20070054928	A1	20070308	US 2006-586751	20061026
US 9174947	B2	20151103		
US 20070225307	A1	20070927	US 2007-753462	20070524
US 8178532	B2	20120515		
US 20070244116	A1	20071018	US 2007-753503	20070524
US 8476298	B2	20130702		
US 20090105299	A1	20090423	US 2007-753514	20070524
US 8067436	B2	20111129		
US 20090170896	A1	20090702	US 2009-393806	20090226
US 7579473	B2	20090825		
JP 2010235631	A	20101021	JP 2010-158335	20100712
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HK 1143068	A1	20120518	HK 2010-109531	20101006
US 20110077233	A1	20110331	US 2010-911442	20101025
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US 20120022065	A1	20120126	US 2011-13249815	20110930
US 8497284	B2	20130730		
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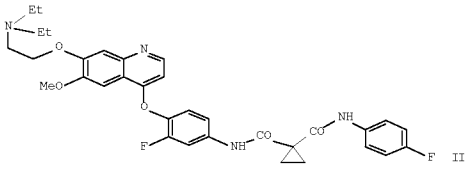
PRIORITY APPLN. INFO.:

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US 2004-60577384	P	20040604
AU 2004-275842	A3	20040924
CA 2004-2537812	A3	20040924
EP 2004-789057	A3	20040924
EP 2011-179942	A3	20040924
EP 2011-179944	A3	20040924
JP 2006-528265	A3	20040924
WO 2004-US31523	W	20040924
US 2006-573336	B1	20060918
US 2006-586751	A1	20061026
US 2007-753462	A1	20070524
US 2007-753503	A1	20070524
US 2007-753514	A1	20070524
JP 2010-158337	A3	20100712
AU 2010-204461	A3	20100727
JP 2010-256317	A3	20101116
US 2011-13249815	A1	20110930
JP 2013-268455	A3	20131226

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 142:373856; MARPAT 142:373856
GI



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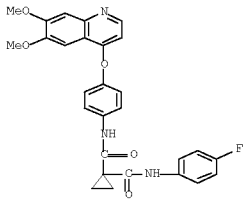


II

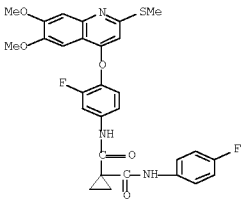
AB The present invention provides compds. (shown as I; variables defined below; e.g. N-[4-[[7-[[2-(diethylamino)ethyl]oxy]-6-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide (shown as II)) for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. More specifically, the invention provides quinazolines and quinolines which inhibit, regulate and/or modulate kinase receptors, particularly c-Met, KDR, c-Kit, flt-3 and flt-4, signal transduction pathways related to the changes in cellular activities as mentioned above, compns. which contain these compds., and methods of using them to treat kinase-dependent diseases and conditions. The present invention also provides methods for making compds. as mentioned above, and compns. which contain these compds. For I: R1 = H, halogen, OR3, NO2, NH2, NR3R4, and (un)substituted lower alkyl; A1 = :N-, :C(H)-, and :C(CN)-; Z = -S(O)0-2-, -O-, and -NR5-; Ar is aryl or heteroaryl; D = -O-, -S(O)0-2-, and -NR15-; R50 = R3 or bicyclic radical; addnl. details are given in the claims. Methods of preparation are claimed and .apprx.80 example prepns. of I and intermediates are included. For example, II was prepared (34 %) from 2-(diethylamino)ethanol and cyclopropane-1,1-dicarboxylic acid N-[3-fluoro-4-[(7-hydroxy-6-methoxyquinolin-4-yl)oxy]phenyl]amide N-(4-fluorophenyl)amide, which was prepared (89 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-[4-[(7-benzyloxy-6-methoxyquinolin-4-yl)oxy]-3-fluorophenyl]amide N-(4-fluorophenyl)amide, which was prepared (48 %) from trifluoromethanesulfonic acid 7-benzyloxy-6-methoxyquinolin-4-yl ester and cyclopropane-1,1-dicarboxylic acid N-(3-fluoro-4-hydroxyphenyl)amide N-(4-fluorophenyl)amide, which was prepared (85 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-(4-benzyloxy-3-fluorophenyl)amide N-(4-fluorophenyl)amide, which was prepared (98 %) from (4-benzyloxy-3-fluorophenyl)amine and 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid; addnl. details are given in the examples.

IT 849217-68-1P 849217-88-2P,
N-[4-[[6,7-Bis(methyloxy)-2-(methylthio)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-90-9P
, N-[4-[[2-Amino-6,7-bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849217-94-3P,
N-[3-Fluoro-4-[[2-(methylamino)-6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849221-39-2P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2-methylphenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849221-41-6P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849221-44-9P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-3,5-difluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849221-45-0P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2,5-difluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849221-47-2P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2,3,5-trifluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849221-48-3P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-5-fluoro-2-methylphenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849221-49-4P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2-chloro-5-methylphenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide 849221-53-0P, N-[4-[[6,7-Bis(methyloxy)quinolin-4-yl]oxy]-2-chloro-5-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinolines and quinazolines as inhibitors of
c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases)

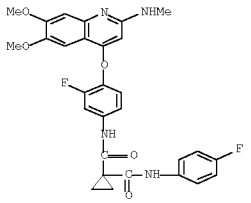
RN 849217-68-1 CAPLUS
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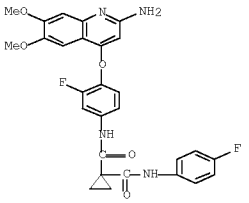
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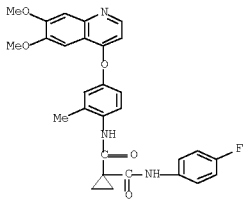
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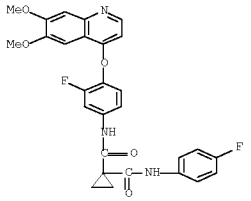
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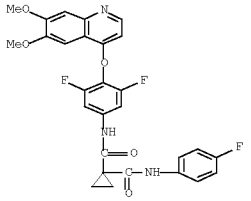
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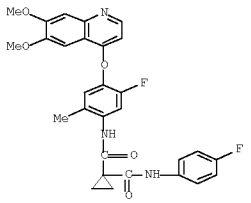
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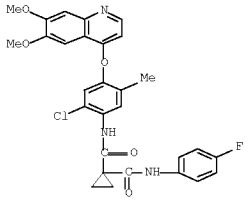
RN 849221-44-9 CAPLUS
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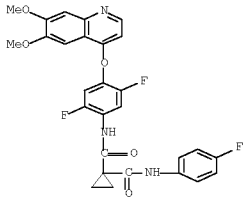
RN 849221-45-0 CAPLUS
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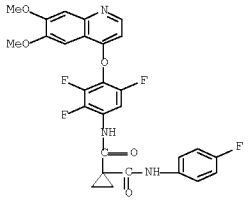
RN 849221-49-4 CAPLUS
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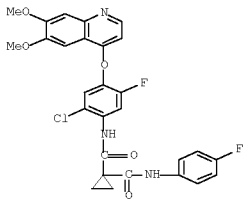
RN 849221-55-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]-5-fluorophenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 849221-47-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-2,3,5-trifluorophenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 849221-48-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-5-fluoro-2-methylphenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 46 THERE ARE 46 CAPLUS RECORDS THAT CITE THIS RECORD (55 CITINGS)

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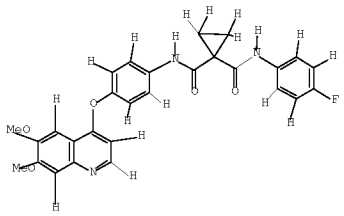
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L5 STRUCTURE UPLOADED

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L5 HAS NO ANSWERS
L5 STR



Structure attributes must be viewed using the Structure Drawing program.

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SEARCH TIME: 00.00.01

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FULL ESTIMATED COST 249.75 3377.34

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FILE LAST UPDATED: 27 Apr 2016 (20160427/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

CAplus includes complete International Patent Classification (IPC) reclassification data for the first quarter of 2016.

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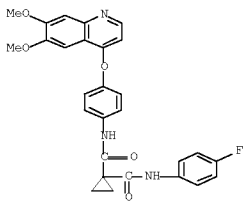
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L8 382 L7

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L8 ANSWER 1 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:559516 CAPLUS Full-text
TITLE: Cabozantinib is selectively cytotoxic in acute myeloid leukemia cells with FLT3-internal tandem duplication (FLT3-ITD)
AUTHOR(S): Lu, Jeng-Wei; Wang, An-Ni; Liao, Heng-An; Chen, Chien-Yuan; Hou, Hsin-An; Hu, Chung-Yi; Tien, Hwei-Fan; Ou, Da-Liang; Lin, Liang-In
CORPORATE SOURCE: Department of Clinical Laboratory Sciences and Medical Biotechnology, National Taiwan University, Taipei, Taiwan
SOURCE: Cancer Letters (New York, NY, United States) (2016), 376(2), 218-225
CODEN: CALEDQ; ISSN: 0304-3835
DIGITAL OBJECT ID: 10.1016/j.canlet.2016.04.004
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is an oral multikinase inhibitor that exhibits anti-tumor activity in several cancers. We found that cabozantinib was significantly cytotoxic to MV4-11 and Molm-13 cells that harbored FLT3-ITD, resulting in IC50 values of 2.4 nM and 2.0 nM, resp. However, K562, OCI-AML3 and THP-1 (leukemia cell lines lacking FLT3-ITD) were resistant to cabozantinib, showing IC50 values in the micromolar range. Cabozantinib arrested MV4-11 cell growth at the G0/G1 phase within 24 h, which was associated with decreased phosphorylation of FLT3, STAT5, AKT and ERK. Addnl., cabozantinib induced MV4-11 cell apoptosis in a dose-dependent manner (as indicated by annexin V staining and high levels of cleaved caspase 3 and PARP-1), down-regulated the anti-apoptotic protein survivin and up-regulated the pro-apoptotic protein Bak. Thus, cabozantinib is selectively cytotoxic to leukemia cells with FLT3-ITD, causing cell-cycle arrest and apoptosis. In mouse xenograft model, cabozantinib significantly inhibited MV4-11 and Molm-13 tumor growth at a dosage of 10 mg/kg and showed longer survival rate. Clin. trials evaluating the efficacy of cabozantinib in acute myeloid leukemia (AML) with FLT3-ITD are warranted.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib as selectively cytotoxic in acute myeloid leukemia cells with FLT3-internal tandem duplication)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



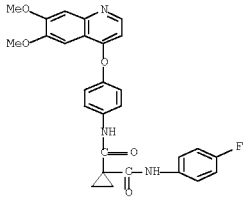
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:552052 CAPLUS Full-text
DOCUMENT NUMBER: 164:447096
TITLE: Pharmaceutical compositions comprising tyrosine kinase inhibitors for treating enveloped viruses
INVENTOR(S): Einav, Shirit; Neveu, Gregory; Barouch-Bentov, Rina
PATENT ASSIGNEE(S): The Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 38pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016054468	A1	20160407	WO 2015-US53638	20151002

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62059449 P 20141003
AB Described are compns. such as tyrosine kinase inhibitors (e.g. erlotinib, sunitinib) and methods for treating an enveloped virus in a patient in need thereof. Exemplary enveloped viruses are those in the family Filoviridae and include Ebola virus.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. comprising tyrosine kinase inhibitors for treating enveloped viruses)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 3 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:551762 CAPLUS Full-text
TITLE: Prediction of response to PARP inhibitors and combinational therapy of cancer targeting c-Met and PARP1
INVENTOR(S): Hung, Mien-Chie; Du, Yi
PATENT ASSIGNEE(S): Board of Regent, The University of Texas System, USA

SOURCE: PCT Int. Appl., 103pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016054055	A1	20160407	WO 2015-US52966	20150929

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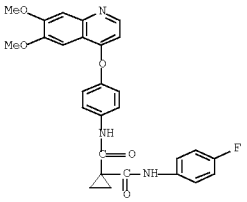
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PRIORITY APPLN. INFO.: US 2014-62057037 P 20140929

AB Provided herein are methods for identifying and treating cancers that are resistant to PARP inhibition. Methods for sensitizing cancers to a PARP inhibitor therapy are also provided. In some aspects, PARP inhibitor cancers are treated with a PARP inhibitor therapy in combination with a c-Met inhibitor therapy.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prediction of response to PARP inhibitors and combinational therapy of cancer targeting c-met and PARP1 and treatment with other therapy)

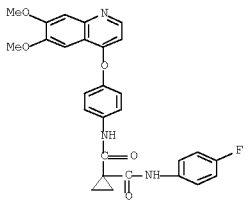
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

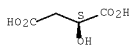
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L8 ANSWER 4 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:534801 CAPLUS Full-text
TITLE: Quick-release medicine phosphatide compound and pharmaceutical composition thereof
INVENTOR(S): Li, Xinsong; Du, Yawei; Ling, Longbing; He, Ruiyu
PATENT ASSIGNEE(S): Southeast University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 54pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

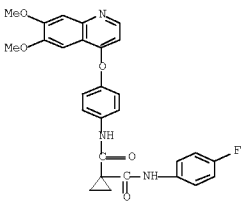
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105457038	A	20160406	CN 2015-10756327	20151109

PRIORITY APPLN. INFO.: CN 2015-10756327 20151109

AB The invention discloses a quick-release medicine phosphatide compd. and pharmaceutical composition thereof. In this compound I, medicine Y1 and Y2 are connected with quick-release hydrophobic spacer arm and enhancement type hydrophobic spacer arm through chemical bond. Two kinds of the spacer arms collaborate with each other and strengthen hydrophobic action to form hydrophobic lipophilic chain. Two hydrophobic chains are connected with phospholipid hydrophilic head to constitute amphipathic mol. Pharmaceutical composition is quick-release medicine phosphatide compound or combined medicinal combination of this compound and pharmaceutically acceptable carrier. The quick-release medicine phosphatide compound and lipidosome nanoparticle thereof can be used as liquid preparation, solid preparation, semi-solid preparation, sterilized preparation and sterile preparation with low toxicity, and can be used for the efficient treatment of diseases such as various tumors.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quick-release medicine phosphatide compound and pharmaceutical composition thereof)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 5 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:501826 CAPLUS Full-text
DOCUMENT NUMBER: 164:433336
TITLE: Prediction of effect of a c-met inhibitor using mutation of KRAS or BRAF
INVENTOR(S): Shim, Seon Hui; Jung, Soo Yeon; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 126pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160090635	A1	20160331	US 2015-14869563	20150929
KR 2016037666	A	20160406	KR 2014-130560	20140929

PRIORITY APPLN. INFO.: KR 2014-130560 A 20140929
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A method for predicting and/or monitoring the efficacy of a c-Met inhibitor using a biomarker; a method for selecting a subject suitable for the application of a c-Met inhibitor using a biomarker; and a method for preventing and/or treating cancer comprising administering a c-Met inhibitor to the selected subject. In particular embodiments, provided are biomarkers for use in predicting and/or monitoring the therapeutic effect of a c-Met inhibitor or selecting a subject suitable for the application of a c-Met inhibitor, including IL-8, bIG-H3, KRAS or BRAF and nucleic acids encoding the proteins. Another embodiment provides a c-Met inhibitor or a pharmaceutical composition including a c-Met inhibitor, for use in inhibiting c-Met and/or treating a cancer in a subject, wherein the subject has a higher level of IL-8 or bIG-H3 compared to a reference sample in which a c-Met inhibitor is not effective, and/or has a mutation of KRAS and/or BRAF. KRAS protein comprises at least one amino acid mutation selected from the group consisting of G12A, G12D, G12R, G12C, G12S, G12V, A146T, A59T, L23R, G13N, G13D, I24F, Q61L, Q61H, G13C, and Q61K; and BRAF protein comprises at least one amino acid mutation selected from the group consisting of G596R, V600E, V600K, V600R, K601E, D594G, K601E, G469A, V600M, G469A, V600L, G466V, V600D, G469V, D594G, D594N, N581S, L597V, L597S, L597Q, K601N, G466V, G466E, G464V, and G469E.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prediction of effect of a c-met inhibitor in cancer therapy using mutation of KRAS or BRAF)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

L8 ANSWER 6 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:467583 CAPLUS Full-text
DOCUMENT NUMBER: 164:424395
TITLE: Combination therapies for treatment of cancer
INVENTOR(S): Janes, Matthew Robert; Patricelli, Matthew Peter; Li,

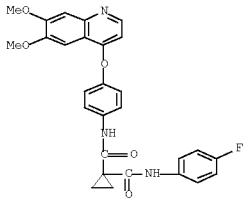
Liansheng; Ren, Pingda; Liu, Yi
PATENT ASSIGNEE(S): Araxes Pharma LLC, USA
SOURCE: PCT Int. Appl., 397pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016044772	A1	20160324	WO 2015-US51030	20150918

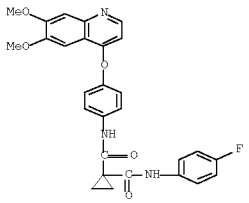
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62052332 P 20140918
US 2015-62195633 P 20150722

AB Combination therapies for treatment of cancers assocd. with mutations in the KRAS gene are provided. Compns. comprising therapeutic agents for treatment of cancers associated with mutations in the KRAS gene are also provided.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapies for treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:381187 CAPLUS Full-text
DOCUMENT NUMBER: 164:368125
TITLE: Biomarker for predicting sensitivity to protein kinase inhibitor and use thereof
INVENTOR(S): Kim, Tae Won; Jin, Dong Hoon; Hong, Seung Woo; Moon, Jai Hee; Shin, Jae Sik; Lee, Ha Reum; Choi, Eun Kyoung; Kim, Seung Mi; Jung, Soo A.; Ha, Seung Hee; Jung, Ha Na; Lee, Dae Hee; Jung, Seang Hwan; Lee, Jung Shin; Choi, Eun Kyung; Lee, Jae Lyun; Hong, Yong Sang; Kim, Kyu Pyo; Kim, Jeong Eun; Park, Seong Joon; Kim, Bong Choel
PATENT ASSIGNEE(S): CJ HealthCare Corporation, S. Korea
SOURCE: PCT Int. Appl., 60pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016036172	A1	20160310	WO 2015-KR9322	20150903

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

KR 2016028399	A	20160311	KR 2015-125055	20150903

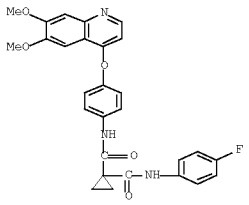
PRIORITY APPLN. INFO.: KR 2014-116787 A 20140903

L8 ANSWER 7 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:448327 CAPLUS Full-text
TITLE: Expression profiling of small intestinal neuroendocrine tumors identifies subgroups with clinical relevance, prognostic markers and therapeutic targets
AUTHOR(S): Andersson, Ellinor; Arvidsson, Yvonne; Swaerd, Christina; Hofving, Tobias; Waengberg, Bo; Kristiansson, Erik; Nilsson, Ola
CORPORATE SOURCE: Sahlgrenska Cancer Center, Department of Pathology, Institute of Biomedicine, Sahlgrenska Academy at the University of Gothenburg, Goeteborg, Swed.
SOURCE: Modern Pathology (2016) Ahead of Print
CODEN: MODPEO; ISSN: 0893-3952
DIGITAL OBJECT ID: 10.1038/modpathol.2016.48
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We wanted to define the transcriptome of small intestinal neuroendocrine tumors in order to identify clin. relevant subgroups of tumors, prognostic markers and novel targets for treatment. Genome-wide expression profiling was conducted on tumor biopsies from 33 patients with well-differentiated neuroendocrine tumors of the distal ileum and metastatic disease at the time of diagnosis. Unsupervised hierarchical clustering anal. identified three groups of tumors. The largest group, comprising half of the tumors, was characterized by longer patient survival and higher expression of neuroendocrine markers, including SSTR2. Tumors with higher grade (G2/3) or gain of chromosome 14 were associated with shorter patient survival and increased expression of cell cycle-promoting genes. Pathway anal. predicted the prostaglandin E receptor 2 (PTGER2) as the most significantly activated regulator in tumors of higher grade, whereas Forkhead box M1 (FOXM1) was the most significantly activated regulator in tumors with gain of chromosome 14. Druggable genes identified from expression profiles included clin. proven SSTR2 and also novel targets, for example, receptor tyrosine kinases (RET, FGFR1/3, PDGFRB and FLT1), epigenetic regulators, mol. chaperones and signal transduction mols. Evaluation of candidate drug targets on neuroendocrine tumors cells (GOT1) showed significant inhibition of tumor cell growth after treatment with tyrosine kinase inhibitors or inhibitors of HDAC, HSP90 and AKT. In conclusion, we have defined the transcriptome of small intestinal neuroendocrine tumors and identified novel subgroups with clin. relevance. We found specific gene expression patterns associated with tumor grade and chromosomal alterations. Our data also suggest novel prognostic biomarkers and therapies for these patients.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression profiling of small intestinal neuroendocrine tumors identifies subgroups with clin. relevance, prognostic markers and therapeutic targets)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

AB The present invention relates to a biomarker for predicting the sensitivity of cells to a protein kinase inhibitor and a use thereof, a composition, a kit, and a prediction method. The biomarker comprises splicing variant or mutant of RON gene. According to the present invention, an effect of predicting sensitivity to a protein kinase inhibitor is excellent, and thus the present invention can be useful for cancer treatment.
IT 1140909-48-3, XL-184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active RON-containing biomarker for predicting cell sensitivity to protein
kinase inhibitor)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

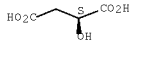
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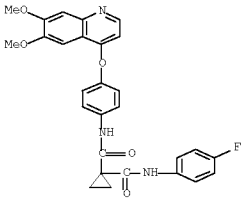
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CMF C4 H6 O5

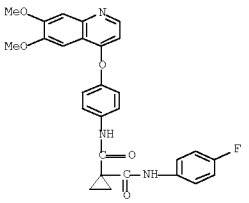
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REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:352953 CAPLUS Full-text
TITLE: Delineation of Polypharmacology across the Human Structural Kinome Using a Functional Site Interaction Fingerprint Approach
AUTHOR(S): Zhao, Zheng; Xie, Li; Xie, Lei; Bourne, Philip E.
CORPORATE SOURCE: National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, MD, 20894, USA
SOURCE: Journal of Medicinal Chemistry (2016) Ahead of Print
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/acs.jmedchem.5b02041
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Targeted polypharmacol. of kinases has emerged as a promising strategy to design efficient and safe therapeutics. Here, we perform a systematic study of kinase-ligand binding modes for the human structural kinome at scale (208 kinases, 1777 unique ligands, and their complexes) by integrating chemical genomics and structural genomics data and by introducing a functional site interaction fingerprint (Fs-IFP) method. New insights into kinase-ligand binding modes were obtained. We establish relationships between the features of binding modes, the ligands, and the binding pockets, resp. We also drive the intrinsic binding specificity and which correlation with amino acid conservation. Third, we explore the landscape of the binding modes and highlight the regions of "selectivity pocket" and "selectivity entrance". Finally, we demonstrate that Fs-IFP similarity is directly correlated to the exptl. determined profile. These improve our understanding of kinase-ligand interactions and contribute to the design of novel polypharmacol. therapies targeting kinases.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delineation of polypharmacol. across structural kinome using functional site interaction fingerprint approach)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





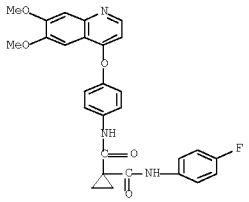
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:333433 CAPLUS Full-text
TITLE: Population pharmacokinetic/pharmacodynamic modeling of tumor growth kinetics in medullary thyroid cancer patients receiving cabozantinib
AUTHOR(S): Miles, Dale R.; Wada, David R.; Jumbe, Nelson L.; Lacy, Steven A.; Nguyen, Linh T.
CORPORATE SOURCE: Exelixis Inc., San Francisco, CA, USA
SOURCE: Anti-Cancer Drugs (2016), 27(4), 328-341
CODEN: ANTDEV; ISSN: 0959-4973
DIGITAL OBJECT ID: 10.1097/CAD.0000000000000330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Nonlinear mixed effects models were developed to describe the relationship between cabozantinib exposure and target lesion tumor size in a phase III study of patients with progressive metastatic medullary thyroid cancer. These models used cabozantinib exposure ests. from a previously published population pharmacokinetic model for cabozantinib in cancer patients that was updated with data from healthy-volunteer studies. Semi-mechanistic models predict well for tumors with static, increasing, or decreasing growth over time, but they were not considered adequate for predicting tumor sizes in medullary thyroid cancer patients, among whom an early reduction in tumor size was followed by a late stabilization phase in those receiving cabozantinib. A semi-empirical tumor model adequately predicted tumor profiles that were assumed to have a net growth rate constant that was piecewise continuous in the regions of 0-110 and 110-280 days. Emax models relating average concentration to average change in tumor size predicted that an average concentration of 79 and 58 ng/mL, resp., would yield 50% of the maximum possible tumor reduction during the first 110 days of dosing and during the subsequent 110-280 days of dosing. Simulations of tumor responses showed that daily doses of 60 mg or greater are expected to provide a similar tumor reduction Both model evaluation of observed data and simulation results suggested that the two protocol-defined cabozantinib dose redns. from 140 to 100 mg/day and from 100 to 60 mg/day are not projected to result in a marked reduction in target lesion regrowth.
IT INDEXING IN PROGRESS

REFERENCE COUNT: 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:342498 CAPLUS Full-text
DOCUMENT NUMBER: 164:380608
TITLE: Exploiting Temporal Collateral Sensitivity in Tumor Clonal Evolution
AUTHOR(S): Zhao, Boyang; Sedlak, Joseph C.; Srinivas, Raja; Creixell, Pau; Pritchard, Justin R.; Tidor, Bruce; Lauffenburger, Douglas A.; Hemann, Michael T.
CORPORATE SOURCE: Computational and Systems Biology Program, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SOURCE: Cell (Cambridge, MA, United States) (2016), 165(1), 234-246
CODEN: CELLB5; ISSN: 0092-8674
DIGITAL OBJECT ID: 10.1016/j.cell.2016.01.045
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The prevailing approach to addressing secondary drug resistance in cancer focuses on treating the resistance mechanisms at relapse. However, the dynamic nature of clonal evolution, along with potential fitness costs and cost compensations, may present exploitable vulnerabilities-a notion that we term "temporal collateral sensitivity.". Using a combined pharmacol. screen and drug resistance selection approach in a murine model of Ph+ acute lymphoblastic leukemia, we indeed find that temporal and/or persistent collateral sensitivity to non-classical BCR-ABL1 drugs arises in emergent tumor subpopulations during the evolution of resistance toward initial treatment with BCR-ABL1-targeted inhibitors. We determined the sensitization mechanism via genotypic, phenotypic, signaling, and binding measurements in combination with computational models and demonstrated significant overall survival extension in mice. Addnl. stochastic math. models and small-mol. screens extended our insights, indicating the value of focusing on evolutionary trajectories and pharmacol. profiles to identify new strategies to treat dynamic tumor vulnerabilities.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exploiting temporal collateral sensitivity in tumor clonal evolution)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(population pharmacokinetic/pharmacodynamic modeling of tumor growth kinetics in medullary thyroid cancer patients receiving cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:249149 CAPLUS Full-text
DOCUMENT NUMBER: 164:320714
TITLE: The discovery of 2-substituted phenol quinazolines as potent RET kinase inhibitors with improved KDR selectivity
AUTHOR(S): Newton, Rebecca; Bowler, Katherine A.; Burns, Emily M.; Chapman, Philip J.; Fairweather, Emma E.; Fritzl, Samantha J. R.; Goldberg, Kristin M.; Hamilton, Niall M.; Holt, Sarah V.; Hopkins, Gemma V.; Jones, Stuart D.; Jordan, Allan M.; Lyons, Amanda J.; Nikki March, H.; McDonald, Neil Q.; Maguire, Laura A.; Mould, Daniel P.; Purkiss, Andrew G.; Small, Helen F.; Stowell, Alexandra I. J.; Thomson, Graeme J.; Waddell, Ian D.; Waszkowycz, Bohdan; Watson, Amanda J.; Ogilvie, Donald J.
CORPORATE SOURCE: Cancer Research UK Manchester Institute, Drug Discovery Unit, University of Manchester, Withington, M20 4BX, UK
SOURCE: European Journal of Medicinal Chemistry (2016), 112, 20-32
CODEN: EJMCA5; ISSN: 0223-5234
DIGITAL OBJECT ID: 10.1016/j.ejmech.2016.01.039
PUBLISHER: Elsevier Masson SAS
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Deregulation of the receptor tyrosine kinase RET has been implicated in medullary thyroid cancer, a small percentage of lung adenocarcinomas,

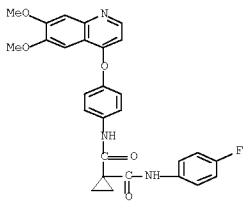
endocrine-resistant breast cancer and pancreatic cancer. There are several clin. approved multi-kinase inhibitors that target RET as a secondary pharmacol. but addnl. activities, most notably inhibition of KDR, lead to dose-limiting toxicities. There is, therefore, a clin. need for more specific RET kinase inhibitors. Herein we report our efforts towards identifying a potent and selective RET inhibitor using vandetanib 1 as the starting point for structure-based drug design. Phenolic anilinoquinazolines exemplified by 6 showed improved affinities towards RET but, unsurprisingly, suffered from high metabolic clearance. Efforts to mitigate the metabolic liability of the phenol led to the discovery that a flanking substituent not only improved the hepatocyte stability, but could also impart a significant gain in selectivity. This culminated in the identification of 36; a potent RET inhibitor with much improved selectivity against KDR.

IT 849217-68-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenol quinazolines preparation as RET kinase inhibitors with improved KDR selectivity and potential as antitumor agents)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:237680 CAPLUS Full-text

TITLE: Patterns in target-directed breast cancer research

AUTHOR(S): Torres, Sofia; Simmons, Christine; Boileau, Jean-Francois; McLeod, Deanna; Martins, Ilidio; Trudeau, Maureen

CORPORATE SOURCE: Sunnybrook Health Sciences Centre, Toronto, ON, M4N 3M5, Can.

SOURCE: SpringerPlus (2016), 5(1), 1-15
CODEN: SPRIFB; ISSN: 2193-1801

DIGITAL OBJECT ID: 10.1186/s40064-016-1736-1

PUBLISHER: Springer International Publishing AG

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB We undertake an anal. of ongoing BC targeted therapy trials registered to CT.gov to describe patterns of ongoing clin. research, highlight gaps in current research programs and identify ways of optimizing ongoing initiatives. A search of clinicaltrials.gov was conducted on Sept. 4, 2013 to identify ongoing randomized phase II and III trials of targeted therapies in BC. A total of 280 trials were analyzed, the majority conducted in either human epidermal growth factor receptor 2 (HER2)-pos. (n = 79, 28.2 %) or hormone receptor (HR)-pos. (n = 104, 37.1 %) populations. Less than half of all trials were conducted in populations selected to match the agent under investigation (n = 126, 45 %). HER2-directed therapy is the single most investigated class of targeted agents (n = 73, 26.1 %), but trials investigating anti-angiogenic agents are also common (n = 49, 17.5 %). The most common new classes of agents under investigation in HR-pos. and triple neg. (TN)/BRCA-pos. disease, are non-receptor protein kinase-inhibitors (n = 12; 11.5 %) and poly (ADP-ribose) polymerase inhibitors (n = 6; 30 %), resp. The majority of regimens combine new targeted agents with either chemotherapy (n = 164, 58.6 %) or endocrine therapy (n = 113, 40.4 %); a total of 8 trials (2.8 %) investigated peptide-drug conjugates. The most frequently utilized end-points were pathol. complete response in the neo-adjuvant setting (n = 36, 52.9 %) and time-to-event end-points in the adjuvant and advanced settings (77.3 and 72.6 %, resp.). Our findings suggest a need for more target-matched agent development, maintenance of a value-based focus in research and a need for the clin. development of agents to treat TN/BRCA-pos. and HR-pos. BC.

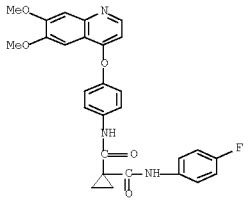
IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(patterns in target-directed breast cancer research)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:226918 CAPLUS Full-text

TITLE: Chemical Proteomics Reveals Ferrochelatase as a Common Off-target of Kinase Inhibitors

AUTHOR(S): Klaeger, Susan; Gohlke, Bjoern; Perrin, Jessica; Gupta, Vipul; Heinzlmeir, Stephanie; Helm, Dominic; Qiao, Huichao; Bergamini, Giovanna; Handa, Hiroshi; Savitski, Mikhail M.; Bantscheff, Marcus; Medard, Guillaume; Preissner, Robert; Kuster, Bernhard

CORPORATE SOURCE: Chair of Proteomics and Bioanalytics, Technical University of Munich, Freising, Germany

SOURCE: ACS Chemical Biology (2016) Ahead of Print
CODEN: ACBCCT; ISSN: 1554-8929

DIGITAL OBJECT ID: 10.1021/acschembio.5b01063

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

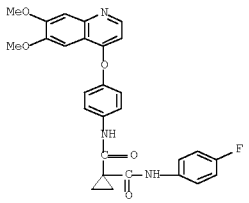
AB Many protein kinases are valid drug targets in oncol. because they are key components of signal transduction pathways. The number of clin. kinase inhibitors is on the rise, but these mols. often exhibit polypharmacol., potentially eliciting desired and toxic effects. Therefore, a comprehensive assessment of a compound's target space is desirable for a better understanding of its biol. effects. The enzyme ferrochelatase (FECH) catalyzes the conversion of protoporphyrin IX into heme and was recently found to be an off-target of the BRAF inhibitor Vemurafenib, likely explaining the phototoxicity associated with this drug in melanoma patients. This raises the question of whether FECH binding is a more general feature of kinase inhibitors. To address this, we applied a chemical proteomics approach using kinobeads to evaluate 226 clin. kinase inhibitors for their ability to bind FECH. Surprisingly, low or submicromolar FECH binding was detected for 29 of all compds. tested and isothermal dose response measurements confirmed target engagement in cells. We also show that Vemurafenib, Linsitinib, Neratinib, and MK-2461 reduce heme levels in K562 cells, verifying that drug binding leads to a loss of FECH activity. Further biochem. and docking expts. identified the protoporphyrin pocket in FECH as one major drug binding site. Since the genetic loss of FECH activity leads to photosensitivity in humans, our data strongly suggest that FECH inhibition by kinase inhibitors is the mol. mechanism triggering photosensitivity in patients. We therefore suggest that a FECH assay should generally be part of the preclin. mol. toxicol. package for the development of kinase inhibitors.

IT 849217-68-1, Cabozantinib

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical proteomics reveals ferrochelatase as a common off-target of kinase inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:224790 CAPLUS Full-text

DOCUMENT NUMBER: 164:293822

TITLE: Drug combinations to treat multiple myeloma

INVENTOR(S): Aftab, Dana T.; Lamb, Peter

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016022697	A1	20160211	WO 2015-US43825	20150805

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62033386 P 20140805

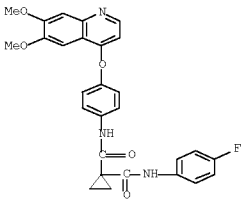
OTHER SOURCE(S): MARPAT 164:293822

AB This invention relates to the combination of a C-Met inhibitor and a proteasome inhibitor to treat cancer, particularly multiple myeloma.

IT 849217-68-1P

RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug combinations to treat multiple myeloma)

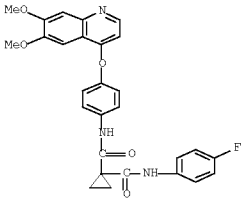
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P 1365530-43-3P 1634653-27-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug combinations to treat multiple myeloma)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

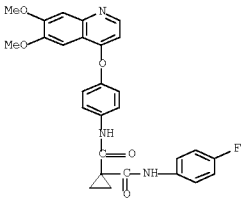


CM 2

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

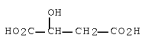
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

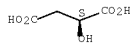
CRN 6915-15-7
CMF C4 H6 O5



IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations to treat multiple myeloma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

CRN 97-67-6
CMF C4 H6 O5

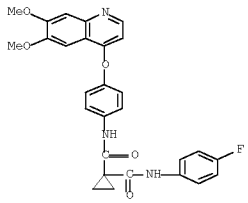
Absolute stereochemistry. Rotation (-).



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

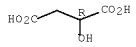
CRN 849217-68-1
CMF C28 H24 F N3 O5



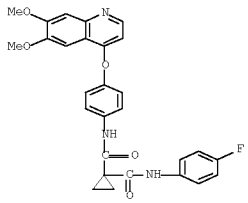
CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



RN 1634653-27-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with



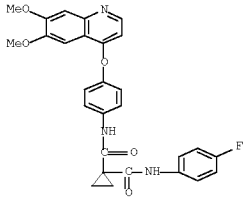
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:222043 CAPLUS Full-text
DOCUMENT NUMBER: 164:270659
TITLE: Interaction of new kinase inhibitors cabozantinib and tofacitinib with human serum alpha-1 acid glycoprotein. A comprehensive spectroscopic and molecular Docking approach
AUTHOR(S): Ajmal, Mohammad Rehan; Abdelhameed, Ali Saber; Alam, Parvez; Khan, Rizwan Hasan
CORPORATE SOURCE: Interdisciplinary Biotechnology Unit, Aligarh Muslim University, Aligarh, 202002, India
SOURCE: Spectrochimica Acta, Part A: Molecular and Biomolecular Spectroscopy (2016), 159, 199-208
CODEN: SAMCAS; ISSN: 1386-1425
DIGITAL OBJECT ID: 10.1016/j.saa.2016.01.049
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In the current study we have investigated the interaction of newly approved kinase inhibitors namely Cabozantinib (CBZ) and Tofacitinib (TFB) with human Alpha-1 acid glycoprotein (AAG) under simulated physiol. conditions using fluorescence quenching measurements, CD, dynamic light scattering and mol. docking methods. CBZ and TFB binds to AAG with significant affinity and the calculated binding constant for the drugs lie in the order of 104. With the increase in temperature the binding constant values decreased for both CBZ and TFB. The fluorescence resonance energy transfer (FRET) from AAG to CBZ and TFB suggested the fluorescence intensity of AAG was quenched by the two studied drugs via the formation of a non-fluorescent complex in the static manner. The mol. distance r value calculated from FRET is around 2 nm for both drugs, fluorescence spectroscopy data was employed for the study of thermodn. parameters, standard Gibbs free energy change at 300K was calculated as - 5.234 kcal mol- 1 for CBZ-AAG interaction and - 6.237 kcal mol- 1 for TFB-AAG interaction, standard enthalpy change and standard entropy change for CBZ-AAG interaction are - 9.553 kcal mol- 1 and - 14.618 cal mol- 1K- 1 resp. while for AAG-TFB interaction, standard enthalpy and standard entropy change was calculated as 4.019 kcal mol- 1 and 7.206 cal mol- 1K- 1 resp. Protein binding of the two drugs caused the tertiary structure

alterations. Dynamic light scattering measurements demonstrated the reduction in the hydrodynamic radii of the protein. Furthermore mol. docking results suggested the Hydrophobic interaction and hydrogen bonding were the interactive forces in the binding process of CBZ to AAG while in case of TFB only hydrophobic interactions were found to be involved, overlap of the binding site for two studied drugs on the AAG mol. was revealed by docking results.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor drugs cabozantinib and tofacitinib interaction with serum α1-acid glycoprotein)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



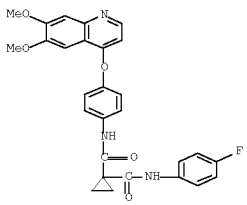
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:219788 CAPLUS Full-text
TITLE: Phase 1 dose escalation trial of the safety and pharmacokinetics of cabozantinib concurrent with temozolomide and radiotherapy or temozolomide after radiotherapy in newly diagnosed patients with high-grade gliomas
AUTHOR(S): Schiff, David; Desjardins, Annick; Cloughesy, Timothy; Mikkelsen, Thomas; Glantz, Michael; Chamberlain, Marc C.; Reardon, David A.; Wen, Patrick Y.
CORPORATE SOURCE: Department of Neurology, Neuro-Oncology Center, University of Virginia Medical Center, Charlottesville, VA, USA
SOURCE: Cancer (Hoboken, NJ, United States) (2016), 122(4), 582-587
CODEN: CANCAR; ISSN: 0008-543X
DIGITAL OBJECT ID: 10.1002/cncr.29798
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB BACKGROUND : Cabozantinib inhibits mesenchymal-epithelial transition factor (MET) and vascular endothelial growth factor receptor 2 (VEGFR2) and has demonstrated activity in patients with recurrent glioblastoma, warranting evaluation of the addition of cabozantinib to radiotherapy (RT) and temozolomide (TMZ) for patients with newly diagnosed high-grade glioma. METHODS : Cabozantinib doses of 40 mg and 60 mg were explored. Patients on the concurrent treatment arm received cabozantinib daily with standard TMZ and after RT continued cabozantinib daily with adjuvant TMZ. In the maintenance arm, patients who completed RT and ≥1 adjuvant cycle of TMZ continued adjuvant TMZ with added cabozantinib (3 schedules: days 1-28, days 1-14, or days 8-21). RESULTS : A total of 26 patients (25 with recurrent glioblastoma and 1 patient with anaplastic astrocytoma) aged 30 to 72 years were enrolled (10 to the concurrent arm and 16 to the maintenance arm). The median number of post-RT TMZ cycles was 4.5 (range, 0-14 cycles) in the concurrent arm and 5.5 (range, 1-12 cycles) in the maintenance arm. Cabozantinib at a dose of 60 mg daily was the maximum administered dose and a dose of 40 mg daily was determined to be the maximum tolerated dose for both treatment arms (schedule of days 1-28). The most frequent grade 3/4 adverse events were thrombocytopenia (31% of patients), leukopenia (27% of patients, including 5 patients with neutropenia), and deep vein thrombosis and/or pulmonary embolism (23% of patients) (adverse events were graded according to the National Cancer Institute Common Terminol. Criteria for Adverse Events [version 3.0]). CONCLUSIONS : Cabozantinib at a dose of 40 mg daily with RT plus TMZ and post-RT TMZ for patients with newly diagnosed high-grade glioma was generally well tolerated, and demonstrated no pharmacokinetic interactions with concurrent TMZ. Given the strong theor. rationale for combining anti-VEGF and anti-MET activity with standard therapy, cabozantinib at a dose of 40 mg daily warrants evaluation in combination with standard therapy for patients with newly diagnosed glioblastoma. Cancer 2016;122:582-587. © 2015 American Cancer Society.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phase 1 dose escalation trial of safety and pharmacokinetics of cabozantinib concurrent with temozolomide and radiotherapy or temozolomide after radiotherapy in newly diagnosed patients with high-grade gliomas)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 18 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:196080 CAPLUS Full-text
DOCUMENT NUMBER: 164:318691
TITLE: Hydrophilic drug phospholipid, its pharmaceutical composition and application
INVENTOR(S): Li, Xinsong; Xu, Chen; Du, Yawei; Ling, Longbing; Hou, Yongpeng
PATENT ASSIGNEE(S): Southeast University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 38pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

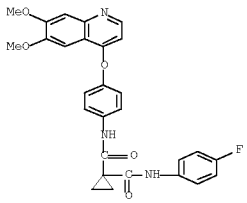
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105288648	A	20160203	CN 2015-10661316	20151014

PRIORITY APPLN. INFO.: CN 2015-10661316 20151014
OTHER SOURCE(S): MARPAT 164:318691

AB The present invention discloses a hydrophilic drug phospholipid, its pharmaceutical composition and application. the pharmaceutical composition is hydrophilic drug phospholipid or the composition of the combination drug of hydrophilic drug phospholipid and pharmacodynamic acceptable carrier, it can be liquid formulation, solid prepns., semi-solid formulation, capsules, granules, gels, injection. the pharmaceutical composition is liposomal nanoparticle formed by hydrophilic drug phospholipid or hydrophilic drug phospholipid and additives, the particle size is 10-1000 nm. the hydrophilic drug phospholipid and its liposomal nanoparticles can be used as the liquid formulations, solid prepns., semi-solid formulation, sterilized prepns. and sterile preparation, have low toxicity, can be used effective treatment for various tumors.

IT 849217-68-1, Cabozantinib
RL: NANO (Nanomaterial); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic drug phospholipid, its pharmaceutical composition and application)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 19 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:193681 CAPLUS Full-text
DOCUMENT NUMBER: 164:245721
TITLE: Use of HSP90 as marker for predicting efficacy of c-Met inhibitor in treatment of cancer
INVENTOR(S): Lee, Ji Min; Kim, Bo Gyou; Oh, Seung Ja; Kim, Kyung Ah; Lee, Saet Byoul; Hwang, Jae Woong
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 94pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

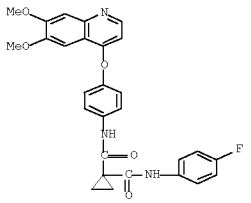
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160030559	A1	20160204	US 2015-14814278	20150730
KR 2016015076	A	20160212	KR 2014-97560	20140730

PRIORITY APPLN. INFO.: KR 2014-97560 A 20140730
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to the use of heat shock protein 90 (Hsp90) as marker for predicting an efficacy of a c-Met inhibitor, selecting a subject for application of a c-Met inhibitor, or monitoring an efficacy of a c-Met inhibitor, and a relevant method of using Hsp90 for treatment of cancer.

IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of HSP90 as marker for predicting efficacy of c-Met inhibitor in treatment of cancer)

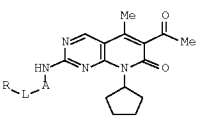
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



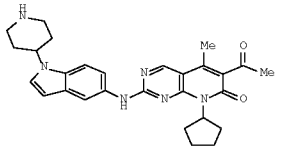
L8 ANSWER 20 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:188602 CAPLUS Full-text
DOCUMENT NUMBER: 164:277127
TITLE: Preparation of acetylcyclopentylmethylaminopyridopyrimidinone derivatives for use as CDK small-molecule inhibitors
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 117pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015597	A1	20160204	WO 2015-CN84983	20150723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294681	A	20160203	CN 2015-10439329	20150723
CN 105294682	A	20160203	CN 2015-10439488	20150723
CN 105294736	A	20160203	CN 2015-10443167	20150724

PRIORITY APPLN. INFO.: CN 2014-10361634 A 20140726
CN 2015-10076030 A 20150212
OTHER SOURCE(S): MARPAT 164:277127
GI

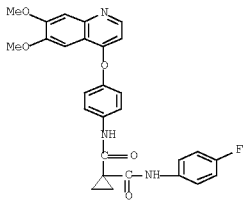


I



II

AB The invention provides substituted 2-aminopyrido[2,3-d]pyrimidin-7(8H)-one compds. of formula I, which can be used for treating inflammation and cell proliferation diseases. The compound of the invention is a powerful cyclin-dependent kinase 4 (CDK 4) or cyclin-dependent kinase 6 (CDK 6) inhibitor. Compds. of formula I wherein L is a bond, (un)substituted C0-4 alkylene, (un)substituted amino-C0-4 alkyl, (un)substituted O-C0-4 alkyl, etc.; A is bicyclic heteroaryl, and bicyclic heterocyclyl; R is H, C3-9 cycloalkyl, C1-9 heteroaryl, C2-9 heterocyclyl, etc.; and stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). The invention compds. were evaluated for their CDK inhibitory activity. From the assay, it was determined that compound II exhibited IC50 values of 6.8 nM and 29.2 nM toward CDK4 and CDK6, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of aminopyridopyrimidinone derivs. as CDK inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



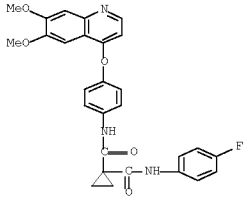
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:186216 CAPLUS Full-text
DOCUMENT NUMBER: 164:277126
TITLE: 2-Aminopyrido[2,3-d]pyrimidin-7(8H)-one derivatives as CDK inhibitors and their preparation
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015598	A1	20160204	WO 2015-CN84984	20150723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294681	A	20160203	CN 2015-10439329	20150723
CN 105294682	A	20160203	CN 2015-10439488	20150723
CN 105294736	A	20160203	CN 2015-10443167	20150724

PRIORITY APPLN. INFO.: CN 2014-10361634 A 20140726
CN 2015-10076030 A 20150212
OTHER SOURCE(S): MARPAT 164:277126
GI

AB Title compds. I [B = Ph, pyridazinyl, pyrimidinyl, pyrazinyl, etc.; L = bond, CH2, CH2CH2, CH2NHCH2, etc.; R1 and R2 independently = H, F, Cl, Br, OH, alkyl, etc.; R3 = H, heteroaryl, cycloalkyl, heterocyclyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as CDK small-mol. inhibitors. Thus, e.g., II was prepared by a multistep procedure (preparation given). Select I were evaluated in CDK4 and CDK6 enzymic inhibition activity assays, e.g., II demonstrated IC50 values of 18 nM and 35 nM, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of acetylcyclopentylmethylaminopyridopyrimidinone derivs. for use as CDK small-mol. inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

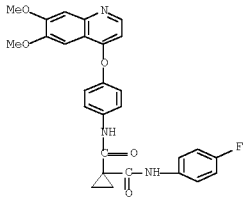
L8 ANSWER 22 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:185751 CAPLUS Full-text
DOCUMENT NUMBER: 164:277125
TITLE: 6-[2-(Pyridinyl-2-ylamino)pyrimidin-4-yl]imidazole compounds as CDK inhibitors and their preparation
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 278pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015605	A1	20160204	WO 2015-CN85036	20150724
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR,				

IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CN 105294683	A	20160203	CN 2015-10444529		20150724
CN 105294655	A	20160203	CN 2015-10447867		20150724
PRIORITY APPLN. INFO.:			CN 2014-10362374	A	20140726
			CN 2015-10015255	A	20150113

OTHER SOURCE(S): MARPAT 164:277125
GI



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

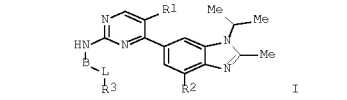
AB The invention provides substituted 6-[2-(pyridinyl-2-ylamino)pyrimidin-4-yl]imidazole compds. of formula I, which can be used for treating inflammation and cell proliferation diseases. The compound of the invention is a powerful cyclin-dependent kinase 4 (CDK 4) or cyclin-dependent kinase-6 (CDK 6) inhibitor. Compds. of formula I wherein R1 and R2 are independently H, F, Cl, Br, OH, C1-4 alkyl, etc.; L1 is a bond, (un)substituted C0-4 alkylene, (un)substituted C0-4 alkoxy-C0-4 alkylene, (un)substituted C0-4 alkylamino-C0-4 alkyl, etc.; R3 is (spiro/bridge/fused) C5-12 heterobicyclyl, C1-9 heteroaryl, C6-12 aryl, etc.; and stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). The invention compds. were evaluated for their CDK inhibitory activity (some data given).
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of [(pyridinylamino)pyrimidinyl]benzimidazoles as CDK
inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

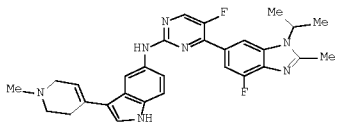
L8 ANSWER 23 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:185021 CAPLUS Full-text
DOCUMENT NUMBER: 164:264663
TITLE: Preparation of isopropylmethylbenzoimidazolylpyrimidine derivatives for use as CDK small-molecule inhibitors
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 125pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015604	A1	20160204	WO 2015-CN85034	20150724
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294683	A	20160203	CN 2015-10444529	20150724
CN 105294655	A	20160203	CN 2015-10447867	20150724
PRIORITY APPLN. INFO.:			CN 2014-10362374 A	20140726
			CN 2015-10015255 A	20150113

OTHER SOURCE(S): MARPAT 164:264663
GI

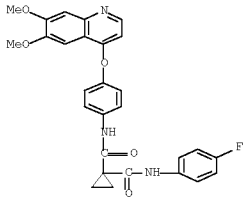


I



II

AB Title compds. I [B = Ph, pyridazinyl, pyrimidinyl, pyrazinyl, etc.; L = bond, CH2, CH2CH2, CH2NHCH2, etc.; R1 and R2 independently = H, F, Cl, Br, OH, alkyl, etc.; R3 = H, heteroaryl, cycloalkyl, heterocyclyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as CDK small-mol. inhibitors. Thus, e.g., II was prepared by amination of 6-(2-chloro-5-fluoropyrimidin-4-yl)-4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazole with 3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1H-indol-5-amine. Select I were evaluated in enzymic inhibition activity assays (data given).
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of isopropylmethylbenzoimidazolylpyrimidine derivs.
for use as CDK small-mol. inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:184907 CAPLUS Full-text
DOCUMENT NUMBER: 164:251528
TITLE: Method of preparing fluorine-18 labeled cabozantinib and its analogs
INVENTOR(S): Xu, Wei; Donnelly, David J.; Chow, Patrick L.; Henley, Benjamin J.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016019285	A1	20160204	WO 2015-US43195	20150731
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2014-62031471 P	20140731

OTHER SOURCE(S): MARPAT 164:251528
GI

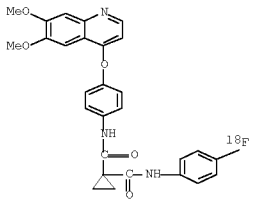
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a method of prepg. compds. of I [wherein R1 and R2 = independently alkoxy or haloalkoxy; R3 - H, F, Cl, etc.; R4 = F, 18F, Cl, etc.] such as cabozantinib II, R4 = F, and [18F]-II, R4 = 18F, comprising the reaction of 4-aminophenol with 4-chloro-6,7-dimethoxyquinoline yielding the ether intermediate, III, which undergoes coupling with 1-carboxycyclopropanecarbonyl chloride providing IV, followed by amidation of IV with 4-fluoroaniline or [18F]-4-fluoroaniline under microwave heating yielding cabozantinib or [18F]-labeled cabozantinib. [18F]-II was administered to mice implanted with U87 tumors (glioblastoma) and to tumor-free animals. PET imaging resulted in visualization of the tumors in the brains of the tumor bearing animals and little or no uptake of [18F]-II in control animals suggesting [18F]-II does not cross the blood brain barrier in tumor-free mice but has significant uptake in U87 implanted mice.

IT 1870908-84-2P
RL: DGN (Diagnostic use); IMF (Industrial manufacture); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of preparing fluorine-18 labeled cabozantinib and its analogs)

RN 1870906-64-1 CAPLUS

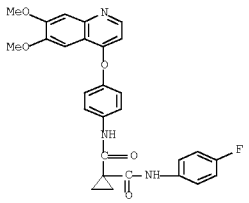
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[4-(fluoro-18F)phenyl]- (CA INDEX NAME)



IT 849217-68-1P, Cabozantinib
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of preparing fluorine-18 labeled cabozantinib and its analogs)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:145903 CAPLUS Full-text

TITLE: Integrating Murine and Clinical Trials with Cabozantinib to Understand Roles of MET and VEGFR2 as Targets for Growth Inhibition of Prostate Cancer

AUTHOR(S): Varkaris, Andreas; Corn, Paul G.; Parikh, Nila U.; Efstathiou, Eleni; Song, Jian H.; Lee, Yu-Chen; Aparicio, Ana; Hoang, Anh G.; Gaur, Sanchaika; Thorpe, Lynnelle; Maity, Sankar N.; Bar Eli, Menashe; Czerniak, Bogdan A.; Shao, Yiping; Alauddin, Mian; Lin, Sue-Hwa; Logothetis, Christopher J.; Gallick, Gary E.

CORPORATE SOURCE: Department of Genitourinary Medical Oncology, David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

SOURCE: Clinical Cancer Research (2016), 22(1), 107-121
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-0235

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

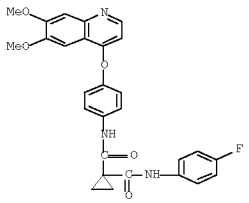
AB Purpose: We performed parallel investigations in cabozantinib-treated patients in a phase II trial and simultaneously in patient-derived xenograft (PDX) models to better understand the roles of MET and VEGFR2 as targets for prostate cancer therapy. Exptl. Design: In the clin. trial, radiog. imaging and serum markers were examined, as well as mol. markers in tumors from bone biopsies. In mice harboring PDX intrafemurally or s.c., cabozantinib effects on tumor growth, MET, PDX in which MET was silenced, VEGFR2, bone turnover, angiogenesis, and resistance were examined Results: In responsive patients and PDX, islets of viable pMET–pos. tumor cells persisted, which rapidly regrew after drug withdrawal. Knockdown of MET in PDX did not affect tumor growth in mice nor did it affect cabozantinib-induced growth inhibition but did lead to induction of FGFR1. Inhibition of VEGFR2 and MET in endothelial cells reduced the vasculature, leading to necrosis. However, each islet of viable cells surrounded a VEGFR2–neg. vessel. Reduction of bone turnover was observed in both cohorts. Conclusions: Our studies demonstrate that MET in tumor cells is not a persistent therapeutic target for metastatic castrate-resistant prostate cancer (CRPC), but inhibition of VEGFR2 and MET in endothelial cells and direct effects on osteoblasts are responsible for cabozantinib-induced tumor inhibition. However, vascular heterogeneity represents one source of primary therapy resistance, whereas induction of FGFR1 in tumor cells suggests a potential mechanism of acquired resistance. Thus, integrated cross-species investigations demonstrate the power of combining preclin. models with clin. trials to understand mechanisms of activity and resistance of investigational agents. Clin Cancer Res; 22(1); 107-21. ©2015 AACR.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib treatment-induced inhibition of VEGFR2, FGFR1 and MET signaling which responsible for tumor inhibition in in-vitro human prostate cancer cells and in in-vivo mouse model)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2016:145922 CAPLUS Full-text

TITLE: A Phase II Trial of the Multitargeted Tyrosine Kinase Inhibitor Lenvatinib (E7080) in Advanced Medullary Thyroid Cancer

AUTHOR(S): Schlumberger, Martin; Jarzab, Barbara; Cabanillas, Maria E.; Robinson, Bruce; Pacini, Furio; Ball, Douglas W.; McCaffrey, Judith; Newbold, Kate; Allison, Roger; Martins, Renato G.; Licitra, Lisa F.; Shah, Manisha H.; Bodenner, Donald; Elisei, Rossella; Burmeister, Lynn; Funahashi, Yasuhiro; Ren, Min; O'Brien, James P.; Sherman, Steven I.

CORPORATE SOURCE: Department of Nuclear Medicine and Endocrine Oncology, Institut Gustave-Roussy and University Paris-Sud, Villejuif, Fr.

SOURCE: Clinical Cancer Research (2016), 22(1), 44-53
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-1127

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

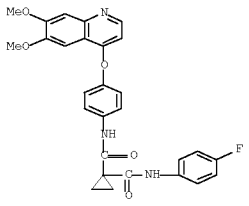
AB Purpose: Pos. results of phase I studies evaluating lenvatinib in solid tumors, including thyroid cancer, prompted a phase II trial in advanced medullary thyroid carcinoma (MTC). Exptl. Design: Fifty-nine patients with unresectable progressive MTC per Response Evaluation Criteria In Solid Tumors (RECIST) v1.0 within the prior 12 mo received lenvatinib (24-mg daily, 28-day cycles) until disease progression, unmanageable toxicity, withdrawal, or death. Prior anti–VEGFR therapy was permitted. The primary endpoint was objective response rate (ORR) by RECIST v1.0 and independent imaging review. Results: Lenvatinib ORR was 36% [95% confidence interval (CI), 24%–49%]; all partial responses. ORR was comparable between patients with (35%) or without (36%) prior anti-VEGFR therapy. Disease control rate (DCR) was 80% (95% CI, 67%–89%); 44% had stable disease. Among responders, median time to response (TTR) was 3.5 mo (95% CI, 1.9–3.7). Median progression-free survival (PFS) was 9.0 mo (95% CI, 7.0–not evaluable). Common toxicity criteria grade 3/4 treatment-emergent adverse events included diarrhea (14%), hypertension (7%), decreased appetite (7%), fatigue, dysphagia, and increased alanine aminotransferase levels (5% each). Ret proto-oncogene status did not correlate with outcomes. Low baseline levels of angiopoietin-2, hepatocyte growth factor, and IL8 were associated with tumor reduction and prolonged PFS. High baseline levels of VEGF, soluble VEGFR3, and platelet-derived growth factor BB, and low baseline levels of soluble Tie-2, were associated with tumor reduction Conclusions: Lenvatinib had a high ORR, high DCR, and a short TTR in patients with documented progressive MTC. Toxicities were managed with dose modifications and medications. Clin Cancer Res; 22(1); 44-53. ©2015 AACR.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(efficacy and safety of multitargeted tyrosine kinase inhibitor lenvatinib was evaluated for treatment of advanced medullary thyroid cancer in patients)

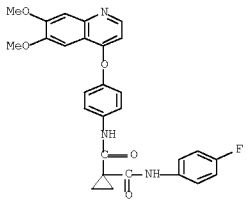
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

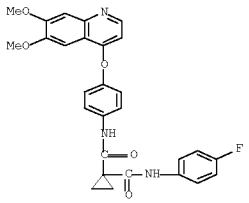
L8 ANSWER 27 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:126388 CAPLUS Full-text
DOCUMENT NUMBER: 164:244992
TITLE: AutoT&T v.2: An Efficient and Versatile Tool for Lead Structure Generation and Optimization
AUTHOR(S): Li, Yan; Zhao, Zhixiong; Liu, Zhihai; Su, Minyi; Wang, Renxiao
CORPORATE SOURCE: State Key Laboratory of Bioorganic and Natural Products Chemistry, Collaborative Innovation Center of Chemistry for Life Sciences, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Journal of Chemical Information and Modeling (2016), 56(2), 435-453
CODEN: JCISD8; ISSN: 1549-9596
DIGITAL OBJECT ID: 10.1021/acs.jcim.5b00691
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In structure-based drug design, automated de novo design methods are helpful tools for lead discovery as well as lead optimization. In a previous study the authors reported a new de novo design method, namely, Automatic Tailoring and Transplanting (AutoT&T). It overcomes some intrinsic problems in conventional fragment-based buildup methods. In this study, the authors describe an upgraded version, namely, AutoT&T2. Structural operations conducted by AutoT&T2 have been largely optimized by introducing several new algorithms. As a result, its overall speed in multiround optimization jobs has been improved by a few thousand fold. With this improvement, it is now practical to conduct structural crossover among multiple lead mols. using AutoT&T2. Three different test cases are described in this study that demonstrate the new features and versatile applications of AutoT&T2. The AutoT&T2 software suite is available to the public. Besides, a Web portal for running AutoT&T2 online is provided at http://www.sioc-ccbg.ac.cn/software/att2 for testing.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AutoT&T v.2 is efficient and versatile tool for lead structure generation and optimization)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:125847 CAPLUS Full-text
TITLE: Research advances of FLT3 inhibitors in treatment of acute myeloid leukemia
AUTHOR(S): Li, Tonghui; Guo, Hao; Lu, Tao; Wang, Yue; Lu, Shuai; Tang, Weifang
CORPORATE SOURCE: Department of Organic Chemistry, China Pharmaceutical University, Nanjing, 211198, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2015), 46(2), 153-161
CODEN: ZHYXE9; ISSN: 1000-5048
DIGITAL OBJECT ID: 10.11665/j.issn.1000-5048.20150203
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 69 ref. is given on research advances of FLT3 inhibitors in treatment of acute myeloid leukemia. Acute myeloid leukemia (AML) is one of the most common acute leukemia in adults. Those patients with FLT3 mutations have a particularly poor prognosis. Recently, the emergence of a variety of targeted inhibitors has shown the capability of suppressing FLT3 signaling in vivo, which provided a new way to treat AML. In this paper, we reviewed those inhibitors based on their structures, which include indolone-related inhibitors, indolocarbazo-related inhibitors, benzimidazole/benzopyrazole-related inhibitors, quinoline/quinoxaline/quinazoline-related inhibitors, tricyclic inhibitors, pyrimidine-related inhibitors and others.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(research advances of FLT3 inhibitors in treatment of acute myeloid leukemia)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

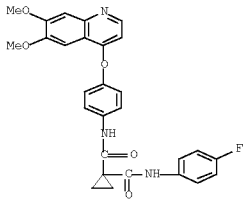


L8 ANSWER 29 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:118025 CAPLUS Full-text
DOCUMENT NUMBER: 164:355574
TITLE: Novel polymorph's of cabozantinib-S-malate
INVENTOR(S): Jetti, Ramakoteswara Rao; Indukuri, Anjaneyaraju; Punde, Dnyandeo; Bohra, Chandersingh; Gadakar, Mahesh Kumar; Gore, Vinayak
PATENT ASSIGNEE(S): Mylan Laboratories Ltd., India
SOURCE: Indian Pat. Appl., 54pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2014CH02561	A	20160115	IN 2014-CH2561	20140523
WO 2015177758	A1	20151126	WO 2015-IB53765	20150522

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

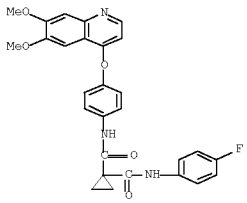
PRIORITY APPLN. INFO.: IN 2014-CH2561 A 20140523
AB The present disclosure provides novel cryst. forms of cabozantinib (S)-malate, designated as form-M1, M2, M3 and M4 and novel crystalline forms of cabozantinib free base, form-M1, M2 and M3 and methods of their production The present disclosure also provides processes for the preparation of crystalline cabozantinib (S)-malate form N-1.
IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(novel polymorph's of cabozantinib-S-malate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3, Cabozantinib (S)-malate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(novel polymorph's of cabozantinib-S-malate)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

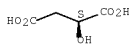
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

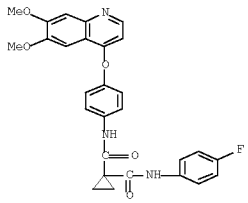
Absolute stereochemistry. Rotation (-).



L8 ANSWER 30 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:117601 CAPLUS Full-text
DOCUMENT NUMBER: 164:421210
TITLE: A photoactivable multi-inhibitor nanoliposome for tumour control and simultaneous inhibition of treatment escape pathways
AUTHOR(S): Spring, Bryan Q.; Bryan Sears, R.; Zheng, Lei Zak; Mai, Zhiming; Watanabe, Reika; Sherwood, Margaret E.; Schoenfeld, David A.; Pogue, Brian W.; Pereira, Stephen P.; Villa, Elizabeth; Hasan, Tayyaba
CORPORATE SOURCE: Wellman Center for Photomedicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Nature Nanotechnology (2016), 11(4), 378-387
CODEN: NNAABX; ISSN: 1748-3387
DIGITAL OBJECT ID: 10.1038/nnano.2015.311
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Nanoscale drug delivery vehicles can facilitate multimodal therapies of cancer by promoting tumor-selective drug release. However, few are effective because cancer cells develop ways to resist and evade treatment. Here, we introduce a photoactivable multi-inhibitor nanoliposome (PMIL) that imparts light-induced cytotoxicity in synchrony with a photoinitiated and sustained release of inhibitors that suppress tumor regrowth and treatment escape signaling pathways. The PMIL consists of a nanoliposome doped with a photoactivable chromophore (benzoporphyrin derivative, BPD) in the lipid bilayer, and a nanoparticle containing cabozantinib (XL184)-a multikinase inhibitor-encapsulated inside. Near-IR tumor irradiation, following i.v. PMIL administration, triggers photodynamic damage of tumor cells and microvessels, and simultaneously initiates release of XL184 inside the tumor. A single PMIL treatment achieves prolonged tumor reduction in two mouse models and suppresses metastatic escape in an orthotopic pancreatic tumor model. The PMIL offers new prospects for cancer therapy by enabling spatiotemporal control of drug release while reducing systemic drug exposure and associated toxicities.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photoactivable multi-inhibitor nanoliposome for tumor control and simultaneous inhibition of treatment escape pathways)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

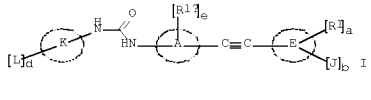


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

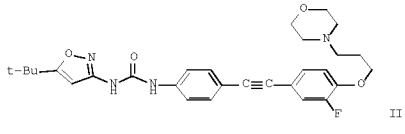
L8 ANSWER 31 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2016:112224 CAPLUS Full-text
DOCUMENT NUMBER: 164:213920
TITLE: Preparation of substituted urea derivatives as protein kinase modulators
INVENTOR(S): Cheng, Changchung; Zhang, Yingjun; Liu, Bing; Long, Bohua; Chen, Yu; Cheng, Zhixin
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 182pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016008433	A1	20160121	WO 2015-CN84253	20150716
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105272930	A	20160127	CN 2015-10422604	20150716
PRIORITY APPLN. INFO.:			CN 2014-10342509 A	20140717

OTHER SOURCE(S): MARPAT 164:213920
GI



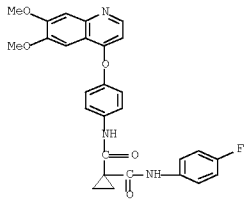
I



II

AB The title compds. I [ring A and ring E = (independently) C6-10 aryl or C1-12 heteroaryl; each J = G(CH2)nR2;each G = (independently) O, S(O)t, S, C(O), etc.; R1, R1a = H, F, Cl, Br, etc.; R2 = alkyl, cycloalkyl, heterocyclyl, etc.; ring K = 5-6 membered heteroaryl;each L = (independently) NH2, NO2, alkylthio, alkyl, etc.; each a and e = (independently) 0-4; each n, d and b = (independently) 1-4; and each t = (independently) 0-2], useful for preventing, managing, treating or lessening a proliferative disease, and modulating the activity of protein kinase, were prepared and claimed. E.g., a multi-step synthesis of the urea II, starting from 2-fluoro-4-iodophenol and N-(3-chloropropyl)morpholine, was described. Exemplified compds. I were tested for their activity against FLT3 kinase (data given for representative compds. I). Pharmaceutical compns. comprising compound I, alone or in combination with other therapeutic agents, were disclosed.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. as protein kinase modulators)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



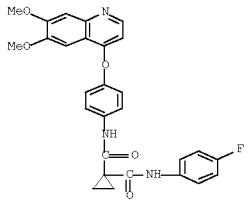
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:2073656 CAPLUS Full-text
TITLE: Hepatocyte growth factor and Met in drug discovery
AUTHOR(S): Sakai, Katsuya; Aoki, Shunsuke; Matsumoto, Kunio
CORPORATE SOURCE: Division of Tumor Dynamics and Regulation, Cancer Research Institute, Kanazawa University, Kanazawa, 920-1192, Japan
SOURCE: Journal of Biochemistry (2015), 157(5), 271-284
CODEN: JOBIAO; ISSN: 0021-924X
DIGITAL OBJECT ID: 10.1093/jb/mvv027
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activation of the hepatocyte growth factor (HGF) -Met pathway evokes dynamic biol. responses that support the morphogenesis, regeneration and survival of cells and tissues. A characterization of conditional Met knockout mice indicates that the HGF-Met pathway plays important roles in the regeneration, protection and homeostasis of cells such as hepatocytes, renal tubular cells and neurons. Preclin. studies in disease models have indicated that recombinant HGF protein and expression plasmid for HGF are biol. drug candidates for the treatment of patients with diseases or injuries that involve impaired tissue function. The phase-I and phase-I/II clin. trials of the intrathecal administration of HGF protein for the treatment of patients with amyotrophic lateral sclerosis and spinal cord injury, resp., are ongoing. Biol. actions of HGF that promote the dynamic movement, morphogenesis and survival of cells also closely participate in invasion-metastasis and resistance to the mol.-targeted drugs in tumor cells. Different types of HGF-Met pathway inhibitors are now in clin. trials for treatment of malignant tumors. Basic research on HGF and Met has lead to drug discoveries in regenerative medicine and tumor biol.

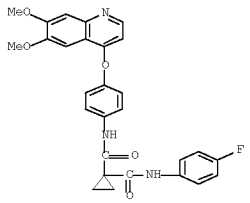
IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hepatocyte growth factor and Met in drug discovery)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 33 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:2060169 CAPLUS Full-text
TITLE: Cabozantinib Inhibits Abiraterone's Upregulation of IGFIR Phosphorylation and Enhances Its Anti-Prostate Cancer Activity
AUTHOR(S): Wang, Xiaodong; Huang, Ying; Christie, Amanda; Bowden, Michaela; Lee, Gwo-Shu Mary; Kantoff, Philip W.; Sweeney, Christopher J.
CORPORATE SOURCE: Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SOURCE: Clinical Cancer Research (2015), 21(24), 5578-5587
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-0824
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Abiraterone improves the overall survival of men with metastatic castration-resistant prostate cancer. However, de novo or adaptive resistance to abiraterone limits its activity. Rational combinations of drugs with different mechanisms of action that overcome resistance mechanisms may improve the efficacy of therapy. To that end, we studied the mol. and phenotypic effects of the combination of cabozantinib plus abiraterone. Exptl. Design: Three prostate cancer cell lines were used to interrogate the in vitro mol. and antiproliferative effects of the single agents and combination of cabozantinib and abiraterone. The in vivo impact of the combination was assessed using the LAPC4-CR xenograft mouse model. Results: In vitro proliferation studies demonstrated single-agent doses between 2 μmol/L and 10 μmol/L for abiraterone and cabozantinib inhibit prostate cancer cell proliferation in a dose-dependent manner, and the anticancer activity of abiraterone is enhanced when combined with cabozantinib. In vivo LAPC4-CR xenograft mouse studies also showed that cabozantinib can improve the antitumor activity of abiraterone. Cabozantinib, a multiple receptor tyrosine kinase inhibitor, enhances the ability of abiraterone to inhibit AR activity in a cell line-dependent manner. In addition, our cell line studies demonstrate abiraterone-stimulated insulin-like growth factor I receptor (IGFIR) phosphorylation with downstream activation of MEK1/2 and ERK1/2, and that this potential adaptive resistance mechanism was inhibited by cabozantinib. Conclusions: Cabozantinib can enhance the efficacy of abiraterone by blocking multiple compensatory survival mechanisms, including IGFIR activation, and supports the assessment of the combination in a clin. trial. Clin Cancer Res; 21(24); 5578-87. ©2015 AACR.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib inhibits abiraterone's upregulation of IGFIR phosphorylation and enhances its anti-prostate cancer activity in LAPC4-CR xenograft mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

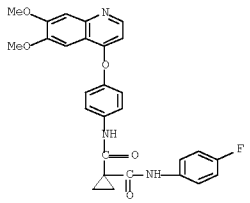
L8 ANSWER 34 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:2059342 CAPLUS Full-text
DOCUMENT NUMBER: 164:119066
TITLE: Methods and devices for treating posterior ocular disorders
INVENTOR(S): Noronha, Glenn; Brooks, Christopher John; Andino, Rafael Victor; Patel, Samirkumar; White, Daniel
PATENT ASSIGNEE(S): Clearside Biomedical, Inc., USA
SOURCE: PCT Int. Appl., 175pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015195842	A1	20151223	WO 2015-US36299	20150617

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.:
US 2014-62013209 P 20140617
US 2014-62018148 P 20140627
US 2014-62063792 P 20141014
US 2015-61155367 P 20150430
US 2015-62156802 P 20150504

AB The present invention relates to a methods and devices for treating uveitis, macular edema associated with uveitis and macular edema associated with retinal vein occlusion in a human subject in need thereof. In certain aspects, devices provided herein include a medicament container defining a lumen configured to contain a medicament, a distal end portion of the medicament container including a coupling portion configured to be removably coupled to a needle assembly, a proximal end portion of the medicament container including a flange and a longitudinal shoulder; a piston assembly including a distal end portion movably disposed within the lumen of the medicament container; and a handle coupled to a proximal end portion of the piston assembly.
IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(methods and devices for treating posterior ocular disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 35 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:2015841 CAPLUS Full-text
DOCUMENT NUMBER: 164:99265
TITLE: Anti-human Tumor endothelial marker TEM8 antibodies and other molecularly targeted agent for combination therapy of cancer
INVENTOR(S): Saha, Saurabh; Zhang, Xiaoyan M.; Dimitrov, Dimiter; Zhu, Zhongyu; St. Croix, Brad; Zudaire, Enrique
PATENT ASSIGNEE(S): Biomed Valley Discoveries, Inc., USA; Untied States Dept. of Health and Human Services
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015191610	A2	20151217	WO 2015-US34941	20150609
WO 2015191610	A3	20160204		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.:
US 2014-62009371 P 20140609

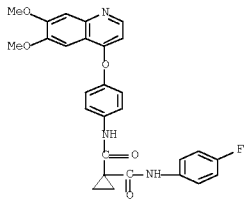
AB The present invention provides, inter alia, methods for treating or ameliorating the effects of a disease, such as cancer, in a subject. The methods include: administering to a subject in need thereof (a) a

therapeutically effective amount of a molecularly targeted agent; and (b) a therapeutically effective amount of a monoclonal antibody or antigen binding fragment thereof, wherein the monoclonal antibody contains: (i) a heavy chain variable region (VH), which includes an amino acid sequence selected from SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, and SEQ ID NO:7; and (ii) a light chain variable region (VL), which includes an amino acid sequence selected from SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8. Compns., including pharmaceutical compns., and kits for treating diseases, such as cancer, are also provided herein.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human Tumor endothelial marker TEM8 antibodies and other molecularly targeted agent for combination therapy of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 36 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:2008346 CAPLUS Full-text

DOCUMENT NUMBER: 164:136379

TITLE: Bioluminescent kinase strips: A novel approach to targeted and flexible kinase inhibitor profiling

AUTHOR(S): Hennek, J.; Alves, J.; Yao, E.; Goueli, S. A.; Zegzouti, H.

CORPORATE SOURCE: R&D Department, Promega Corporation, Madison, WI, 53711, USA

SOURCE: Analytical Biochemistry (2016), 495, 9-20
CODEN: ANBCA2; ISSN: 0003-2697

DIGITAL OBJECT ID: 10.1016/j.ab.2015.11.007

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)

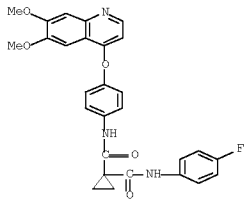
LANGUAGE: English

AB In addn. to target efficacy, drug safety is a major requirement during the drug discovery process and is influenced by target specificity. Therefore, it is imperative that every new drug candidate be profiled against various liability panels that include protein kinases. Here, an effective methodol. to streamline kinase inhibitor profiling is described. An accessible standardized profiling system for 112 protein kinases covering all branches of the kinome was developed. This approach consists of creating different sets of kinases and their corresponding substrates in multi-tube strips. The kinase stocks are pre-standardized for optimal kinase activity and used for inhibitor profiling using a bioluminescent ADP detection assay. The authors show that these strips can routinely generate inhibitor selectivity profiles for small or broad kinase family panels. Lipid kinases were also assembled in strip format and profiled together with protein kinases. The authors identified two specific PI3K inhibitors that have off-target effects on CK2 that were not reported before and would have been missed if compds. were not profiled against lipid and protein kinases simultaneously. To validate the accuracy of the data generated by this method, the authors confirmed that the inhibition potencies observed are consistent with published values produced by more complex technologies such as radioactivity assays.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioluminescent kinase strips as novel approach to targeted and flexible kinase inhibitor profiling)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 37 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1965343 CAPLUS Full-text

TITLE: Repurposing of anticancer drugs: in vitro and in vivo activities against Schistosoma mansoni

AUTHOR(S): Cowan, Noemi; Keiser, Jennifer

CORPORATE SOURCE: Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, CH-4002, Switz.

SOURCE: Parasites & Vectors (2015), 8, 1-9
CODEN: PVAEAK; ISSN: 1756-3305

DIGITAL OBJECT ID: 10.1186/s13071-015-1023-y

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

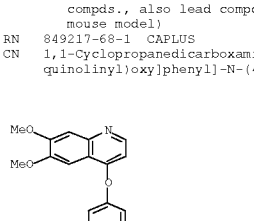
AB Background: Drug discovery for the neglected tropical disease schistosomiasis has a high priority. Anticancer drugs, especially protein kinase inhibitors, might serve as a starting point for drug discovery owing to the importance of protein kinases in helminth growth and development. Furthermore, the Schistosoma mansoni genome encodes several genes for targets of drugs marketed for human use, including several anticancer drugs. Methods: In this study, we screened the approved oncol. drug set of the National Cancer Institute's Developmental Therapeutic Program for antischistosomal activity. Drugs were tested in vitro against the larval and adult stage of S. mansoni. IC50 values and albumin binding were determined for active compds. Lead compds. were tested in the chronic S. mansoni mouse model. Results: Eleven of the 114 compds. tested revealed IC50 values ≤ 10 μM against both S. mansoni stages. Five of these lost activity against adult S. mansoni in the presence of serum albumin. Of 6 compds. studied in vivo, the highest activity was observed from two kinase inhibitors trametinib, and vandetanib, which reduced worm burden by 63.6 and 48.1 % resp., after a single oral dose of 400 mg/kg body weight Conclusion: Our study has confirmed that oncol. drugs possess antischistosomal activity. There is space for further investigation, including elucidation of the mechanisms of action of schistosome-active cancer drugs, application of different treatment courses, and structure-activity relationship studies for improving drug potency.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro drug testing against larval and adult stage of Schistosoma mansoni and determination of IC50 values and albumin binding for active compds., also lead compds. were tested in chronic Schistosoma mansoni mouse model)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 38 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1955534 CAPLUS Full-text

TITLE: Defining the Schistosoma haematobium kinome enables the prediction of essential kinases as anti-schistosome drug targets

AUTHOR(S): Stroehlein, Andreas J.; Young, Neil D.; Jex, Aaron R.; Sternberg, Paul W.; Tan, Patrick; Boag, Peter R.; Hofmann, Andreas; Gasser, Robin B.

CORPORATE SOURCE: Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Parkville, Australia

SOURCE: Scientific Reports (2015), 5, 17759
CODEN: SRCEC3; ISSN: 2045-2322

DIGITAL OBJECT ID: 10.1038/srep17759

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

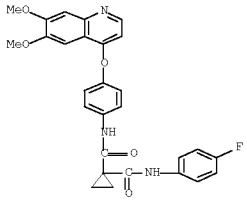
AB The blood fluke Schistosoma haematobium causes urogenital schistosomiasis, a neglected tropical disease (NTD) that affects more than 110 million people. Treating this disease by targeted or mass administration with a single chemical, praziquantel, carries the risk that drug resistance will develop in this pathogen. Therefore, there is an imperative to search for new drug targets in S. haematobium and other schistosomes. In this regard, protein kinases have potential, given their essential roles in biol. processes and as targets for drugs already approved by the US Food and Drug Administration (FDA) for use in humans. In this context, we defined here the kinome of S. haematobium using a refined bioinformatic pipeline. We classified, curated and annotated predicted kinases, and assessed the developmental transcription profiles of kinase genes. Then, we prioritised a panel of kinases as potential drug targets and inferred chems. that bind to them using an integrated bioinformatic pipeline. Most kinases of S. haematobium are very similar to those of its congener, S. mansoni, offering the prospect of designing chems. that kill both species. Overall, this study provides a global insight into the kinome of S. haematobium and should assist the repurposing or discovery of drugs against schistosomiasis.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(defining Schistosoma haematobium kinome enables prediction of essential kinases as anti-schistosome drug targets)

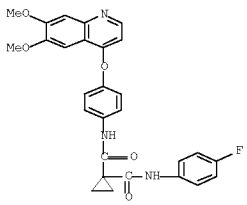
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

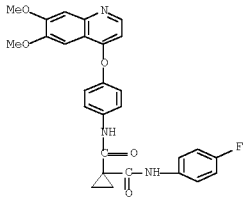
L8 ANSWER 39 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1916188 CAPLUS Full-text
TITLE: Clinical observation of liver cancer patients treated with axitinib and cabozantinib after failed sorafenib treatment: a case report and literature review
AUTHOR(S): Zhang, Bin; Zhang, Xia; Zhou, Tao; Liu, Jiwei
CORPORATE SOURCE: Department of Oncology, The First Affiliated Hospital of Dalian Medical University, Dalian, Peop. Rep. China
SOURCE: Cancer Biology & Therapy (2015), 16(2), 215-218
CODEN: CBTAAO; ISSN: 1555-8576
DIGITAL OBJECT ID: 10.4161/15384047.2014.962318
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Hepatocellular carcinoma (HCC) is a major pathol. type of primary liver cancer. Sorafenib has demonstrated definite efficacy in targeted therapy for HCC. However, when treatment with sorafenib fails, suitable drugs must be found for further treatment. This article reports a case of an HCC patient who was treated with angiogenesis inhibitor axitinib and c-Met inhibitor cabozantinib following treatment with sorafenib. The report focuses on clin. treatment and toxicity. Rational application of targeted therapy is also explored.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(clin. observation of liver cancer patients treated with axitinib and cabozantinib after failed sorafenib treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 41 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1892326 CAPLUS Full-text
DOCUMENT NUMBER: 163:709974
TITLE: Novel polymorphs of cabozantinib (S)-malate and cabozantinib free base
INVENTOR(S): Jetti, Ramakoteswara Rao; Indukuri, Anjaneyaraju; Punde, Dnyandeo; Bohra, Chandersingh; Gadakar, Mahesh Kumar; Gore, Vinayak
PATENT ASSIGNEE(S): Mylan Laboratories Ltd., India
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

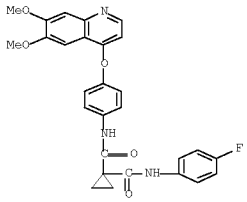
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015177758	A1	20151126	WO 2015-IB53765	20150522
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
IN 2014CH02561	A	20160115	IN 2014-CH2561	20140523



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 40 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1897715 CAPLUS Full-text
TITLE: Cabozantinib: an orphan drug for thyroid cancer
AUTHOR(S): Viola, D.; Cappagli, V.; Matrone, A.; Mazzeo, S.; Elisei, R.
CORPORATE SOURCE: Endocrine Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56124, Italy
SOURCE: Expert Opinion on Orphan Drugs (2015), 3(12), 1469-1477
CODEN: EOODAJ; ISSN: 2167-8707
DIGITAL OBJECT ID: 10.1517/21678707.2015.1112789
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Until recently, no therapeutic options were available for the treatment of advanced medullary thyroid cancer (MTC). Cabozantinib (XL184) is a novel tyrosine kinase inhibitor (TKI) that inhibits several tyrosine kinase receptors, in particular those coded by MET, VEGFR-2 and RET oncogenes that are considered to be involved in the pathogenesis of MTC. This article provides an overview of the phase I and III trials that demonstrated the efficacy of cabozantinib in two cohorts of advanced MTC patients who were naive or previously treated with other TKIs. The benefits in terms of progression-free survival (PFS), overall survival (OS) and the demog. clin. and mutational status of the two cohorts of MTC patients are reported and discussed. The possibility to have a therapeutic option for the treatment of patients with advanced and progressive MTC and, in particular, the evidence that the drug can be active also in those patients who already experienced disease progression while taking another TKI is a great opportunity as demonstrated in cases treated with cabozantinib after vandetanib such as the one reported in this paper.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib, an orphan drug for thyroid cancer)

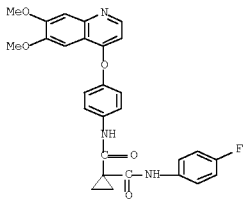
PRIORITY APPLN. INFO.: IN 2014-CH2561 A 20140523
AB The present disclosure provides novel cryst. forms of cabozantinib (S)-malate, designated as form-M1, M2, M3 and M4 and novel crystalline forms of cabozantinib free base, form-M1, M2 and M3 and methods of their production The present disclosure also provides processes for the preparation of crystalline cabozantinib (S)-malate form N-1. Formula (I).
IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(novel polymorphs of cabozantinib (S)-malate and cabozantinib free base)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P, Cabozantinib (S)-malate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(novel polymorphs of cabozantinib (S)-malate and cabozantinib free base)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

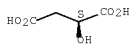
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CM 2

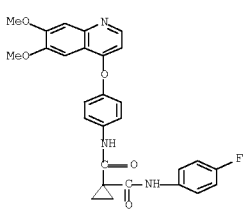
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

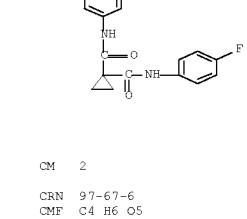


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 42 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1833484 CAPLUS Full-text
DOCUMENT NUMBER: 164:370558
TITLE: Identification of Bone-Derived Factors Conferring De Novo Therapeutic Resistance in Metastatic Prostate Cancer
AUTHOR(S): Lee, Yu-Chen; Lin, Song-Chang; Yu, Guoyu; Cheng, Chien-Jui; Liu, Bin; Liu, Hsuan-Chen; Hawke, David H.; Parikh, Nila U.; Varkaris, Andreas; Corn, Paul; Logothetis, Christopher; Satcher, Robert L.; Yu-Lee, Li-Yuan; Gallick, Gary E.; Lin, Sue-Hwa
CORPORATE SOURCE: Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Cancer Research (2015), 75(22), 4949-4959
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-15-1215
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Resistance to currently available targeted therapies significantly hampers the survival of patients with prostate cancer with bone metastasis. Here we demonstrate an important resistance mechanism initiated from tumor-induced bone. Studies using an osteogenic patient-derived xenograft, MDA-PCa-118b, revealed that tumor cells resistant to cabozantinib, a Met and VEGFR-2 inhibitor, reside in a "resistance niche" adjacent to prostate cancer-induced bone. We performed secretome anal. of the conditioned medium from tumor-induced bone to identify proteins (termed "osteocrines") found within this resistance niche. In accordance with previous reports demonstrating that activation of integrin signaling pathways confers therapeutic resistance, 27 of the 90 osteocrines identified were integrin ligands. We found that following cabozantinib treatment, only tumor cells positioned adjacent to the newly formed woven bone remained viable and expressed high levels of pFAK-Y397 and pTalin-S425, mediators of integrin signaling. Accordingly, treatment of C4-2B4 cells with integrin ligands resulted in increased pFAK-Y397 expression and cell survival, whereas targeting integrins with FAK inhibitors PF-562271 or defactinib inhibited FAK phosphorylation and reduced the survival of PC3-mm2 cells. Moreover, treatment of MDA-PCa-118b tumors with PF-562271 led to decreased tumor growth, irresp. of initial tumor size. Finally, we show that upon treatment cessation, the combination of PF-562271 and cabozantinib delayed tumor recurrence in contrast to cabozantinib treatment alone. Our studies suggest that identifying paracrine de novo resistance mechanisms may significantly contribute to the generation of a broader set of potent therapeutic tools that act combinatorially to inhibit metastatic prostate cancer. Cancer Res; 75(22); 4949-59. ©2015 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(paracrine de novo resistance factors significantly contribute to generation of bone formation, therapeutic resistance and inhibit metastatic prostate cancer cells and in human and mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



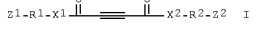
L8 ANSWER 43 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1818418 CAPLUS Full-text
TITLE: Advances in receptor tyrosine kinase inhibitors taking c-Met as anti-tumor target
AUTHOR(S): Zhang, Yuan; Cheng, Yulan; Zhou, Jinpei; Zhang, Huibin
CORPORATE SOURCE: Dept. of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2015), 46(1), 16-27
CODEN: ZHYXE9; ISSN: 1000-5048
DIGITAL OBJECT ID: 10.11665/j.issn.1000-5048.20150102
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 52 refs. on the c-Met signaling pathway and the resistance of kinase inhibitors caused by the cross-talk between c-Met and other membrane receptors and the progress of single-target and multi-target c-Met inhibitors.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reviewing the advances in receptor tyrosine kinase inhibitors taking c-Met as anti-tumor target)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



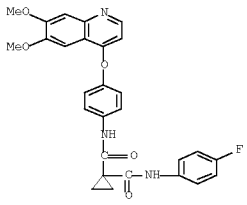
L8 ANSWER 44 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1805828 CAPLUS Full-text
DOCUMENT NUMBER: 163:694481
TITLE: Acetylenedicarboxyl linkers and their uses in specific conjugation of a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: U.S. Pat. Appl. Publ., 80pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150322155	A1	20151112	US 2015-14799666	20150715
PRIORITY APPLN. INFO.:			US 2015-14799666	20150715

OTHER SOURCE(S): CASREACT 163:694481; MARPAT 163:694481
GI



AB Provided are novel acetylenedicarboxyl linkers used for the specific conjugation of compds./cytotoxic agents to a cell-binding mol., through bridge linking pairs of thiols on the cell-binding mol. Also provided are methods of making such linkers, and of using such linkers in making homogeneous conjugates, as well as of application of the conjugates in treatment of cancers, infections and autoimmune disorders. Particularly provided is a bridge linker compound of the Formula (I), wherein:The acetylenedicarboxyl group is capable of reacting with a pair of sulfur atoms of the cell-binding agent; Z1 and Z2 are the same or different a function group that enables to react with a cytotoxic drug; R1 and R2 are the same or different linear alkyl; X1 and X2 are independently selected from NH, N(R3), O, S or CH2; R3 is H, linear alkyl.
IT 849217-68-1, Cabozan-tinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-therapy with; acetylenedicarboxyl linkers and their uses in specific conjugation of cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 45 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1783974 CAPLUS Full-text
TITLE: New molecularly targeted therapies against advanced hepatocellular carcinoma: From molecular pathogenesis to clinical trials and future directions

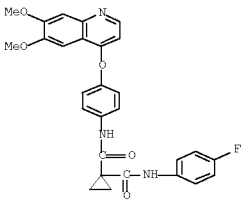
AUTHOR(S): Chuma, Makoto; Terashita, Katsumi; Sakamoto, Naoya
CORPORATE SOURCE: Department of Gastroenterology and Hepatology, Hokkaido University, Sapporo, Japan
SOURCE: Hepatology Research (2015), 45(10), E1-E11
CODEN: HPRSFM; ISSN: 1386-6346
DIGITAL OBJECT ID: 10.1111/hepr.12459
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

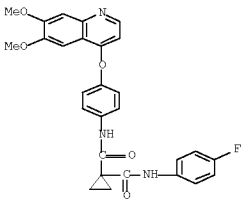
AB A review. Hepatocellular carcinoma (HCC) can be lethal due to its aggressive course and lack of effective systemic therapies for advanced disease. Sorafenib is the only systemic therapy that has demonstrated an overall survival benefit in patients with advanced HCC, and new agents for treatment of advanced HCC are needed. The multiple pathways involved in HCC oncogenesis, proliferation and survival provide many opportunities for the development of molecularly targeted therapies. Mol. targets of interest have expanded from angiogenesis to cancer cell-directed oncogenic signaling pathways for treatment of advanced HCC. Agents targeting vascular endothelial growth factor receptor, epidermal growth factor receptor, fibroblast growth factor receptor, platelet-derived growth factor receptor, c-mesenchymal-epithelial transition factor-1 and mammalian target of rapamycin signaling have been actively explored. This article focuses on the evaluation of mol. agents targeting pathogenic HCC and provides a review of recently completed phase III drug studies (e.g. involving sorafenib, sunitinib, brivanib, linifanib, erlotinib, everolimus, ramucirumab or orantinib) and ongoing drug studies (e.g. involving lenvatinib, regorafenib, tivantinib or cabozantinib) of molecularly targeted agents in advanced HCC, including a brief description of the biol. rationale behind these agents.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of sorafenib, sunitinib, brivanib, linifanib, erlotinib, everolimus, ramucirumab/orantinib and lenvatinib, regorafenib, tivantinib/cabozantinib of molecularly targeted agents in patients with advanced hepatocellular carcinoma)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 47 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1726025 CAPLUS Full-text
DOCUMENT NUMBER: 163:628844
TITLE: Method of treating lung adenocarcinoma
INVENTOR(S): Aftab, Dana T.; Yu, Peiwen
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015164869	A1	20151029	WO 2015-US27800	20150427

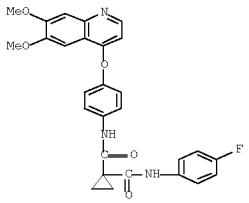
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61984599 P 20140425
OTHER SOURCE(S): CASREACT 163:628844; MARPAT 163:628844

AB This invention is directed to the treatment of cancer in a patient, particularly a patient with lung adenocarcinoma, and more particularly a patient with SLC34A2-ROS1, CD74-ROS1, or FIG-ROS1 fusion-pos. non-small cell lung cancer, with an inhibitor of MET, VEGFR2, and ROS1.

IT 849217-68-1
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(treating lung adenocarcinoma)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

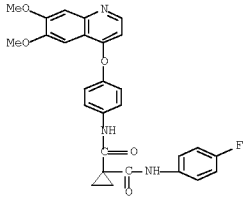


IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treating lung adenocarcinoma)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 46 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1783428 CAPLUS Full-text
DOCUMENT NUMBER: 163:681013
TITLE: Cabozantinib for the treatment of progressive metastatic medullary thyroid cancer
AUTHOR(S): Krajewska, Jolanta; Olczyk, Tomasz; Jarzab, Barbara
CORPORATE SOURCE: Nuclear Medicine and Endocrine Oncology Department, M.Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Pol.
SOURCE: Expert Review of Clinical Pharmacology (2016), 9(1), 69-79
CODEN: ERCPAG; ISSN: 1751-2433
DIGITAL OBJECT ID: 10.1586/17512433.2016.1102052
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib (XL-184) is a potent inhibitor of MET, VEGFR 2/KDR, RET and other receptor tyrosine kinases, such as KIT, AXL and FLT3. Its efficacy against MTC has been demonstrated in a prospective, randomized, placebo-controlled study (EXAM). Cabozantinib comparing to placebo significantly prolonged progression free survival both in hereditary and sporadic MTC, 11.2 vs. 4.0 mo, resp. Final anal. showed no global differences in overall survival (OS) between cabozantinib and placebo. However, in a subgroup with RET M918T mutation the difference in OS was significant: 44.3 vs. 18.9 mo, resp. Among the most frequent cabozantinib-related adverse events (AEs), observed in >30% of patients were diarrhea, palmar-plantar erythrodysesthesia, decreased weight, decreased appetite, nausea, fatigue, dysgeusia, hair color changes and hypertension. Expert Commentary: Cabozantinib constitutes an effective treatment option with acceptable toxicity in MTC patients showing either germinal or sporadic tumor RET M918T mutation as the drug prolonged OS in these subjects.

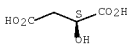
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of progressive metastatic medullary thyroid cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

CM 2

CRN 97-67-6
CMF C4 H6 O5

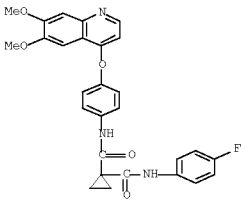
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating lung adenocarcinoma)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

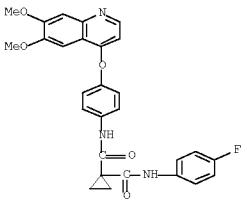
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

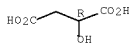


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 49 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1694942 CAPLUS Full-text
DOCUMENT NUMBER: 163:596944
TITLE: Methods for treating cancer using TOR kinase inhibitor combination therapy
INVENTOR(S): Fultz, Kimberly Elizabeth; Tran, Tam Minh; Xu, Shuichan; Xu, Weiming; Trowe, Torsten; Filvaroff, Ellen
PATENT ASSIGNEE(S): Signal Pharmaceuticals, LLC, USA
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015160868	A1	20151022	WO 2015-US25843	20150415
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
NZ 629860	A	20160129	NZ 2014-629860	20140902
US 20150297590	A1	20151022	US 2015-14686872	20150415
PRIORITY APPLN. INFO.:			US 2014-61980124 P	20140416

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 48 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1723003 CAPLUS Full-text
DOCUMENT NUMBER: 163:632038
TITLE: Hepatocyte growth factor as marker of prognosis in small cell lung cancer (SCLC)
INVENTOR(S): Arriola Aperribay, Edurne; Canadas Castillo, Israel; Rovira Guerin, Ana; Albanell Mestres, Joan
PATENT ASSIGNEE(S): Fundacio Institut Mar d'Investigacions Mediques (IMIM), Spain
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

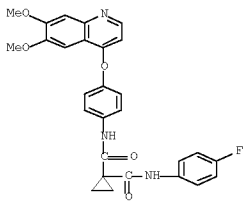
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015161885	A1	20151029	WO 2014-EP58375	20140424
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			WO 2014-EP58375	20140424

AB The invention relates to a new marker, the hepatocyte growth factor (HGF) in serum or plasma for the prognosis of small-cell lung cancer (SCLC). The invention also provides methods for selecting subjects suffering from SCLC that are candidate to respond to certain substances inhibiting certain kinases expressed in the tumors. There are also encompassed the use of immunoassay and nucleic acid reagents for detecting HGF in serum or plasma, said reagents for carrying out the prognostic method.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatocyte growth factor in serum or plasma as prognostic marker of small-cell lung cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

AB Provided are methods for treating or preventing cancer, comprising administering an effective amount of a 3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one TOR kinase inhibitor and an effective amount of a second active agent to a patient. Cancers treated by the method include solid tumors of the head, neck, breast, lung, ovaries, colon, rectum, stomach, prostate, urinary bladder, uterine, cervix, and other reproductive organs, wherein the tumors include relapsed, refractory or advanced solid tumors.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy using pyrazinopyrazine TOR kinase inhibitors for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

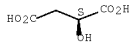
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



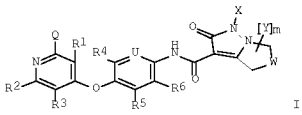
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 50 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1694572 CAPLUS Full-text
DOCUMENT NUMBER: 163:601731
TITLE: Preparation of bicyclic pyrazolone compounds for inhibiting or modulating the activity of receptor tyrosine kinases
INVENTOR(S): Xi, Ning; Wu, Yanjun
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: U.S. Pat. Appl. Publ., 52pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

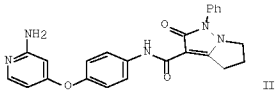
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150299219	A1	20151022	US 2015-14687992	20150416
WO 2015164161	A1	20151029	WO 2015-US26062	20150416

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61982729 P 20140422
OTHER SOURCE(S): CASREACT 163:601731; MARPAT 163:601731
GI

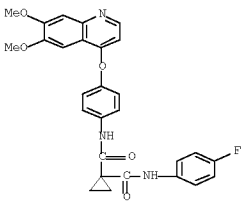


I



II

AB The title compds. I [Q = H, (un)substituted OH, NH2, etc.; U = CR7 or N; X = H, alkyl, cycloalkyl, etc.; Y = alkyl, cycloalkyl, aryl, etc.; m = 0-4; W = (CH2)n, (CH2)nO, (CH2)nNH, (CH2)nS (wherein n = 0-4); R1-R7 = H, F, Cl, Br, etc.; with the provisos], which are used to inhibit or modulate the activity of receptor tyrosine kinases, especially Axl, Mer, c-Met and Ron, were prepared E.g., a multi-step synthesis of II, starting from phenylhydrazine and 4-chlorobutanoyl chloride, was described. Exemplified compds. I were tested for their biol. activity (data given for representative compds. I). The invention also provides pharmaceutical compns. comprising the compound I, and a method of preventing, treating or lessening the severity of a proliferative disorder in a patient with the compds. I or the pharmaceutical compns. comprising I.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of bicyclic pyrazolone compds. for inhibiting or modulating the activity of receptor tyrosine kinases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

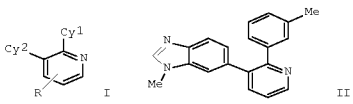


L8 ANSWER 51 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1654358 CAPLUS Full-text
DOCUMENT NUMBER: 163:601695
TITLE: 2,3-Disubstituted pyridine compounds as TGF-beta inhibitors and their preparation
INVENTOR(S): Singh, Rajinder; Bhamidipati, Somasekhar; Ding, Pingyu; Payan, Donald; Gelman, Marina; Kinsella, Todd
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 406pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015157093	A1	20151015	WO 2015-US24146	20150402

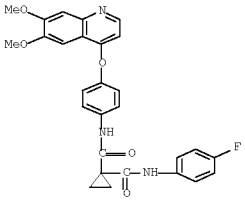
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61976880 P 20140408
US 2014-62019577 P 20140701
OTHER SOURCE(S): MARPAT 163:601695
GI



I II

AB The invention described compds. of formula I and a method of treating cancer comprising administering to a subject having cancer one of the compds. in conjunction with another therapeutic treatment of cancer. The compds. I inhibit signaling by a member of the TGF-β superfamily such as nodal or activin. Compds. of formula I wherein Cy1 is (un)substituted Ph, benzofuranyl, (un)substituted C1-3 alkyl, etc.; Cy2 is pyrazolo[1,5-a]pyrimidinyl, benzothiazolyl, imidazo[1,2-a]pyridinyl, (un)substituted phenylsulfonyl, etc.; R is (un)substituted Ph, (un)substituted heteroaryl and (un)substituted heterocycloalkyl; and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by cross-coupling of 2-chloro-2-(3-methylphenyl)pyridine with 1-methyl-1H-benzimidazole-6-boronic acids. The invention compds. were evaluated for their TGF-β inhibitory activity (some data given).
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of disubstituted pyridine compds. as TGF-β inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 52 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1650548 CAPLUS Full-text
DOCUMENT NUMBER: 163:585951
TITLE: Preparation of bridge linkers used for specific conjugation of two or more cytotoxic agents to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin; Zhao, Robert
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 162pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015155753	A2	20151015	WO 2015-IB56083	20150810

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

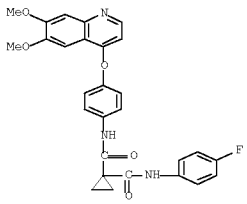
US 20150284416 A1 20151008 US 2015-14740403 20150616
PRIORITY APPLN. INFO.: US 2015-14740403 T0 20150616
OTHER SOURCE(S): MARPAT 163:585951
GI

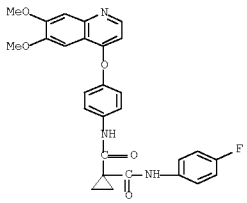
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to novel linkers contg. a 2,3-disubstituted succinic group, or 2-monosubstituted, or 2,3-disubstituted fumaric or maleic (trans (E)- or cis (Z)-butenedioic) group, e.g., (I), for conjugation of two or more compds./cytotoxic agents per linker to a cell-binding mol., through bridge linking pairs of thiols (reduced from the interchain disulfide bonds of the cell-binding agent by a reducing agent, such as dithiothreitol, dithioerythritol, L-glutathione and tris(2-carboxyethyl)phosphine (TCEP), or/and β-mercaptoethanol) on the cell-binding mol. specifically. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by treating reaction with drugs and to their use for cancers, infections and autoimmune disorders. Thus, linker I was prepared by cyclization of 2,3-dibromosuccinic acid in CH2Cl2 in the presence of P2O5. R1-COCHBrCHBrCO-R (II) was prepared in 3 steps from I and R1-H (preparation given) using R = H (preparation given). A herceptin antibody conjugate with II was prepared by reacting herceptin with and TCEP and II. The resulting conjugate was evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 889 and for SK-OV-3 cell was over 800. Five-week-old female BALB/c Nude mice inoculated s.c. in the area under the right shoulder with N-87 carcinoma cells treated with the conjugate had completely no tumor measurable at day 13 till day 60 (the end of experiment) in an in vivo antitumor activity study.

IT **849217-68-1**, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of two or
more cytotoxic agents to a cell-binding mol.)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

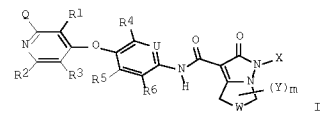


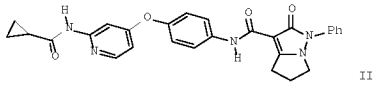


L8 ANSWER 54 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1640328 CAPLUS Full-text
DOCUMENT NUMBER: 163:618028
TITLE: Preparation of bicyclopyrazolone compounds as tyrosine kinase inhibitors
INVENTOR(S): Xi, Ning; Wu, Yanjun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 81pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104974162	A	20151014	CN 2015-10167125	20150409
PRIORITY APPLN. INFO.:			CN 2014-10141156 A	20140409

OTHER SOURCE(S): MARPAT 163:618028
GI

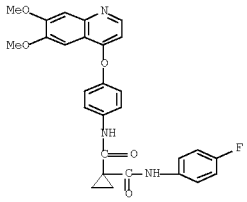




AB The invention provides bicyclopyrazolone compds. I [wherein Q = H, (un)substituted OH, NH2, etc.; U = (un)substituted CH or N; X = H, alkyl, alkenyl, alkynyl, etc.; Y = independently H, alkyl, alkenyl, etc.; W = (CH2)n, (CH2)nO, (CH2)nNH, or (cH2)nS; n = 0-4; R1-R6 = independently H, F, Cl, Br, CN, N3, etc.; m = 1-4; with provisos], stereoisomers, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts, or prodrugs thereof for suppressing the activity of receptor tyrosine kinase, especially Axl, Mer, c-Met and Ron kinases. The invention also provides pharmaceutical compns. comprising the title compds., and application of the title compds. and pharmaceutical compns. for preventing and treating proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 3 and 26 nM against Mer and c-Met tyrosine kinases, resp.

IT **849217-68-1**, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of bicyclopyrazolone compds. as tyrosine kinase inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 53 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1646639 CAPLUS Full-text
DOCUMENT NUMBER: 163:612041
TITLE: Method for screening antitumor drug biomarkers, and application thereof
INVENTOR(S): Xiong, Lei
PATENT ASSIGNEE(S): HTS Biotechnology (Shanghai) Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 23pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

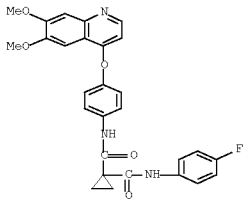
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104975063	A	20151014	CN 2014-10130154	20140401
PRIORITY APPLN. INFO.:			CN 2014-10130154	20140401

AB The invention discloses method for screening antitumor drug biomarkers, and application thereof. The method comprises the steps of: (1) providing tumor cells as starting cells, and tumor cells are from identical tumor tissue of the same object, (2) performing passage of the starting cells, establishing cell lines, and detecting genomic information of the cell lines so as to obtain at least 5 tumor cell lines that have genomic differences and are highly homologous, (3) performing antitumor drug sensitivity testing of the tumor cell lines, and typing the tumor cell lines based on the testing results, and (4) based on the typing results, analyzing the genomic information of the tumor cell lines to determine anti-tumor drug biomarkers. The method can maximally reduce background noise between different tumor cell lines, and can help to efficiently and accurately screen biomarkers of antitumor drugs.

IT **849217-68-1**, Cabozantinib
RL: ANT (Analyte); BUU (Biological use, unclassified); PAC (Pharmacological activity); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(method for screening antitumor drug biomarkers, and application thereof)

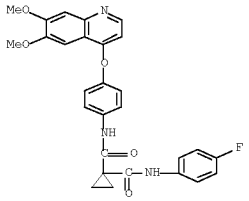
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

L8 ANSWER 55 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1635205 CAPLUS Full-text
TITLE: Selective targeting of CTNNB1-, KRAS- or MYC-driven cell growth by combinations of existing drugs
AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; Spijkers-Hagelstein, Jill A. P.; de Vetter, Judith R. F.; de Man, Jos; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE: Netherlands Translational Research Center B.V., Oss, Neth.
SOURCE: PLoS One (2015), 10(5), e0125021/1-e0125021/22
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0125021
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The aim of combination drug treatment in cancer therapy is to improve response rate and to decrease the probability of the development of drug resistance. Preferably, drug combinations are synergistic rather than additive, and, ideally, drug combinations work synergistically only in cancer cells and not in non-malignant cells. We have developed a workflow to identify such targeted synergies, and applied this approach to selectively inhibit the proliferation of cell lines with mutations in genes that are difficult to modulate with small mols. The approach is based on curve shift anal., which we demonstrate is a more robust method of determining synergy than combination matrix screening with Bliss-scoring. We show that the MEK inhibitor trametinib is more synergistic in combination with the BRAF inhibitor dabrafenib than with vemurafenib, another BRAF inhibitor. In addition, we show that the combination of MEK and BRAF inhibitors is synergistic in BRAF-mutant melanoma cells, and additive or antagonistic in, resp., BRAF-wild type melanoma cells and non-malignant fibroblasts. This combination exemplifies that synergistic action of drugs can depend on cancer genotype. Next, we used curve shift anal. to identify new drug combinations that specifically inhibit cancer cell proliferation driven by difficult-to-drug cancer genes. Combination studies were performed with compds. that as single agents showed preference for inhibition of cancer cells with mutations in either the CTNNB1 gene (coding for β-catenin), KRAS, or cancer cells expressing increased copy nos. of MYC. We demonstrate that the Wnt-pathway inhibitor ICG-001 and trametinib acted synergistically in Wnt-pathway-mutant cell lines. The ERBB2 inhibitor TAK-165 was synergistic with trametinib in KRAS-mutant cell lines. The EGFR/ERBB2 inhibitor neratinib acted synergistically with the spindle poison docetaxel and with the Aurora kinase inhibitor GSK-1070916 in cell lines with MYC amplification. Our approach can therefore efficiently discover novel drug combinations that selectively target cancer genes.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (selective targeting of CTNNB1-, KRAS-or MYC-driven human cancer cell growth by combinations of existing drugs)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

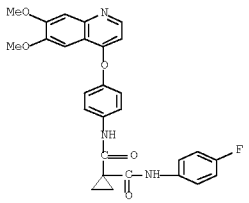
L8 ANSWER 57 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1626773 CAPLUS Full-text
TITLE: Evaluation of the effect of food and gastric pH on the single-dose pharmacokinetics of cabozantinib in healthy adult subjects
AUTHOR(S): Nguyen, Linh; Holland, Jaymes; Mamelok, Richard; Laberge, Marie-Kristine; Grenier, Julie; Swearingen, Dennis; Armas, Danielle; Lacy, Steven
CORPORATE SOURCE: Exelixis, Inc., San Francisco, CA, USA
SOURCE: Journal of Clinical Pharmacology (2015), 55(11), 1293-1302
CODEN: JCPCBR; ISSN: 0091-2700
DIGITAL OBJECT ID: 10.1002/jcph.526
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is a small mol. tyrosine kinase inhibitor that has been approved for the treatment of patients with progressive, metastatic medullary thyroid cancer. Cabozantinib exhibits a pH-dependent solubility profile in vitro. Two phase 1 clin. pharmacol. studies were conducted in healthy subjects to evaluate whether factors that may affect cabozantinib solubility and gastric pH could alter cabozantinib bioavailability: a food effect study (study 1) and a drug-drug interaction (DDI) study with the proton pump inhibitor (PPI) esomeprazole (study 2). Following a high-fat meal (study 1), cabozantinib Cmax and AUC were increased (40.5% and 57%, resp.), and the median tmax was delayed by 2 h. Cabozantinib should thus not be taken with food (patients should not eat for at least 2 h before and at least 1 h after administration). In the DDI study (study 2), the 90% confidence intervals (CIs) around the ratio of least-squares means of cabozantinib with esomeprazole vs.



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 56 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1634096 CAPLUS Full-text
TITLE: Pharmacokinetic interaction study of combining cabozantinib with erlotinib in rats by UPLC-MS/MS
AUTHOR(S): Wang, Zhiyi; Zhang, Qingwei; Zhang, Meiling; Wu, Haiya; Zhang, Yuan
CORPORATE SOURCE: The Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, 325000, Peop. Rep. China
SOURCE: Latin American Journal of Pharmacy (2015), 34(2), 313-318
CODEN: LAJPA9; ISSN: 0326-2383
PUBLISHER: Colegio de Farmaceuticos de la Provincia de Buenos Aires
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study examd. whether oral administration of erlotinib to rats with cabozantinib led to any pharmacokinetic interactions or not. Twenty four rats were randomly divided into 3 groups, cabozantinib group (cabozantinib 30 mg/kg, n = 8), erlotinib group (erlotinib 25 mg/kg, n = 8) and co-administration group (erlotinib 25 mg/kg and cabozantinib 30 mg/kg, n = 8). The concentration of cabozantinib and erlotinib in rat plasma was determined by a sensitive and simple UPLC-MS/MS method. There was statistical pharmacokinetics difference for cabozantinib in the cabozantinib group and co-administration group, when co-oral administration cabozantinib with erlotinib, the AUC(0-t) and Cmax increased ($p < 0.01$). There was statistical pharmacokinetics difference for erlotinib in the erlotinib group and co-administration group, when co-oral administration erlotinib with cabozantinib, the AUC(0-t) increased and CL decreased ($p < 0.05$). These data indicate erlotinib could influence the pharmacokinetic profile of cabozantinib in rats, and vice versa, which might cause drug-drug interactions when using cabozantinib with erlotinib.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic interaction study of combining cabozantinib with erlotinib in rats by ultra-performance liquid chromatog.-mass spectrum/mass spectrum)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

cabozantinib alone for AUC0-inf were within the 80%-125% limits; the upper 90%CI for Cmax was 125.1%. Because of the low apparent risk of a DDI, concomitant use of PPIs or weaker gastric pH-altering agents with cabozantinib is not contraindicated.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (evaluation of effect of food and gastric hydrogen ion concentration on single-dose pharmacokinetics of cabozantinib in healthy adult subjects)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



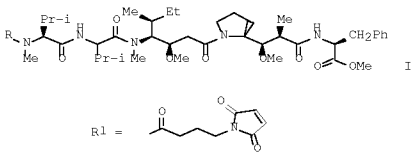
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 58 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623830 CAPLUS Full-text
DOCUMENT NUMBER: 163:553993
TITLE: Preparation of cytotoxic auristatin analogs and their conjugates with cell-binding molecules
INVENTOR(S): Liang, Qingliang; Zhao, Robert Y.; Ye, Hangbo; Gai, Shun; Jia, Junxiang; Huang, Yuanyuan; Li, Xing; Guo, Huihui; Xie, Hongsheng; Li, Wenjun; Zhou, Xiaomai; Yang, Chengyu; Zhuo, Xiaotao; Zhao, Linyao; Cao, Minjun; Lin, Chen; Peng, Jie; Ye, Zhicang; Xu, Jun
PATENT ASSIGNEE(S): Hangzhou DAC Biotech Co, Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 127pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151079	A2	20151008	WO 2015-IB54653	20150620

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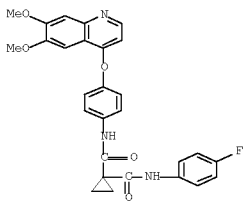
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IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA,
MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA,
PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK,
SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, ZA, ZM, ZW
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ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,
SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: WO 2015-IB54653 20150620
OTHER SOURCE(S): MARPAT 163:553993
GI



AB The invention is related to the prepn. of cytotoxic auristatin analogs, e.g., I, in particular monomethyl auristatin F (MMAF) conjugates of such cytotoxic agents with a cell-binding agent, methods of using them to arrest or retard abnormal cell growth and /or proliferation and to their use for targeted treatment of cancer, autoimmune disease, and infectious diseases. Thus, I [R = H] was prepared and coupled to 4-maleimidobutyric acid to provide I [R = R1] linker drug conjugate. A herceptin antibody-I [R = R1] conjugate was prepared and evaluated for its in vitro potency against N-87 human gastric carcinoma cells.

IT 849217-68-1, Cabozantinib 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug, synergistic agent; preparation of auristatin analogs and their conjugates with cell-binding mols. useful as antiproliferative and antitumor agents)

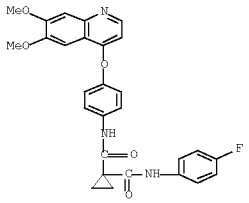
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

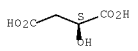
CRN 849217-68-1
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

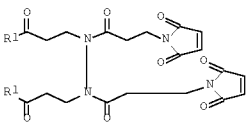


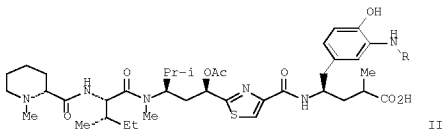
L8 ANSWER 59 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623829 CAPLUS Full-text
DOCUMENT NUMBER: 163:553992
TITLE: Preparation of bridge linkers used for specific conjugation of a cytotoxic agent to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 112pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151081	A2	20151008	WO 2015-IB55264	20150712
US 20150314017	A1	20151105	US 2015-14799712	20150715

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2015-IB55264 T0 20150712
OTHER SOURCE(S): CASREACT 163:553992; MARPAT 163:553992
GI

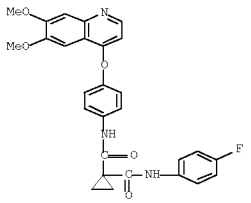




AB The invention is related to the prepn. of novel linkers contg. a hydrazine unit, e.g., I, used for the specific conjugation in particular cytotoxic agents to a cell-binding mol., through bridge linking a pair of thiols on the cell-binding mol. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by reaction with drugs and to their use for treating especially cancer. Thus, the linker I [R1 = OH] was prepared by a multi-step synthesis starting from O-benzylhydroxylamine hydrochloride and tert-Bu acrylate using tert-Bu 3-aminopropanoate and 3-maleimidopropanoic acid. Reaction of I with oxalyl chloride, and treatment of the diacid dichloride with II [R = H] gave I [R1 = II wherein R is absent]. A herceptin antibody-I [R1 = II wherein R is absent] conjugate was prepared and evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 105 and for SK-OV-3 cell was over 3136.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.

L8 ANSWER 60 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623828 CAPLUS Full-text
DOCUMENT NUMBER: 163:585947
TITLE: Preparation of novel bridge linkers containing an acetylenedicarbonyl group for specific conjugation of a cytotoxic agent to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 113pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151080	A2	20151008	WO 2015-IB55051	20150704

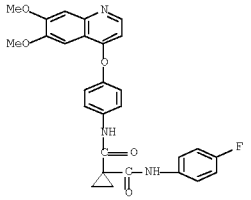
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2015-IB55051 20150704
OTHER SOURCE(S): MARPAT 163:585947
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of novel bridge linkers contg. an acetylenedicarboxylic group, e.g., I, to link two drugs to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by reaction with drugs and to their use for treating especially cancer. Thus, I [R = 2,5-dioxopyrrolidin-1-yloxy] was prepared by reacting 13-amino-bis(4,7,10-trioxadodecanoic acid) (preparation given) with bis(2,5-dioxopyrrolidin-1-yl)but-2-ynedioate (preparation given) and treatment of the tetraacid with NHS. Amidation of I [R = 2,5-dioxopyrrolidin-1-yloxy] with tubulysin analog R1-H gave R1-I [R = absent] containing 4 tubulysins analog per bridge linker. A herceptin antibody-R1-I [R = absent] conjugate was prepared and evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 270 (IC50>10/IC50 = 0.037), and for SK-OV-3 cell was over 344.

IT 849217-68-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.

L8 ANSWER 61 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1623827 CAPLUS Full-text
DOCUMENT NUMBER: 163:553991
TITLE: Preparation of hydrophilic linkers for the conjugation of a cytotoxic agent or a chromophore to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151078	A2	20151008	WO 2015-IB54521	20150615
WO 2015151078	A3	20160310		

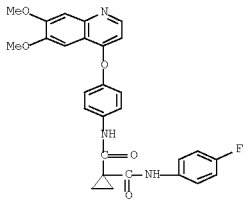
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PRIORITY APPLN. INFO.: WO 2015-IB54521 20150615
OTHER SOURCE(S): MARPAT 163:553991
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of hydrophilic linkers contg. phosphamide, phosphinate, sulfonamide, sulfonyl, sulfonimide, and/or sulfoxide groups, e.g., I, to link drugs, in particular, cytotoxic agents or a chromophore mols. to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (e.g. cytotoxic agent) conjugates comprising either modification of the drugs with these hydrophilic linkers first, followed by reaction with cell-binding agents; or modification of cell-binding agents with these hydrophilic linkers first, followed by reaction with drugs. Thus, linker I was prepared from N-methylethane-1,2-diamine and succinic anhydride using POCl3, 3-(methylamino)propanoic acid and NHS. Conjugation of I with the tubulysin analog II [R = H] gave the drug-linker conjugate II [R = R1]. An antiHer2-II [R= R1] antibody conjugate of was prepared and evaluated for its in vitro cytotoxicity. The specificity of the conjugate for N87 cell was over 1315 (IC50> 50/IC50= 0.038), and for SK-OV-3 cell was over 1560.

IT 849217-68-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.

L8 ANSWER 62 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1617130 CAPLUS Full-text
DOCUMENT NUMBER: 163:553989
TITLE: Preparation of hydrophilic linkers for the conjugation of a cytotoxic agent or a chromophore to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: U.S. Pat. Appl. Publ., 69pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

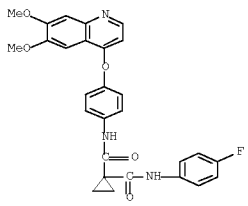
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150284416	A1	20151008	US 2015-14740403	20150616
WO 2015155753	A2	20151015	WO 2015-IB56083	20150810

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR,

HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2015-14740403 T0 20150616
OTHER SOURCE(S): CASREACT 163:553989
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of hydrophilic linkers contg. phosphamide, phosphinate, sulfonamide, sulfonyl, sulfonimide, and/or sulfoxide groups, e.g., I, to link drugs, in particular, cytotoxic agents or a chromophore mols. to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (e.g. cytotoxic agent) conjugates comprising either modification of the drugs with these hydrophilic linkers first, followed by reaction with cell-binding agents; or modification of cell-binding agents with these hydrophilic linkers first, followed by reaction with drugs. Thus, linker I was prepared from N-methylethane-1,2-diamine and succinic anhydride using POCl3, 3-(methylamino)propanoic acid and NHS. Conjugation of I with the tubulysin analog II [R = H] gave the drug-linker conjugate II [R = Rl]. An antiHer2-II [R= Rl] antibody conjugate of was prepared and evaluated for its in vitro cytotoxicity. The specificity of the conjugate for N87 cell was over 1315 (IC50> 50/IC50= 0.038), and for SK-OV-3 cell was over 1560.
IT 849217-68-1P, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

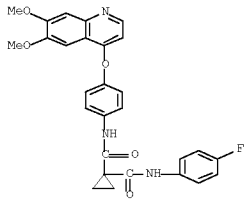


RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 63 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1617114 CAPLUS Full-text
DOCUMENT NUMBER: 163:551060
TITLE: Combination therapy comprising anti-angiogenesis agents and OX40 binding agonists
INVENTOR(S): Walsh, Kevin; De Almeida, Patricia; Du, Changchun; Kim, Jeong; Zhu, Jing; Bevers, Jack; Andya, James; Shen, Ye
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 166pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

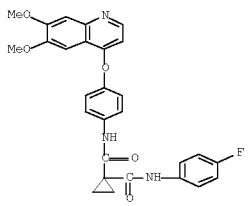
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015153514	A1	20151008	WO 2015-US23434	20150330
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150307617	A1	20151029	US 2015-14673792	20150330
PRIORITY APPLN. INFO.:			US 2014-61973193 P	20140331
			US 2014-61989448 P	20140506
			US 2014-62073873 P	20141031
			US 2014-62080171 P	20141114
			US 2015-62113345 P	20150206

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose a cancer treatment method comprising the administering of an anti-angiogenesis agent and an OX40 binding agonist. In the one example, anti-VEGF antibody treatment resulted in reduced tumor growth, compared to anti-gp120 (control), in a syngeneic mouse colon carcinoma model. Anti-OX40 antibody treatment exhibited little activity alone. Anti-OX40 treatment in combination with anti-VEGF treatment demonstrated superior tumor growth inhibition when compared to single agent administration or anti-gp120 treatment.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-angiogenesis agents in combination with OX40 agonists for treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 64 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1606231 CAPLUS Full-text
TITLE: Antitumor Effects and Mechanisms of AZD4547 on FGFR2-Deregulated Endometrial Cancer Cells
AUTHOR(S): Kwak, Yeonui; Cho, Hanna; Hur, Wooyoung; Sim, Taebo
CORPORATE SOURCE: KU-KIST Graduate School of Converging Science and Technology, Korea University, Seoul, S. Korea
SOURCE: Molecular Cancer Therapeutics (2015), 14(10), 2292-2302
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-15-0032
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Uncontrolled activation of FGFRs induces the progression of various cancers. It was recently reported that FGFR2-activating mutants are implicated in about 12% of endometrial carcinomas. AZD4547, a potent pan-FGFR inhibitor, is currently being evaluated in clin. trials for several FGFR-driven cancers. However, AZD4547 has not been examined yet against FGFR2 mutant-driven endometrial cancers. Thus, we evaluated the activity of AZD4547 against four different endometrial cancer cells, including AN3-CA, MFE296, MFE280, and HEC1A, where all but HEC1A cells express distinctive FGFR2 mutations. We found that AZD4547 exhibits potent antiproliferative activity (EC50 = 31 nmol/L) against AN3-CA cells harboring FGFR2-K310R/N550K mutant. Anal. using a phospho-kinase array revealed that AZD4547 blocks FGFR2 downstream signaling, such as p38, ERK1/2, JNK, p70S6K, and PLCγ. Moreover, oral administration of AZD4547 (30 mg/kg, every day) remarkably delayed tumor growth in a mouse xenograft model of AN3-CA cells. Unbiased reporter gene assay showed that AZD4547 antagonizes the aFGF-induced activation of several transcription factors, including EGR1, ELK-1/SRF, AP-1, and NFκB. Genome-wide transcriptome anal. revealed that AZD4547 perturbs a number of transcriptions, and EGR1 was identified as one of the major targets of AZD4547. The significance of the FGFR2-EGR1 axis in endometrial cancer progression has not been reported. In addition, using kinome-wide inhibition profiling anal., we first identified potential new target kinases of AZD4547, including MAP4K3, MAP4K5, IRR, RET, and FLT3. Our study demonstrated that AZD4547 exhibits its therapeutic activity against endometrial cancer cells by perturbing various regulatory mechanisms related to FGFR signaling. Mol Cancer Ther; 14(10); 2292-302. ©2015 AACR.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antitumor effects and mechanisms of AZD4547 on FGFR2-deregulated endometrial cancer cells)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 65 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1604658 CAPLUS Full-text
DOCUMENT NUMBER: 163:569777
TITLE: Preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid salt and their crystal forms
INVENTOR(S): Chen, Minhua; Zhang, Yanfeng; Li, Jiaoyang; Zhang, Xiaoyu; Lu, Fei
PATENT ASSIGNEE(S): Crystal Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104961681	A	20151007	CN 2014-10641139	20141113
PRIORITY APPLN. INFO.:			CN 2014-10641139	20141113

AB The title N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid salt has higher

solubility than N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide malate, and plays important roles in improving the bioavailability, treatment effect, and safety of drug.

IT 1817759-89-9P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crystal structure; preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid and their crystal forms)

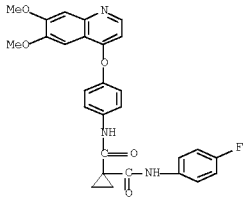
RN 1817759-89-9 CAPLUS

CN Galactaric acid, compd. with N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1

CMF C28 H24 F N3 O5

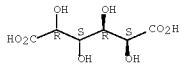


CM 2

CRN 526-99-8

CMF C6 H10 O8

Relative stereochemistry.



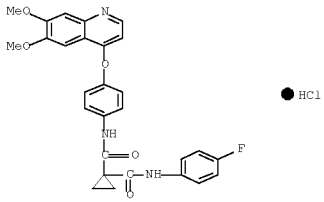
IT 849217-68-1, Cabozantinib

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid and their crystal forms)

RN 1817759-42-4 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrochloride (1:1) (CA INDEX NAME)



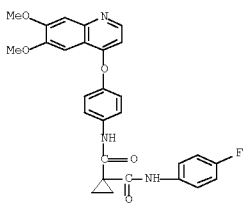
IT 849217-68-1, Cabozantinib

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 67 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1602738 CAPLUS Full-text

TITLE: TAMing resistance to multi-targeted kinase inhibitors through Axl and Met inhibition

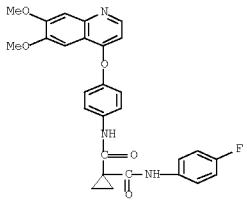
AUTHOR(S): Pinato, D. J.; Chowdhury, S.; Stebbing, J.

CORPORATE SOURCE: Department of Surgery and Cancer, Imperial College

forms)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 66 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1604653 CAPLUS Full-text

DOCUMENT NUMBER: 163:569776

TITLE: Preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms

INVENTOR(S): Chen, Minhua; Zhang, Yanfeng; Li, Jiaoyang; Zhang, Xiaoyu; Lu, Fei

PATENT ASSIGNEE(S): Crystal Pharmatech Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104961680	A	20151007	CN 2014-10626255	20141107

PRIORITY APPLN. INFO.: CN 2014-10626255 20141107

AB The title N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride has higher solubility than N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide malate, and plays important roles in improving the bioavailability, treatment effect, and safety of drug.

IT 1817759-42-4P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crystal structure; preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms)

London, London, UK

SOURCE: Oncogene (2015) Ahead of Print
CODEN: ONCNES; ISSN: 0950-9232

DIGITAL OBJECT ID: 10.1038/onc.2015.374

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. TAM (Tyro3-Axl-Mer) receptor tyrosine kinases and Met are implicated in several hallmarks of cancer progression including sustained angiogenesis, enhanced motility, tissue invasion and acquisition of metastatic potential through the upregulation of epithelial-to-mesenchymal transition. Increasing evidence has confirmed Axl and Met as emerging central drivers of adaptive resistance to targeted therapies across a wide variety of cancers. In this issue of Oncogene, Zhou et al. describe the mechanisms linking Axl and Met activation to acquired resistance to sunitinib in renal cell carcinoma (RCC), providing a pre-clin. rationale for the development of Axl and Met inhibitors including cabozantinib in anti-angiogenic resistant RCC.

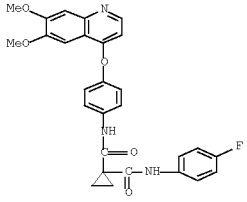
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(TAMing resistance to multi-targeted kinase inhibitors through Axl and Met inhibition)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 68 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1593218 CAPLUS Full-text

DOCUMENT NUMBER: 163:673623

TITLE: Cabozantinib in Thyroid Cancer

AUTHOR(S): Fallahi, Poupak; Ferrari, Silvia M.; Di Bari, Flavia; Materazzi, Gabriele; Benvenga, Salvatore; Miccoli, Paolo; Antonelli, Alessandro

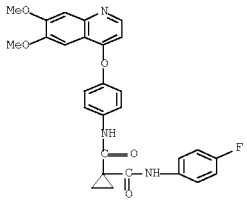
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56126, Italy

SOURCE: Recent Patents on Anti-Cancer Drug Discovery (2015), 10(3), 259-269
CODEN: RPADDY; ISSN: 1574-8928
DIGITAL OBJECT ID: 10.2174/1574892810666150708110816
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib is an oral once-daily multitarget tyrosine kinase inhibitor of MET, VEGFR2, RET, acting against KIT, AXL, FLT3 and Tie-2. Cabozantinib has shown anti-cancer effects in preclin. and clin. models of cancers derived from both epithelial and mesenchymal origins [prostate cancer, non small lung cancer, medullary thyroid cancer (MTC) and differentiated thyroid cancer (DTC), renal cell carcinoma, etc.]. In a Phase III clin. study, cabozantinib improved PFS (11.2 mo vs. 4.0 mo in the placebo group) of patients with MTC (independently of age, bone metastases, RET status and prior treatment). Cabozantinib was approved in 2012 by FDA for metastatic MTC and in 2013 by EMA. Cabozantinib has been also evaluated in metastatic DTC patients, because they have activation on tyrosine kinases, including MET, VEGFR2 and RET, suggesting the possible use of cabozantinib in metastatic DTC. Actually, two Phase II trials of cabozantinib in DTC patients resistant to RAI are ongoing. To increase the antineoplastic effect of cabozantinib, and to overcome the occurrence of drug resistance, combination studies with other anticancer agents are ongoing. In conclusion, cabozantinib has shown to exert an important therapeutic effect in patients with MTC improving PFS. In DTC patients, cabozantinib has shown promising results.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of tyrosine kinase inhibitor cabozantinib in thyroid cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



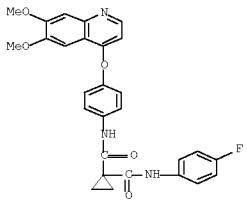
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 152 THERE ARE 152 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 69 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1592351 CAPLUS Full-text
TITLE: Sensitivity of neuroblastoma to the novel kinase inhibitor cabozantinib is mediated by ERK inhibition
AUTHOR(S): Zhang, Linna; Scorsone, Kathleen; Woodfield, Sarah E.; Zage, Peter E.
CORPORATE SOURCE: Department of Pediatrics, Section of Hematology-Oncology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Cancer Chemotherapy and Pharmacology (2015), 76(5), 977-987
CODEN: CCPHDZ; ISSN: 0344-5704
DIGITAL OBJECT ID: 10.1007/s00280-015-2871-z
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Purpose: Children with high-risk neuroblastoma have poor survival rates, and novel therapies are needed. We hypothesized that cabozantinib would be effective against neuroblastoma tumor cells and tumors in preclin. models via inhibition of receptor tyrosine kinase signaling pathways. Methods: We determined neuroblastoma cell viability after treatment with cabozantinib alone and in combination with 13-cis-retinoic acid, topotecan, and temozolomide using MTT assays. Inhibition of RET and intracellular signaling was measured by Western blot anal. of treated and untreated cells. To investigate the efficacy of cabozantinib against neuroblastoma tumors in vivo, neuroblastoma cells were injected orthotopically into immunocompromised mice, and mice were treated with oral cabozantinib. Tumors were evaluated for growth by determination of in vivo luminescence and final tumor wts. Results: All neuroblastoma cell lines were sensitive to cabozantinib, and IC50 values ranged from 1.6 to 16.2 μM. Cabozantinib treatment was synergistic with 13-cis-retinoic acid and chemotherapy agents topotecan and temozolomide. Cabozantinib treatment inhibited RET phosphorylation in all cell lines and ERK phosphorylation in more sensitive neuroblastoma cell lines. In mice with neuroblastoma xenograft tumors, cabozantinib treatment significantly reduced tumor growth. Conclusions: Treatment of neuroblastoma tumor cells with cabozantinib inhibits RET and ERK phosphorylation and is effective against neuroblastoma tumor cell lines alone and in combination with 13-cis-retinoic acid, topotecan, and temozolomide. Cabozantinib treatment is also effective in reducing tumor growth in vivo. Cabozantinib therefore represents a novel therapeutic agent for neuroblastoma, and further preclin. and clin. studies are warranted.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(efficacy of cabozantinib against neuroblastoma tumor cells and tumors in preclin. immunocompromised mouse models via inhibition of receptor tyrosine kinase signaling pathways)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



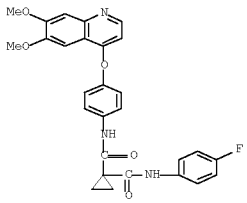
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 70 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1582731 CAPLUS Full-text
TITLE: MET/HGF targeted drugs as potential therapeutic strategies in non-small cell lung cancer
AUTHOR(S): Perez-Ramirez, Cristina; Canadas-Garre, Marisa; Molina, Miguel Angel; Faus-Dader, Maria Jose; Calleja-Hernandez, Miguel Angel
CORPORATE SOURCE: Pharmacogenetics Unit, UGC Provincial de Farmacia de Granada, Instituto de Investigacion Biosanitaria de Granada, Complejo Hospitalario Universitario de Granada, Granada, Spain
SOURCE: Pharmacological Research (2015), 102, 90-106
CODEN: PHMREP; ISSN: 1043-6618
DIGITAL OBJECT ID: 10.1016/j.phrs.2015.09.016
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. This article discusses about MET pathway signaling and dysregulation development of MET inhibitors like tivantinib, cabozantinib, crizotinib and foretinib to block HGF/MET signaling pathway and use of c-Met protein /hepatocyte growth factor targeted drugs as potential therapeutic strategies in non-small cell lung cancer in human and mouse model.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of c-Met protein/hepatocyte growth factor targeted drugs as potential therapeutic strategies in non-small cell lung cancer in human and mouse model)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 202 THERE ARE 202 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 71 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1579900 CAPLUS Full-text
DOCUMENT NUMBER: 163:512733
TITLE: Cancer treatment with c-MET antagonists and correlation of the latter with HGF expression
INVENTOR(S): Yu, Wei; Shames, David; Koeppen, Hartmut; Phan, See; Rost, Sandra
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 178pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015148531	A1	20151001	WO 2015-US22282	20150324
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2014-61969706 P 20140324
US 2014-61985316 P 20140428

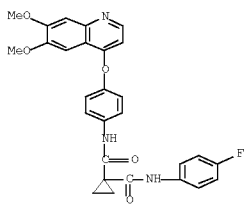
AB The present invention concerns cancer biomarkers. In particular, the invention concerns HGF as a biomarker for patient selection and patient prognosis in cancer, as well as methods of therapeutic treatment, articles of manufacture and methods for making them, diagnostic kits, methods of

detection and methods of advertising related thereto. Cancer patients are treated with an anti-c-met antibody in combination with an anti-VEGF antibody.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer treatment with c-MET antagonists and correlation of the latter with HGF expression)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 72 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1577497 CAPLUS Full-text

TITLE: Rapid modification of the bone microenvironment following short-term treatment with Cabozantinib in vivo

AUTHOR(S): Haider, Marie-Therese; Hunter, Keith D.; Robinson, Simon P.; Graham, Timothy J.; Corey, Eva; Dear, T. Neil; Hughes, Russell; Brown, Nicola J.; Holen, Ingunn

CORPORATE SOURCE: Department of Oncology, University of Sheffield, Sheffield, UK

SOURCE: Bone (New York, NY, United States) (2015), 81, 581-592
CODEN: BONEDL; ISSN: 1873-2763

DIGITAL OBJECT ID: 10.1016/j.bone.2015.08.003

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Bone metastasis remains incurable with treatment restricted to palliative care. Cabozantinib (CBZ) is targeted against multiple receptor tyrosine kinases involved in tumor pathobiol., including hepatocyte growth factor receptor (MET) and vascular endothelial growth factor receptor 2 (VEGFR-2). CBZ has demonstrated clin. activity in advanced prostate cancer with resolution of lesions visible on bone scans, implicating a potential role of the bone microenvironment as a mediator of CBZ effects. We characterised the effects of short-term administration of CBZ on bone in a range of in vivo models to determine how CBZ affects bone in the absence of tumor. Studies were performed in a variety of in vivo models including male and female BALB/c nude mice (age 6-17-wk). Animals received CBZ (30 mg/kg, 5 × weekly) or sterile H2O control for 5 or 10 days. Effects on bone integrity (μCT), bone cell activity (PINP, TRAP ELISA), osteoblast and osteoclast number/mm trabecular bone surface, area of epiphyseal growth plate cartilage, megakaryocyte nos. and bone marrow composition were assessed. Effects of longer-term treatment (15-day & 6-wk administration) were assessed in male NOD/SCID and beige SCID mice. CBZ treatment had significant effects on the bone microenvironment, including reduced osteoclast and increased osteoblast nos. compared to control. Trabecular bone structure was altered after 8 administrations. A significant elongation of the epiphyseal growth plate, in particular the hypertrophic chondrocyte zone, was observed in all CBZ treated animals irresp. of administration schedule. Both male and female BALB/c nude mice had increased megakaryocyte nos./mm2 tissue after 10-day CBZ treatment, in addition to vascular ectasia, reduced bone marrow cellularity and extravasation of red blood cells into the extra-vascular bone marrow. All CBZ-induced effects were transient and rapidly lost following cessation of treatment. Short-term administration of CBZ induces rapid, reversible effects on the bone microenvironment in vivo highlighting a potential role in mediating treatment responses.

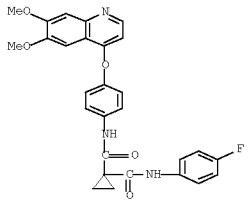
IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rapid modification of bone microenvironment following short-term treatment with cabozantinib in vivo)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 73 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1577278 CAPLUS Full-text

DOCUMENT NUMBER: 164:288433

TITLE: Stromal expression of VEGF-A and VEGFR-2 in prostate tissue is associated with biochemical and clinical recurrence after radical prostatectomy

AUTHOR(S): Nordby, Yngve; Andersen, Sigve; Richardsen, Elin; Ness, Nora; Al-Saad, Samer; Melbo-Jorgensen, Christian; Patel, Hiten R. H.; Donnem, Tom; Busund, Lill-Tove; Bremnes, Roy M.

CORPORATE SOURCE: Department Clinical Medicine, The Arctic University of Norway, Tromso, Norway

SOURCE: Prostate (Hoboken, NJ, United States) (2015), 75(15), 1682-1693
CODEN: PRSTDS; ISSN: 0270-4137

DIGITAL OBJECT ID: 10.1002/pros.23048

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

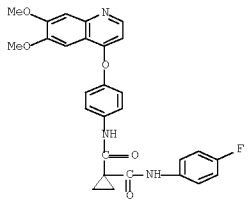
AB Background : There is probably significant overtreatment of patients with prostate cancer due to a lack of sufficient diagnostic tools to predict aggressive disease. Vascular endothelial growth factors (VEGFs) and their receptors (VEGFRs) are potent mediators of angiogenesis and tumor proliferation, but have been examined to a limited extent in large prostate cancer studies. Meanwhile, recent promising results on VEGFR-2 inhibition have highlighted their importance, leading to the need for further investigations regarding their expression and prognostic impact. Design : Using tissue microarray and immunohistochem., the expression of VEGFs (VEGF-A and VEGF-C) and their receptors (VEGFR-2 and VEGFR-3) were measured in neoplastic tissue and corresponding stroma from radical prostatectomy specimens in 535 Norwegian patients. Their expression was evaluated semiquantatively and assocns. with event-free survival were calculated Results : High expression of VEGFR-2 in either stroma or epithelium was independently associated with a higher incidence of prostate cancer relapse (HR = 4.56, P = 0.038). A high combined expression of either VEGF-A, VEGFR-2 or both in stroma was independently associated with a higher incidence of biochem. failure (HR = 1.77, P = 0.011). Conclusions : This large study highlights the prognostic importance of VEGF-A and VEGFR-2 stromal expression. Analyses of these biomarkers may help distinguish which patients will benefit from radical treatment. Together with previous studies showing efficiency of targeting VEGFR-2 in prostate cancer, this study highlights its potential as a target for therapy, and may aid in future selection of prostate cancer patients for novel anti-angiogenic treatment. Prostate 75:1682-1693, 2015. 2015 Wiley Periodicals, Inc.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stromal expression of VEGF-A and VEGFR-2 in prostate tissue was associated with biochem. and clin. recurrence in human after radical prostatectomy)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 74 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1545892 CAPLUS Full-text

DOCUMENT NUMBER: 163:469529

TITLE: Target inhibition map system for combination antitumor therapy design and methods of using same

INVENTOR(S): Pal, Ranadip; Keller, Charles, III; Berlow, Noah E.; Seguin, Bernard

PATENT ASSIGNEE(S): Texas Tech University System, USA; Colorado State University Research Foundation

SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150269307	A1	20150924	US 2015-14661918	20150318
PRIORITY APPLN. INFO.:			US 2014-61955068 P	20140318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

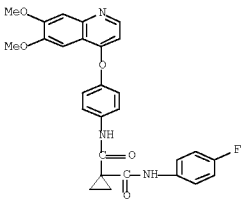
AB Disclosed is a system and method for targeted therapy designs which model a cancer pathway for predicting the effectiveness of targeted anti-cancer drugs. The disclosed system and method includes utilization of a computer processor allowing for the selection of a set of drugs from available drugs using approximation algorithms utilizing cell viability data associated with a testable culture of a patient's tumor for generating a probabilistic target inhibition map (PTIM) from viability data for considering the selection of a set of drugs from available drugs, and further supports a wide variety of scenarios for personalized cancer therapy, related products and services.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL-184

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(target inhibition map system for combination therapy design and methods of using same)

RN 849217-68-1 CAPLUS

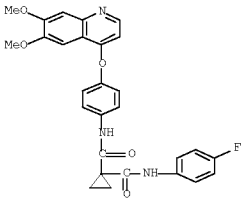
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

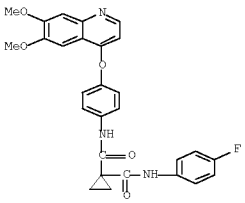
CRN 849217-68-1
CMF C28 H24 F N3 O5



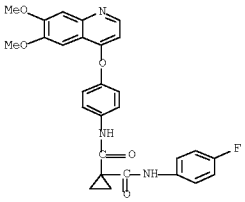
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

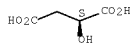


IT 1628542-34-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dosing of cabozantinib formulations)
RN 1628542-34-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, monohydroxy deriv. (CA INDEX NAME)



D1—OH

IT 1621681-63-7
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosing of cabozantinib formulations)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)

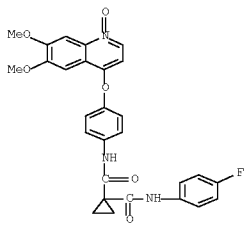


L8 ANSWER 75 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1542977 CAPLUS Full-text
DOCUMENT NUMBER: 163:469542
TITLE: Dosing of cabozantinib formulations
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

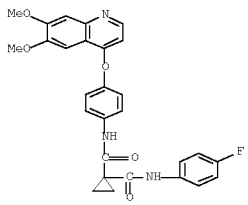
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015142928	A1	20150924	WO 2015-US21072	20150317

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61954352 P 20140317
OTHER SOURCE(S): CASREACT 163:469542
AB The invention relates to administration of various pharmaceutical formulations of N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1- dicarboxamide, (cabozantinib) a c-Met inhibitor, and its metabolites, to achieve desirable pharmacokinetic and pharmacodynamic effects.
IT 1809822-99-8
RL: ANT (Analyte); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dosing of cabozantinib formulations)
RN 1809822-99-8 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, labeled with carbon-14 (CA INDEX NAME)



IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosing of cabozantinib formulations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



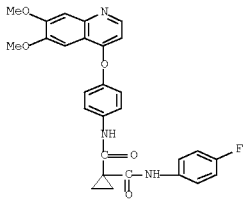
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 76 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1518424 CAPLUS Full-text
DOCUMENT NUMBER: 163:693610
TITLE: Cabozantinib for the treatment of non-small cell lung cancer with KIF5B-RET fusion. An example of swift repositioning
AUTHOR(S): Song, Minsoo; Kim, Seong-Heon; Yoon, Suk Kyoon
CORPORATE SOURCE: New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Taegu, 701-310, S. Korea

SOURCE: Archives of Pharmacal Research (2015), 38(12), 2120-2123
CODEN: APHRDQ; ISSN: 0253-6269
DIGITAL OBJECT ID: 10.1007/s12272-015-0660-1
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A new chimeric fusion transcript of KIF5B (the kinesin family 5B gene) and the RET (Rearranged during Transcription) oncogene, KIF5B-RET, was found in 1-2 % of lung adenocarcinomas (LADCs) in 2012. Several related clin. trials for non-small cell lung cancer (NSCLC) with KIF5B-RET rearrangements using existing RET inhibitors, such as cabozantinib, lenvatinib, vandetanib, sunitinib, ponatinib, and AUY922, have been swiftly initiated by the discovery of the KIF5B-RET fusion gene. Anti-RET activity and the status of clin. development of cabozantinib for KIF5B-RET fusion-pos. NSCLC are discussed.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of non-small cell lung cancer with KIF5B-RET fusion. An example of swift repositioning)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

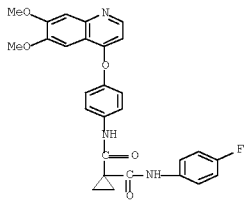


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 77 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1512965 CAPLUS Full-text
TITLE: Design, synthesis and pharmacological evaluation of novel 4-phenoxyquinoline derivatives as potential antitumor agents
AUTHOR(S): Hu, Hao; Jiang, Mingyan; Xie, Lijun; Hu, Gang; Zhang, Cuirong; Zhang, Lixia; Zhou, Shunguang; Zhang, Meihui; Gong, Ping
CORPORATE SOURCE: Key Laboratory of Structure-based Drug Design and Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Chemical Research in Chinese Universities (2015), 31(5), 746-755
CODEN: CRCUED; ISSN: 1005-9040
DIGITAL OBJECT ID: 10.1007/s40242-015-5166-3
PUBLISHER: Jilin University
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB A series of novel 4-phenoxyquinoline derivs. contg. 3-amino-2-cyano-acrylamide framework was designed and synthesized, and the in vitro cytotoxic activities of them against five cancer cell lines(HT-29, H460, A549, MKN-45, and U87MG) were evaluated. Most of the compds. exhibited moderate-to-significant cytotoxicity and high selectivity against one or more cell lines as compared with Foretinib. The studies of their preliminary structure-activity relationships(SARs) indicate that the compds. containing Me groups, especially Me groups at 4-position of the Ph ring(moiety B) are more effective. Among them, compound 36 shows the most potent antitumor activities with IC50 values of 0.04, 0.09, 0.67, 0.39 and 1.10 μmol/L against HT-29, H460, A549, MKN-45 and U87MG cell lines, resp.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(design, synthesis and pharmacol. evaluation of novel 4-phenoxyquinoline derivs. as potential antitumor agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

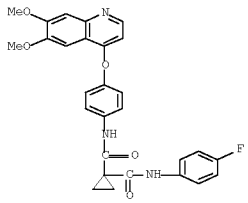


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 78 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1496569 CAPLUS Full-text
TITLE: Oral adverse events in cancer patients treated with VEGFR-directed multitargeted tyrosine kinase inhibitors
AUTHOR(S): Yuan, Anna; Kurtz, Sharyn L.; Barysauskas, Constance M.; Pilotte, Amy P.; Wagner, Andrew J.; Treister, Nathaniel S.
CORPORATE SOURCE: Division of Oral Medicine, Brigham and Women's Hospital, Boston, MA, 02115, USA
SOURCE: Oral Oncology (2015), 51(11), 1026-1033
CODEN: EJCCER; ISSN: 1368-8375
DIGITAL OBJECT ID: 10.1016/j.oraloncology.2015.09.003
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB This study characterized the incidence and clin. features of oral adverse events among cancer patients who received VEGFR-directed multitargeted tyrosine kinase inhibitor (VR-TKI) therapies.Electronic medical records of adult cancer patients treated with sunitinib, sorafenib, regorafenib, pazopanib, cabozantinib, imatinib, and bevacizumab therapy at Dana-Farber Cancer Institute from 2009 to 2012 were reviewed. Data collected included patient characteristics, oral and non-oral adverse events, and time to onset. Time oral adverse event-free was the primary outcome.A total of 747 patients with 806 individual courses of therapy were treated for a median of 3.9 mo with sunitinib (n = 161), sorafenib (n = 172), regorafenib (n = 15), pazopanib (n = 132), cabozantinib (n = 23), imatinib (n = 144), or bevacizumab (n = 159) for lung cancer (21%), gastrointestinal stromal tumor (15%), and metastatic renal cell carcinoma (13%). An oral adverse event was reported in 23.7% of patients at a median of 1.9 mo after starting therapy. The most commonly reported oral adverse event was oral mucosal sensitivity (dysesthesia), occurring in 12% of patients, typically without clin. findings. Multivariate models showed patients who received VR-TKI therapy were at greater risk of any oral adverse event compared with patients treated with imatinib or bevacizumab. Patients receiving VR-TKI therapy who developed an oral adverse event were also at increased risk for hand-foot skin reaction (15.9%).VR-TKI associated oral adverse events are characterized primarily by dysesthesia with lack of clin. signs. Oral dysesthesia is more commonly associated with VR-TKIs than with bevacizumab or imatinib. Management is largely empirical and requires further investigation.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oral adverse events in cancer patients treated with VEGFR-directed multitargeted tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



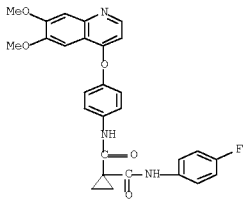
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 79 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1474667 CAPLUS Full-text
DOCUMENT NUMBER: 164:415926
TITLE: Antioxidant and Anticoagulant Status Were Improved by Personalized Dietary Intervention Based on Biochemical and Clinical Parameters in Cancer Patients
AUTHOR(S): Lee, Ga-Yi; Lee, Jong Jyun; Lee, Seung-Min
CORPORATE SOURCE: Program of Clinical Nutrition, Yonsei Graduate School of Human Environmental Sciences, Seoul, S. Korea
SOURCE: Nutrition and Cancer (2015), 67(7), 1083-1092
CODEN: NUCADQ; ISSN: 0163-5581
DIGITAL OBJECT ID: 10.1080/01635581.2015.1073754
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB We investigated whether personalized dietary intervention could improve clin. measurements such as immune cell-mediated cytotoxicity, serum albumin, derivs. of reactive oxygen metabolites (D-ROMS), D-dimer, and fibrinogen. Cancer patients received either a treatment support diet (TD, for those with chemotherapy), or a remission support diet (RD; for those in remission) for at least 3 wk (21-61 days). Both diets were low glycemic, low fat, and high plant protein diets; the diet for the TD group contained an addnl. 0.5 servings of protein. Based on clin. values, addnl. amts. of garlic, onion, tomato, shiitake, rice bran, kale, blueberry, pineapples, and/or turmeric powder were provided in regular meals. Estimated daily intake of protein, plant fat, garlic, onion, allicin, and quercetin was greater in the TD compared to the RD. An increased intake of vitamin A, vitamin C, vitamin E and selenium and a reduction in D-dimer were noted compared to baseline diets in both groups. A decrease in D-ROMS in the RD and an increase in albumin and an increased tendency in cytotoxicity in the TD were observed In conclusion, personalized diets with supplemented functional ingredients improved antioxidant status and/or anticoagulant activity in cancer patients undergoing chemotherapy and in remission.

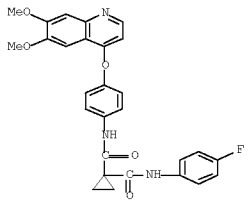
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant and anticoagulant status were improved by personalized

dietary intervention based on biochem. and clin. parameters in cancer patients)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

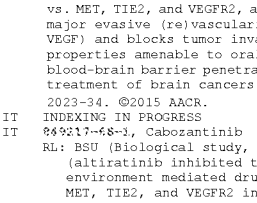
L8 ANSWER 80 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1456151 CAPLUS Full-text
DOCUMENT NUMBER: 163:418831
TITLE: Structural insight into selectivity and resistance profiles of ROS1 tyrosine kinase inhibitors
AUTHOR(S): Davare, Monika A.; Vellore, Nadeem A.; Wagner, Jacob P.; Eide, Christopher A.; Goodman, James R.; Drilon, Alexander; Deininger, Michael W.; O'Hare, Thomas; Druker, Brian J.
CORPORATE SOURCE: Knight Cancer Institute, Oregon Health & Science University, Portland, OR, 97239, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2015), 112(39), E5381-E5390
CODEN: PNASA6; ISSN: 0027-8424
DIGITAL OBJECT ID: 10.1073/pnas.1515281112
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Oncogenic ROS1 fusion proteins are mol. drivers in multiple malignancies, including a subset of non-small cell lung cancer (NSCLC). The phylogenetic proximity of the ROS1 and anaplastic lymphoma kinase (ALK) catalytic domains led to the clin. repurposing of the Food and Drug Administration (FDA)-approved ALK inhibitor crizotinib as a ROS1 inhibitor. Despite the antitumor activity of crizotinib observed in both ROS1- and ALK-rearranged NSCLC patients, resistance due to acquisition of ROS1 or ALK kinase domain mutations has been observed clin., spurring the development of second-generation inhibitors. Here, we profile the sensitivity and selectivity of seven ROS1 and/or ALK inhibitors at various levels of clin. development. In contrast to crizotinib's dual ROS1/ALK activity, cabozantinib (XL-184) and its structural analog foretinib (XL-880) demonstrate a striking selectivity for ROS1 over ALK. Mol. dynamics simulation studies reveal structural features that distinguish the ROS1 and ALK kinase domains and contribute to differences in binding site and kinase selectivity of the inhibitors tested. Cell-based resistance profiling studies demonstrate that the ROS1-selective inhibitors retain efficacy against the recently reported CD74-ROS1G2032R mutant whereas the dual ROS1/ALK inhibitors are ineffective. Taken together, inhibitor profiling and stringent characterization of the structure-function differences between the ROS1 and ALK kinase domains will facilitate future rational drug design for ROS1- and ALK-driven NSCLC and other malignancies.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural insight into selectivity and resistance profiles of ROS1 tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L8 ANSWER 81 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1433158 CAPLUS Full-text
TITLE: Altiratinib Inhibits Tumor Growth, Invasion, Angiogenesis, and Microenvironment-Mediated Drug Resistance via Balanced Inhibition of MET, TIE2, and VEGFR2
AUTHOR(S): Smith, Bryan D.; Kaufman, Michael D.; Leary, Cynthia B.; Turner, Benjamin A.; Wise, Scott C.; Ahn, Yu Mi; Booth, R. John; Caldwell, Timothy M.; Ensinger, Carol L.; Hood, Molly M.; Lu, Wei-Ping; Patt, Tristan W.; Patt, William C.; Rutkoski, Thomas J.; Samarakoon, Thiwanka; Telikepalli, Hanumaiah; Vogeti, Lakshminarayana; Vogeti, Subha; Yates, Karen M.; Chun, Lawrence; Stewart, Lance J.; Clare, Michael; Flynn, Daniel L.

CORPORATE SOURCE: Deciphera Pharmaceuticals, Lawrence, KS, USA
SOURCE: Molecular Cancer Therapeutics (2015), 14(9), 2023-2034
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-14-1105
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Altiratinib (DCC-2701) was designed based on the rationale of engineering a single therapeutic agent able to address multiple hallmarks of cancer (1). Specifically, altiratinib inhibits not only mechanisms of tumor initiation and progression, but also drug resistance mechanisms in the tumor and microenvironment through balanced inhibition of MET, TIE2 (TEK), and VEGFR2 (KDR) kinases. This profile was achieved by optimizing binding into the switch control pocket of all three kinases, inducing type II inactive conformations. Altiratinib durably inhibits MET, both wild-type and mutated forms, in vitro and in vivo. Through its balanced inhibitory potency vs. MET, TIE2, and VEGFR2, altiratinib provides an agent that inhibits three major evasive (re)vascularization and resistance pathways (HGF, ANG, and VEGF) and blocks tumor invasion and metastasis. Altiratinib exhibits properties amenable to oral administration and exhibits substantial blood-brain barrier penetration, an attribute of significance for eventual treatment of brain cancers and brain metastases. Mol Cancer Ther; 14(9); 2023-34. ©2015 AACR.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(altiratinib inhibited tumor growth, invasion, angiogenesis, and micro environment mediated drug resistance through balanced inhibition of MET, TIE2, and VEGFR2 in human cancer cell lines and mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

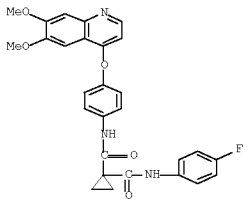


REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 82 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1392691 CAPLUS Full-text
DOCUMENT NUMBER: 163:345656
TITLE: Use of ibrutinib to treat EGFR mutant cancer
INVENTOR(S): Fang, Bingliang; Roth, Jack A.; Wang, Michael; Wang, Li; Wu, Shuhong; Heymach, John V.; Swisher, Stephen G.; Hofstetter, Wayne L.
PATENT ASSIGNEE(S): The University of Texas System, USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015127234	A1	20150827	WO 2015-US16859	20150220
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2014-61942255 P 20140220
AB Provided herein are methods of using irreversible BTK inhibitors, such as, for example, ibrutinib (PCI-32765), to treat EGFR mutant cancers, HER2 amplified cancers, and/or HER2 overexpressing cancers. In certain aspects, the method further comprises administering at least a second anticancer therapy to the subject.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of ibrutinib to treat EGFR mutant cancer and combination with other therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 83 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1362724 CAPLUS Full-text
DOCUMENT NUMBER: 163:299275
TITLE: Preparation of crystalline solid forms of cabozantinib
INVENTOR(S): Aftab, Dana T.; Guz, Nathan; Lau, Stephen; Hamill, Noel; Walker, Tracy; Galbraith, Jana; Yau, Simon; Shah, Khalid
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

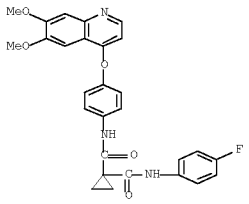
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015123639	A1	20150820	WO 2015-US16052	20150216

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61939985 P 20140214
AB The invention relates to novel cryst. solid forms of cabozantinib., and solvates thereof, including hydrates, that are useful for the treatment of cancer. Also disclosed are pharmaceutical compns. comprising the crystalline solid forms and processes for making the crystalline solid forms, as well as methods of using them for the treatment of cancer, particularly thyroid cancer, prostate cancer, hepatocellular cancer, renal cancer, and non-small cell lung carcinoma. The crystalline solid forms can be used to make the L-malate salt of cabozantinib.
IT [redacted], Cabozantinib S-malate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystalline solid forms of cabozantinib)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

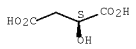
CRN 849217-68-1
CMF C28 H24 F N3 O5



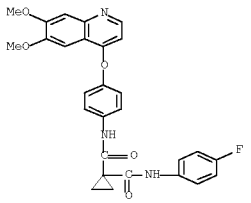
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

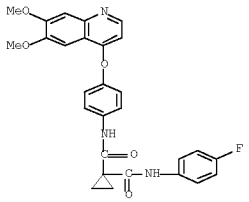


IT [redacted]
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of crystalline solid forms of cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 84 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1349511 CAPLUS Full-text
DOCUMENT NUMBER: 163:449411
TITLE: Identification of triazolo[4,5-b]pyrazine derivatives as hepatocyte growth factor receptor inhibitors through structure-activity relationships and molecular docking simulations
AUTHOR(S): Dong, Minghui; Ren, Yujie; Gao, Xiaodong
CORPORATE SOURCE: School of Chemical and Environmental Engineering, Shanghai Institute of Technology, Shanghai, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2015), 25(19), 4118-4126
CODEN: BMCLE8; ISSN: 0960-894X
DIGITAL OBJECT ID: 10.1016/j.bmcl.2015.08.025
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB C-MET is a receptor tyrosine kinase and potential oncol. target for cancer therapy. The activities of 1,2,3-triazolo[4,5-b]pyrazine series of c-MET inhibitors were analyzed according to the three-dimensional quant. structure-activity relationship and mol. docking methods. The results indicated that the hydrophobic and electrostatic fields play key roles in activity and QSAR model was reliable enough for activity prediction. Moreover, the docking results do validate the predicted 3D-QSAR scores, vital residues Asp1222, Asp1231, Met1160, Tyr1259 and Tyr1230 found in binding site. Four new c-MET inhibitor analogs designed in this Letter which are being currently synthesized by our labs.
IT [redacted], Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triazolo-pyrazine derivs. identification as HGFR inhibitors through SAR and mol. docking simulation)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

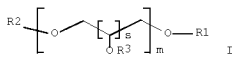
L8 ANSWER 85 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1315537 CAPLUS Full-text
DOCUMENT NUMBER: 163:323284
TITLE: Composition for vectorizing an anti-cancer agent
INVENTOR(S): Robic, Caroline; Mayer, Jean-Francois
PATENT ASSIGNEE(S): Guerbet, Fr.
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015118113	A1	20150813	WO 2015-EP52527	20150206

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

FR 3017295	A1	20150814	FR 2014-50972	20140207

PRIORITY APPLN. INFO.: FR 2014-50972 A 20140207
GI

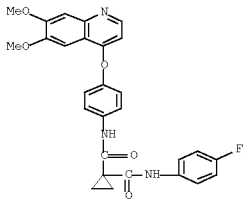


AB The invention relates to a stable water-in-oil emulsion compn. contg.: 20% to 40% (volume/volume) aqueous phase in the form of droplets and containing an anti-cancer agent; and 60% to 80% (volume/volume) lipid phase containing an iodized oil and at least one surfactant, having formula I, in a proportion, of surfactant mass relative to the total volume of the composition, of 0.3% to 5%, formula II for said surfactant being the following in which: s has a value of 0 or 1; m is a whole number from 2 to 30; R1 is a formula I grouping wherein n is a whole number from 4 to 10, o is a whole number from 1 to 4, p is a whole number from 3 to 7; q is a whole number from 2 to 10, and r has a value of 0 or 1; R2 is a hydrogen atom or is identical to R1; and each R3 is, sep., a hydrogen atom or is identical to R1. The invention also relates to an emulsion obtained from said composition, to the preparing method thereof, and to the use thereof for treating cancer and the metastases thereof. An emulsion containing 50 mg doxorubicin, 1% PGPR in Lipidol, and 2.5 mL Xenetix 250 was prepared

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition for vectorizing anti-cancer agent)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 86 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1289334 CAPLUS Full-text

DOCUMENT NUMBER: 163:438199

TITLE: Response to MET Inhibitors in Patients with Stage IV Lung Adenocarcinomas Harboring MET Mutations Causing Exon 14 Skipping

AUTHOR(S): Paik, Paul K.; Drilon, Alexander; Fan, Pang-Dian; Yu, Helena; Rekhtman, Natasha; Ginsberg, Michelle S.; Borsu, Laetitia; Schultz, Nikolaus; Berger, Michael F.; Rudin, Charles M.; Ladanyi, Marc

CORPORATE SOURCE: Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

SOURCE: Cancer Discovery (2015), 5(8), 842-849
CODEN: CDAIB2; ISSN: 2159-8274

DIGITAL OBJECT ID: 10.1158/2159-8290.CD-14-1467

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

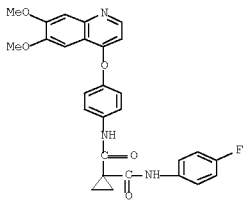
LANGUAGE: English

AB Mutations in the MET exon 14 RNA splice acceptor and donor sites, which lead to exon skipping, deletion of the juxtamembrane domain containing the CBL E3-ubiquitin ligase-binding site, and decreased turnover of the resultant aberrant MET protein, were previously reported to be oncogenic in preclin. models. We now report responses to the MET inhibitors crizotinib and cabozantinib in four patients with stage IV lung adenocarcinomas harboring mutations leading to MET exon 14 skipping, highlighting a new therapeutic strategy for the 4% of lung adenocarcinoma patients whose tumors harbor this previously underappreciated genetic alteration. Significance: Oncogenic mutations in the MET exon 14 splice sites that cause exon 14 skipping occur in 4% of lung adenocarcinomas. We report responses to the MET inhibitors crizotinib and cabozantinib in patients with lung adenocarcinomas harboring MET exon 14 splice site mutations, identifying a new potential therapeutic target in this disease. Cancer Discov; 5(8); 842-9. ©2015 AACR. See related commentary by Ma, p. 802. See related article by Frampton et al., p. 850. This article is highlighted in the In This Issue feature, p. 783.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response to MET inhibitors in patients with stage IV lung adenocarcinomas harboring MET mutations causing exon 14 skipping)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 87 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1265280 CAPLUS Full-text

TITLE: Pharmacokinetic (PK) drug interaction studies of cabozantinib: Effect of CYP3A inducer rifampin and inhibitor ketoconazole on cabozantinib plasma PK and effect of cabozantinib on CYP2C8 probe substrate rosiglitazone plasma PK

AUTHOR(S): Nguyen, Linh; Holland, Jaymes; Miles, Dale; Engel, Caroline; Benrimoh, Natacha; O'Reilly, Terry; Lacy, Steven

CORPORATE SOURCE: Exelixis, Inc., So. San Francisco, CA, USA

SOURCE: Journal of Clinical Pharmacology (2015), 55(9), 1012-1023
CODEN: JCPCBR; ISSN: 0091-2700

DIGITAL OBJECT ID: 10.1002/jcph.510

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

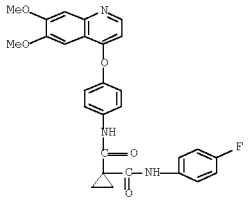
AB Cabozantinib is a small-mol. tyrosine kinase inhibitor that has been approved for the treatment of patients with progressive, metastatic medullary thyroid cancer. In vitro data indicate that (1) cytochrome P 450 (CYP) 3A4 is the primary CYP isoenzyme involved in the metabolism of cabozantinib, and (2) CYP2C8 is the CYP isoenzyme most potently inhibited by cabozantinib with potential for in vivo inhibition at clin. relevant plasma exposures. Pharmacokinetic (PK) drug-drug interactions (DDIs) were evaluated clin. between cabozantinib and (1) a CYP3A inducer (rifampin) in healthy volunteers, (2) a CYP3A inhibitor (ketoconazole) in healthy volunteers, and (3) a CYP2C8 substrate (rosiglitazone) in patients with solid tumors. Compared with cabozantinib given alone, coadministration with rifampin resulted in a 4.3-fold higher plasma clearance (CL/F) of cabozantinib and a 77% decrease in cabozantinib plasma AUC0-inf, whereas coadministration with ketoconazole decreased cabozantinib CL/F by 29% and increased cabozantinib AUC0-inf by 38%. Chronic coadministration with cabozantinib resulted in no significant effect on rosiglitazone plasma Cmax, AUC0-24, or AUC0-inf. In summary, chronic use of strong CYP3A inducers and inhibitors should be avoided when cabozantinib is administered, and cabozantinib at clin. relevant exposures is not anticipated to markedly affect the PK of concomitant medications via CYP enzyme inhibition.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetic drug interaction studies of cabozantinib, effect of CYP3A inducer rifampin and inhibitor ketoconazole on cabozantinib plasma PK and effect of cabozantinib on CYP2C8 probe substrate rosiglitazone plasma pharmacokinetics)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 88 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1258933 CAPLUS Full-text

DOCUMENT NUMBER: 164:142494

TITLE: Small-molecule kinase inhibitors: an analysis of FDA-approved drugs

AUTHOR(S): Wu, Peng; Nielsen, Thomas E.; Clausen, Mads H.

CORPORATE SOURCE: Department of Chemistry, Technical University of Denmark, Kgs. Lyngby, DK-2800, Den.

SOURCE: Drug Discovery Today (2016), 21(1), 5-10
CODEN: DDTOFS; ISSN: 1359-6446

DIGITAL OBJECT ID: 10.1016/j.drudis.2015.07.008

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; (online computer file)

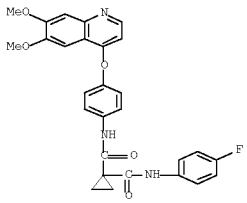
LANGUAGE: English

AB Small-mol. kinase inhibitors (SMKIs), 28 of which are approved by the US Food and Drug Administration (FDA), have been actively pursued as promising targeted therapeutics. Here, we assess the key structural and physicochem. properties, target selectivity and mechanism of function, and therapeutic indications of these approved inhibitors. Our anal. showed that >30% of approved SMKIs have a mol. weight (MW) exceeding 500 and all have a total ring count of between three and five. The assumption that type II inhibitors tend to be more selective than type I inhibitors has been proved to be unreliable. Although previous SMKI research was concentrated on tyrosine kinase inhibitors for cancer treatment, recent progress indicates diversification of SMKI research in terms of new targets, mechanistic types, and therapeutic indications.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural and physicochem. properties, target selectivity and mechanism of function therapeutic indications of FDA approved small-mol. kinase inhibitor)

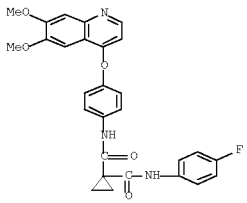
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 89 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1256269 CAPLUS Full-text
TITLE: 2ME2 inhibits the activated hypoxia-inducible pathways by cabozantinib and enhances its efficacy against medullary thyroid carcinoma
AUTHOR(S): Lin, Han; Jiang, Xian; Zhu, Huaqiang; Jiang, Wenjing; Dong, Xuesong; Qiao, Haiquan; Sun, Xueying; Jiang, Hongchi
CORPORATE SOURCE: Key Laboratory of Hepatosplenic Surgery, Department of General Surgery, The First Affiliated Hospital of Harbin Medical University, Harbin, 150001, Peop. Rep. China
SOURCE: Tumor Biology (2016), 37(1), 381-391
CODEN: TUMBEA; ISSN: 1010-4283
DIGITAL OBJECT ID: 10.1007/s13277-015-3816-1
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is a multi-targeted tyrosine kinase inhibitor targeting vascular endothelial growth factor (VEGF) receptor (VEGFR)-2, MET (c-Met, also called hepatocyte growth factor (HGF) receptor), and other receptor tyrosine kinases. Cabozantinib has recently been approved for treating advanced medullary thyroid carcinoma (MTC), but its long-term benefit remains uncertain and dose-dependent adverse events are very common. The present study has demonstrated that 2-methoxyestradiol (2ME2), an inhibitor of hypoxia-inducible factors (HIFs) and a promising anticancer agent under investigation in clin. trials, strengthens anticancer activities of cabozantinib against MTC cells in vitro and in vivo. The activated hypoxia-inducible pathways, which are mainly regulated by HIF-1, contribute to the resistance of hypoxic MTC cells to cabozantinib. Cabozantinib upregulated HIF-1α expression at translational levels and increased the expression of the downstream factors including VEGF, lactate dehydrogenase A (LDHA), HGF, and MET. 2ME2 corrected the activated pathways by cabozantinib through downregulating HIF-1α expression and inhibiting its nuclear translocation in hypoxic MTC cells. Administration of 2ME2 enhanced the efficacy of cabozantinib in suppressing the growth of MTC cell line xenografts and patient-derived xenografts established in mice. Given that 2ME2 targets insensitive hypoxic cancer cells to cabozantinib and can inhibit the activated pathways by cabozantinib, the present results warrant further investigation of 2ME2, particularly in combination with cabozantinib, for the treatment of MTC.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (2ME2 inhibits activated hypoxia-inducible pathways by cabozantinib and enhances its efficacy against medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 90 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1243654 CAPLUS Full-text
DOCUMENT NUMBER: 163:316612
TITLE: Biomarker TTF1 for predicting effect of c-met inhibitor
INVENTOR(S): Kim, Bo Gyou; Lee, Eunjin; Kim, Kyung Ah; Ahn, Tae Jin
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 92pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150212077	A1	20150730	US 2015-14604361	20150123
KR 2015088433	A	20150803	KR 2014-8733	20140124
PRIORITY APPLN. INFO.:			KR 2014-8733 A	20140124

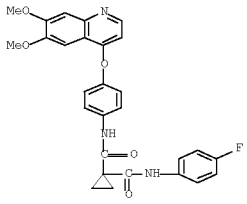
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A method of predicting an effect of a c-Met inhibitor and/or selecting a subject for application of a c-Met inhibitor using trefoil factor 1 (TFF1), a method of monitoring an effect of a c-Met inhibitor using TFF1, and a method of treating and/or preventing cancer including administering a c-Met inhibitor to the selected subject. Herein, the effect of a c-Met inhibitor may refer to the prevention, improvement, alleviation, and/or treatment of a c-Met related disease such as cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biomarker TTF1 for predicting effect of c-met inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

L8 ANSWER 91 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1226166 CAPLUS Full-text
TITLE: The study on synthetic technology of cabozantinib (S)-malate
AUTHOR(S): Qi, Baohui; He, Huan
CORPORATE SOURCE: Department of Bioengineering, Zhuhai Campus, Zunyi Medical College, Zhuhai, 519041, Peop. Rep. China
SOURCE: Guangdong Huagong (2014), 41(19), 22-23
CODEN: GHUAFI; ISSN: 1007-1865
PUBLISHER: Guangdong Huagong Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The cabozantinib(S)-malate, which was used for the treatment of locally advanced or metastatic progressive medullary thyroid cancer, was prepared from 3, 4-dimethoxyacetophenone by nitration, condensation, cyclization, chlorination and substitution, etc. In this synthetic route, raw materials were com. available, and reactive conditions were mild, and the operation was easy, and the yield was higher.
IT INDEXING IN PROGRESS
IT 1140909-48-3, Cabozantinib (S)-malate
RL: SPN (Synthetic preparation); PREP (Preparation)
(study on synthetic technol. of cabozantinib S-malate)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

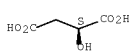
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

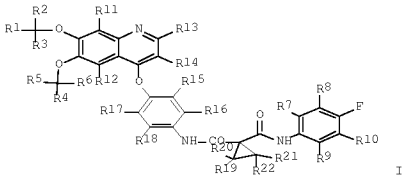
Absolute stereochemistry. Rotation (-).



L8 ANSWER 92 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1213912 CAPLUS Full-text
DOCUMENT NUMBER: 163:271103
TITLE: Preparation of deuterated cabozantinib derivatives and their application as anticancer agents
INVENTOR(S): Chen, Xinghai; Peng, Wei; Parker, Omar; Zheng, Feiming; Fu, Yong
PATENT ASSIGNEE(S): Shanghai Shengkao Pharmaceutical Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 35pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104788372	A	20150722	CN 2014-10361351	20140725
PRIORITY APPLN. INFO.:			CN 2014-10361351	20140725
OTHER SOURCE(S):	MARPAT 163:271103			

GI

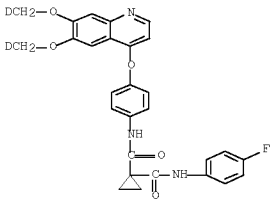


I

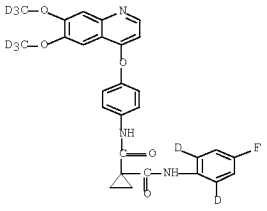
AB The invention is related to the prepn. of deuterated cabozantinib derivs. I and their application as anticancer agents. The invention compound I, wherein R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, and R22 are H or D independently and contain at least one D and their pharmaceutically acceptable salts, crystalline hydrates, solvates, prodrugs, single crystal or polymorph are claimed. Compound I was prepared by multi-step procedure (procedure given). The deuterated cabozantinib derivs. have slow decomposition in vivo, thereby reducing adverse metabolism of drugs. The invention compds. were evaluated for their anticancer activity.

IT 1802168-46-2P 1802168-48-4P 1802168-49-5P
1802168-50-8P 1802168-51-9P 1802168-52-0P
1802168-53-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of deuterated cabozantinib derivs. and their application as anticancer agents)

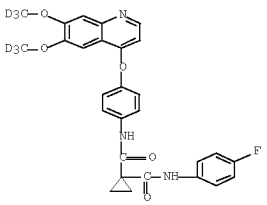
RN 1802168-46-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



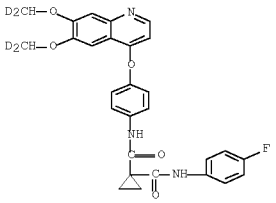
RN 1802168-50-8 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)- (CA INDEX NAME)



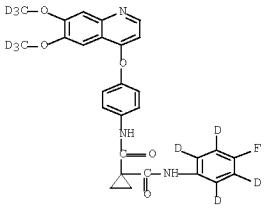
RN 1802168-51-9 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)- (CA INDEX NAME)



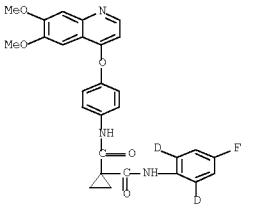
RN 1802168-48-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d2)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



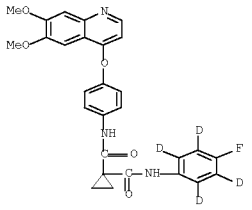
RN 1802168-49-5 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 1802168-52-0 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)- (CA INDEX NAME)



RN 1802168-53-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)- (CA INDEX NAME)

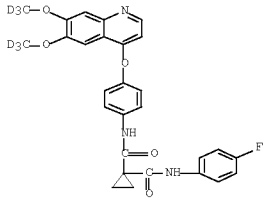


IT 1802168-54-2P 1802168-55-3P 1802168-56-4P
1802168-57-5P 1802168-58-6P 1802168-59-7P
1802168-60-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of deuterated cabozantinib derivs. and their application as anticancer agents)

RN 1802168-54-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with
N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

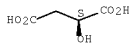
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CMF C28 H18 D6 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

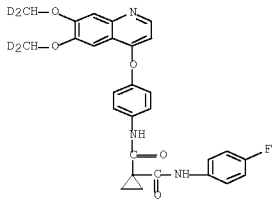
Absolute stereochemistry. Rotation (-).



RN 1802168-55-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with
N-[4-[[6,7-di(methoxy-d2)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

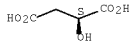
CRN 1802168-48-4
CMF C28 H20 D4 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

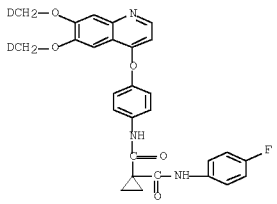
Absolute stereochemistry. Rotation (-).



RN 1802168-56-4 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with
N-[4-[[6,7-di(methoxy-d)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

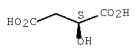
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CMF C28 H22 D2 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

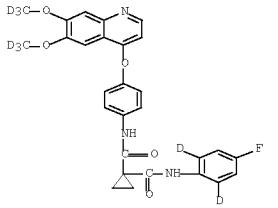
Absolute stereochemistry. Rotation (-).



RN 1802168-57-5 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with
N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

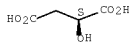
CRN 1802168-50-8
CMF C28 H16 D8 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

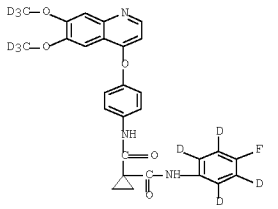
Absolute stereochemistry. Rotation (-).



RN 1802168-58-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with
N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

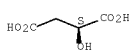
CRN 1802168-51-9
CMF C28 H14 D10 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

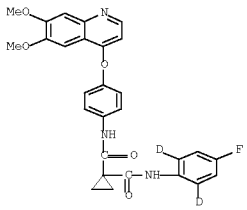


RN 1802168-59-7 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

CRN 1802168-52-0
CMF C28 H22 D2 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

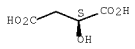
Absolute stereochemistry. Rotation (-).

Linh
CORPORATE SOURCE: Genentech (A member of the Roche Group), South San Francisco, CA, USA
SOURCE: Clinical Pharmacokinetics (2016), 55(1), 93-105
CODEN: CPKNDH; ISSN: 0312-5963
DIGITAL OBJECT ID: 10.1007/s40262-015-0295-x
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background and Objectives: Cabozantinib is a tyrosine kinase inhibitor approved in the USA and EU for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC). The indicated cabozantinib dose is 140 mg/day, with dose modifications allowed for patients who develop adverse events (AEs). The anal. objective was to develop a population pharmacokinetic (PopPK) model in MTC patients and to use the model for exposure-response (ER) anal. of dose modifications. Methods: A PopPK model for cabozantinib was developed using data from three clin. trials (2079 evaluations from 289 patients), including a randomized, double-blind, placebo-controlled phase III study of patients with progressive, metastatic MTC. The PopPK model predictions [model-predicted steady-state area under the plasma concentration-time curve (AUCss,pred)] were used for an ER anal. of the time to first dose modification. Results: The final PopPK model was a one-compartment model with first-order absorption and first-order elimination. Estimated cabozantinib apparent oral clearance (CL/F) and apparent volume of distribution (Vc/F) were 106 L/day [±2.98 % relative standard error (RSE)] (males) and 349 L (±2.73 % RSE), resp. CL/F was reduced by 22 % (to 83 L/day) in females. Sex and body mass index (BMI) were significant covariates that combined contributed 15 % to the variability in cabozantinib CL/F, but did not warrant dose adjustment. Higher cabozantinib AUCss,pred was correlated to an increased risk of early dose modification and a lower average dose through to Day 85. Early cabozantinib dose modification was not associated with a reduction in progression-free survival (PFS). Conclusion: A PopPK model was developed for cabozantinib pharmacokinetics in MTC patients. Higher cabozantinib exposure was associated with earlier first dose modification and a lower average administered dose through to Day 85. Early first dose modification did not appear to impact PFS.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(population pharmacokinetic model of cabozantinib in patients with medullary thyroid carcinoma and its application to exposure)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

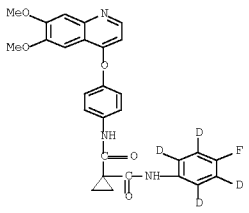


RN 1802168-60-0 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

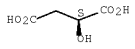
CRN 1802168-53-1
CMF C28 H20 D4 F N3 O5



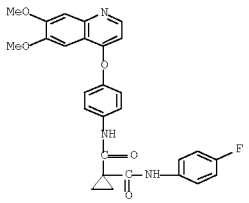
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L8 ANSWER 93 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1181814 CAPLUS Full-text
TITLE: Population Pharmacokinetic Model of Cabozantinib in Patients with Medullary Thyroid Carcinoma and Its Application to an Exposure-Response Analysis
AUTHOR(S): Miles, Dale; Jumbe, Nelson L.; Lacy, Steven; Nguyen,



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 94 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1173698 CAPLUS Full-text
DOCUMENT NUMBER: 163:302461
TITLE: Compositions and methods for the treatment of intraocular neovascularization and/or leakage using tyrosine kinase inhibitors
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 12pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150196649	A1	20150716	US 2015-14593704	20150109
WO 2015108787	A2	20150723	WO 2015-US10867	20150109
WO 2015108787	A3	20151112		

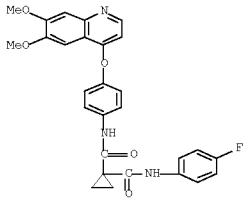
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-61928061 P 20140116
US 2014-61969861 P 20140325
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides compns. and methods for the treatment of intraocular neovascularization and/or leakage including wet age-related macular degeneration. The compns. preferably use tyrosine kinase inhibitors with an IC50 for VEGFR2 of 20 nanomolar or less and an IC50 for c-MET of 20 nanomolar or less.

IT 849217-68-1, Cabozantinib 1235470-36-6 1642298-56-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treatment of intraocular neovascularization and/or leakage using tyrosine kinase inhibitors of VEGFR2 and c-MET)

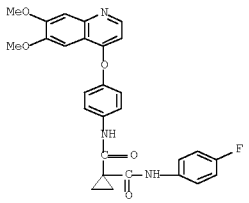
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1235470-36-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

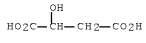
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

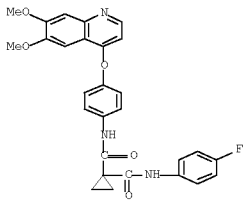
CRN 6915-15-7
CMF C4 H6 O5



RN 1642298-56-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 75-75-2
CMF C H4 O3 S



L8 ANSWER 95 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1169349 CAPLUS Full-text
DOCUMENT NUMBER: 163:218113
TITLE: Preparation of heterocyclic modulators of lipid synthesis for use against cancer and viral infections
INVENTOR(S): Wagman, Allan S.; Johnson, Russell J.; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.; Duke, Greg; Ohol, Yamini; Heuer, Timothy; O'Farrell, Marie
PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015105860	A1	20150716	WO 2015-US10459	20150107
WO 2015105860	A9	20160204		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

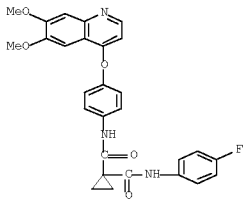
PRIORITY APPLN. INFO.: US 2014-61924520 P 20140107
OTHER SOURCE(S): CASREACT 163:218113; MARPAT 163:218113
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [LAr = II-IV; Ar = V; R1 = H, CN, halo, etc.; R2 = H, halo, alkyl; R3 = H or F; R21 = H, halo, alkyl, etc.; R22 = H, halo, alkyl; R24 = alkoxy, O(alkylene)alkoxy, cycloalkoxy, etc.; R25 = H, halo, alkyl, etc.; with the provisos], useful for treating conditions characterized by dysregulation of a fatty acid synthase pathway, were prepared E.g., a multi-step synthesis of VI, starting from Me propanoate and Me formate, was described. Exemplified compds. I were evaluated for their FASN inhibition (data given for representative compds. I). Pharmaceutical composition comprising I was disclosed.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of heterocyclic modulators of lipid synthesis for use against cancer and viral infections)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 96 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:1169171 CAPLUS Full-text
DOCUMENT NUMBER: 163:217976
TITLE: Preparation of tertiary amines and amine oxides as LXR agonists
INVENTOR(S): Martinez, Eduardo J.; Kaiser, Bernd; Tavazoie, Sohail F.; Kurth, Isabel; Gonsalves, Foster Casimir; Darst, David M., Jr.; Tavazoie, Masoud Fakhr
PATENT ASSIGNEE(S): Rgenix, Inc., USA
SOURCE: PCT Int. Appl., 163pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

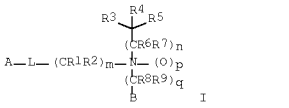
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015106164	A1	20150716	WO 2015-US10909	20150109

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW

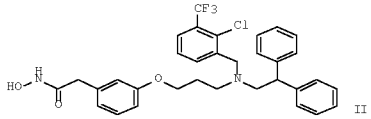
PRIORITY APPLN. INFO.: US 2014-61926150 P 20140110

OTHER SOURCE(S): CASREACT 163:217976; MARPAT 163:217976

GI



I



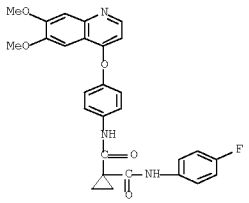
II

AB This invention features compds. of formula I that modulate the activity of liver X receptors, pharmaceutical compns. including the compds. of the invention, and methods of utilizing those compns. for modulating the activity of liver X receptors in the treatment of cancer. Compds. of formula I wherein A is substituted Ph, (un)substituted azacyclyl, and (un)substituted oxobenzopyranyl; L is absent, O, S, amino and CR4R5; m is 2, 3, 4, 5, 6, 7 and 8;, n, p and q are independently 0 and 1; R1, R2, R6, R7, R8 and R9 are independently H, OH, halo, amino, thio, etc.; R3 is H, OH, amino, (un)substituted Cl-6 alkyl, etc.; R4 and R6 are independently H, OH, halo, amino, thio, etc.; and pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by reductive amination of 2-chloro-3-trifluoromethylbenzaldehyde with 2,2-diphenethylamine followed by alkylation with 1,3-dibromopropane; the resulting (3-bromopropyl)({[2-chloro-3-(trifluoromethyl)phenyl]methyl})(2,2-diphenylethyl)amine underwent etherification with Me 3-hydroxyphenylacetate to give Me 2-{3-[3-({[2-chloro-3-(trifluoromethyl)phenyl]methyl}-(2,2-diphenylethyl)- amino)-propoxy]phenyl}acetate, which underwent amidation with hydroxylamine hydrochloride to give compound II. The invention compds. were evaluated for their LXR agonistic activity. From the assay it was determine that compound exhibited ApoE induction . 80% at 1 μM and > 40 % at 10 μM, and EC50 value of 1.0 μM.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of tertiary amines and amine oxides as LXR agonists)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 97 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1144766 CAPLUS Full-text

DOCUMENT NUMBER: 164:320926

TITLE: Salvage systemic therapy for advanced urothelial carcinoma: on the cusp of a sea change?

AUTHOR(S): Sonpavde, Guru; Bellmunt, Joaquim

CORPORATE SOURCE: University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, AL, USA

SOURCE: Oncologist (2015), 20(5), 461-463
CODEN: OCOLF6; ISSN: 1083-7159

DIGITAL OBJECT ID: 10.1634/theoncologist.2015-0077

PUBLISHER: AlphaMed Press

DOCUMENT TYPE: Journal

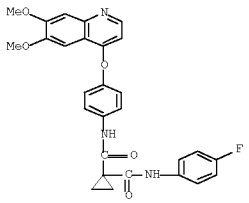
LANGUAGE: English

AB This paper studies about the salvage systemic therapy for advanced urothelial carcinoma.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on salvage systemic therapy for advanced urothelial carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 98 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1144752 CAPLUS Full-text

DOCUMENT NUMBER: 163:384755

TITLE: Prospective comprehensive genomic profiling of advanced gastric carcinoma cases reveals frequent clinically relevant genomic alterations and new routes for targeted therapies

AUTHOR(S): Ali, Siraj M.; Sanford, Eric M.; Klempner, Samuel J.; Rubinson, Douglas A.; Wang, Kai; Palma, Norma A.; Chmielecki, Juliann; Yelensky, Roman; Palmer, Gary A.; Morosini, Deborah; Lipson, Doron; Catenacci, Daniel V.; Braiteh, Fadi; Erlich, Rachel; Stephens, Philip J.; Ross, Jeffrey S.; Ou, Sai-Hong Ignatius; Miller, Vincent A.

CORPORATE SOURCE: Foundation Medicine Inc., Cambridge, MA, USA

SOURCE: Oncologist (2015), 20(5), 499-507
CODEN: OCOLF6; ISSN: 1083-7159

DIGITAL OBJECT ID: 10.1634/theoncologist.2014-0378

PUBLISHER: AlphaMed Press

DOCUMENT TYPE: Journal

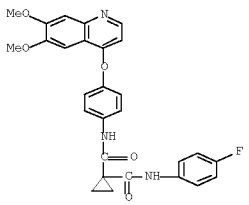
LANGUAGE: English

AB Background: Gastric cancer (GC) is a major global cancer burden and the second most common cause of global cancer-related deaths. The addition of anti-ERBB2 (HER2) targeted therapy to chemotherapy improves survival for ERBB2-amplified advanced GC patients; however, the majority of GC patients do not harbor this alteration and thus cannot benefit from targeted therapy under current practice paradigms. Materials and Methods: Prospective comprehensive genomic profiling of 116 predominantly locally advanced or metastatic (90.0%) gastric cancer cases was performed to identify genomic alterations (GAs) associated with a potential response to targeted therapies approved by the U.S. Food and Drug Administration or targeted therapy-based clin. trials. Results: Overall, 78% of GC cases harbored one clin. relevant GA or more, with the most frequent alterations being found in TP53 (50%), ARID1A (24%), KRAS (16%), CDH1 (15%), CDKN2A (14%), CCND1 (9.5%), ERBB2 (8.5%), PIK3CA (8.6%), MLL2 (6.9%), FGFR2 (6.0%), and MET (6.0%). Receptor tyrosine kinase genomic alterations were detected in 20.6% of cases, primarily ERBB2, FGFR2, and MET amplification, with ERBB2 alterations evenly split between amplifications and base substitutions. Rare BRAF mutations (2.6%) were also observed One MET-amplified GC patient responded for 5 mo to crizotinib, a multitargeted ALK/ROS1/MET inhibitor. Conclusion: Comprehensive genomic profiling of GC identifies clin. relevant GAs that suggest benefit from targeted therapy including MET-amplified GC and ERBB2 base substitutions.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prospective comprehensive genomic profiling of advanced gastric carcinoma cases reveals frequent clin. relevant genomic alterations and new routes for targeted therapies)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 99 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1128572 CAPLUS Full-text

TITLE: Metabolism and disposition of cabozantinib in healthy male volunteers and pharmacologic characterization of its major metabolites

AUTHOR(S): Lacy, Steven; Hsu, Bih; Miles, Dale; Aftab, Dana; Wang, Ronghua; Nguyen, Linh

CORPORATE SOURCE: Department of Non-Clinical Development, Exelixis, Inc., South San Francisco, CA, USA

SOURCE: Drug Metabolism & Disposition (2015), 43(8), 1190-1207
CODEN: DMDSAI; ISSN: 1521-009X

DIGITAL OBJECT ID: 10.1124/dmd.115.063610

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

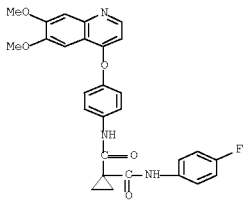
AB Metab. and excretion of cabozantinib, an oral inhibitor of receptor tyrosine kinases, was studied in 8 healthy male volunteers after a single oral dose of 175 mg cabozantinib l-malate containing 14C-cabozantinib (100 μCi/subject). Total mean radioactivity recovery within 48 days was 81.09%; radioactivity was eliminated in feces (53.79%) and urine (27.29%). Cabozantinib was extensively metabolized with 17 individual metabolites identified by liquid chromatog.-tandem mass spectrometry (LC-MS/MS) in plasma, urine, and feces. Relative plasma radioactivity exposures (analyte AUC0-t/total AUC0-t for cabozantinib + major metabolites) were 27.2, 25.2, 32.3, 7, and 6% for cabozantinib and major metabolites monohydroxy sulfate (EXEL-1646), 6-desmethyl amide cleavage product sulfate (EXEL-1644), N-oxide (EXEL-5162), and amide cleavage product (EXEL-5366), resp. Comparable relative plasma exposures determined by LC-MS/MS anal. were 32.4, 13.8, 45.9, 4.9, and 3.1%, resp. These major metabolites each possess in vitro inhibition potencies ≤1/10th of parent cabozantinib against the targeted kinases MET, RET, and VEGFR2/KDR. In an in vitro cytochrome P 450 (CYP) panel, cabozantinib and EXEL-1644 both inhibited most potently CYP2C8 (Kiapp = 4.6 and 1.1 μM, resp.). In an in vitro drug transporter panel, cabozantinib inhibited most potently MATE1 and MATE2-K (IC50 = 5.94 and 3.12 μM, resp.) and was a MRP2 substrate; EXEL-1644 inhibited most potently OAT1, OAT3, OATP1B1, MATE1, and OATP1B3 (IC50 = 4.3, 4.3, 6.1, 16.7, and 20.6 μM, resp.) and was a substrate of MRP2, OAT3, OATP1B1, OATP1B3, and possibly P-gp. Therefore, cabozantinib appears to be the primary pharmacol. active circulating analyte, whereas both cabozantinib and EXEL-1644 may represent potential for drug-drug interactions.

IT INDEXING IN PROGRESS

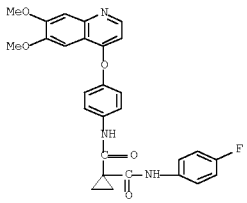
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolism, disposition and pharmacokinetics of cabozantinib and its biotransformation products in healthy male volunteers and pharmacol. characterization of its major metabolites)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 101 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1124138 CAPLUS Full-text

DOCUMENT NUMBER: 163:187706

TITLE: Biomarker for predicting or monitoring efficacy of c-Met inhibitor

INVENTOR(S): Jung, Soo Yeon; Shim, Seon Hui; Song, Yun Jeong; Yoo, Hyeon-Seok

PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea

SOURCE: Eur. Pat. Appl., 147pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2891884	A2	20150708	EP 2015-150360	20150107
EP 2891884	A3	20151014		
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015082121	A	20150715	KR 2015-956	20150106
CN 104762371	A	20150708	CN 2015-10008065	20150107
US 20150192588	A1	20150709	US 2015-14591787	20150107
JP 2015129755	A	20150716	JP 2015-1880	20150107
PRIORITY APPLN. INFO.:			KR 2014-1799 A	20140107
			KR 2015-956 A	20150106

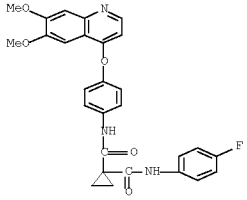
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A biomarker for predicting and/or monitoring the efficacy of a c-Met inhibitor; a composition for predicting and/or monitoring the efficacy of a c-Met inhibitor, comprising a material detecting the biomarker; a composition for selecting a subject suitable for the application of a c-Met inhibitor, comprising a material detecting the biomarker is presented. In addition a method for predicting and/or monitoring the efficacy of a c-Met inhibitor using the biomarker; a method for selecting a subject suitable for the application of a c-Met inhibitor using the biomarker; and a method for preventing and/or treating cancer comprising administering a c-Met inhibitor to the selected subject is given. One embodiment provides a biomarker for use in predicting and/or monitoring the therapeutic effect of a c-Met inhibitor or selecting a subject suitable for the application of a c-Met inhibitor, wherein the biomarker includes at least one selected from the group consisting of IL-8, BIGH3, or MIF and nucleic acids encoding the proteins. Another embodiment provides a c-Met inhibitor or a pharmaceutical composition including a c-Met inhibitor, for use in inhibiting c-Met and/or treating a cancer in a subject, wherein the subject has a high level of IL-8 or a nucleic acid encoding IL-8 compared to a reference sample in which a c-Met inhibitor is not effective; shows a decreased level of IL-8, BIGH3, MIF, and/or nucleic acids encoding them after administering a c-Met inhibitor; and/or has a mutation of KRAS, BRAF, and/or nucleic acids encoding them. A specific example shows the IL-8 levels in cancer cell-implanted mouse models showing relationship between IL-8 level and responsiveness to an anti-c-Met antibody.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biomarker for predicting or monitoring efficacy of c-Met inhibitor)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

L8 ANSWER 102 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1079985 CAPLUS Full-text

DOCUMENT NUMBER: 163:231592

TITLE: Heteroaromatic compound and its application in medicine for treating proliferative diseases

INVENTOR(S): Liu, Bing; Liu, Jinlei; Zhang, Yingjun; Zhang, Jiancun

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 189pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

L8 ANSWER 100 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1127378 CAPLUS Full-text

DOCUMENT NUMBER: 164:142135

TITLE: MET inhibitors for treatment of advanced hepatocellular carcinoma: a review

AUTHOR(S): Qi, Xing-Shun; Guo, Xiao-Zhong; Han, Guo-Hong; Li, Hong-Yu; Chen, Jiang

CORPORATE SOURCE: Department of Gastroenterology, General Hospital of Shenyang Military Area, Shenyang, Liaoning Province, 100840, Peop. Rep. China

SOURCE: World Journal of Gastroenterology (2015), 21(18), 5445-5453
CODEN: WJGAF2; ISSN: 2219-2840

DIGITAL OBJECT ID: 10.3748/wjg.v21.i18.5445

PUBLISHER: Baishideng Publishing Group Inc.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB The current std. treatment option for advanced hepatocellular carcinoma (HCC) is sorafenib, but its clin. benefit is modest. In spite of many attempts, few drugs can provide any significant improvement of survival as the first- or second-line therapy of choice in phase III randomized controlled trials. Recently, the subgroup anal. of a phase II randomized controlled trial has shown that tivantinib, a selective MET inhibitor, can significantly improve the overall survival in patients with MET-pos. advanced HCC after the failure or intolerance of a prior systemic therapy. These findings enlighten the role of MET inhibitors in the treatment of advanced HCC. In this paper, we review all ongoing and completed clin. trials regarding this topic. As for the first-line therapy of advanced HCC, INC280 and foretinib are being evaluated in 2 phase II single-arm trials; and MSC2156119J and golvatinib plus sorafenib are being compared with sorafenib alone in 2 phase II randomized controlled trials. As for the second-line therapy of advanced HCC, tivantinib and cabozantinib are being compared with placebo in 2 phase II randomized controlled trials.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase II and III clin. trials regarding MET inhibitors used for treatment of human advanced hepatocellular carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CN 104744446	A	20150701	CN 2014-10835175		20141229
PRIORITY APPLN. INFO.:			CN 2013-10746766	A	20131230
			CN 2014-10108590	A	20140322

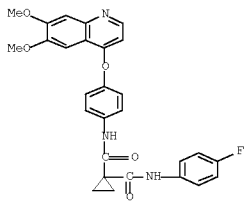
OTHER SOURCE(S): MARPAT 163:231592

AB The invention provides a class of heteroarom. compd. or stereisomer, geometrical isomer, tautomer, racemate, oxynitride, hydrate, solvate, metabolite, metabolic precursor and pharmaceutically acceptable salt, or prodrug thereof, used for the treatment of proliferative disease. The invention also discloses the pharmaceutical composition containing such compound and application of the compound of this invention or its pharmaceutical composition in the preparation of medicine for the treatment of proliferative disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heteroarom. compound and its application in medicine for treating proliferative diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 103 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1073487 CAPLUS Full-text

DOCUMENT NUMBER: 163:480792

TITLE: Response and toxicity of small-molecule tyrosine kinase inhibitors in patients with thyroid carcinoma: a systematic review and meta-analysis

AUTHOR(S): N. Klein Hesselink, E.; Steenvoorden, D.; Kapiteijn, E.; Corssmit, E. P.; van der Horst-Schrivers, A. N. A.; Lefrandt, J. D.; Links, T. P.; Dekkers, O. M.

CORPORATE SOURCE: Department of Endocrinology, Department of Internal Medicine, Division of Vascular Medicine, University Medical Center Groningen, University of Groningen, Groningen, Neth.

SOURCE: European Journal of Endocrinology (2015), 172(5), R215-R225
CODEN: EJOEEP; ISSN: 0804-4643

DIGITAL OBJECT ID: 10.1530/EJE-14-0788

PUBLISHER: BioScientifica Ltd.

DOCUMENT TYPE: Journal; General Review

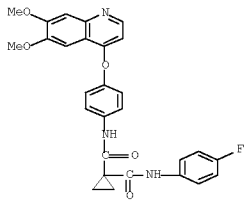
LANGUAGE: English

AB Context: Many tyrosine kinase inhibitors (TKIs) have been studied in patients with thyroid carcinoma (TC). However, the effect and toxicity of various TKIs in differentiated TC (DTC) and medullary TC (MTC) patients have not been directly compared. The aim of the present systematic review and meta-anal. was to systematically summarize response and toxicity of TKIs in TC patients. Methods: All major databases were systematically searched for publications on TKIs in TC. Primary endpoint was objective response; secondary endpoints were clin. benefit, percentage TKI dose reduction/discontinuation, hand-foot syndrome, diarrhea, and nausea/vomiting. Meta-anal. was performed using an exact likelihood approach and a logistic regression. Pooled percentages and 95% CIs were reported. Results: In total, 22 publications were included. For DTC patients, gefitinib induced no objective responses. Pooled percentage was highest for pazopanib, 49 (95% CI 33-64)%, and was 17 (95% CI 12-24)% for sorafenib. For MTC, gefitinib and imatinib induced no objective responses, whereas sunitinib induced objective response in 43 (95% CI 14-77)%. For vandetanib and cabozantinib, these nos. were 40 (95% CI 34-46)% and 27 (95% CI 22-32)% resp. Clin. benefit was found in 53 (95% CI 48-59)% of DTC patients on sorafenib, and in 84 (95% CI 79-88)% and 55 (95% CI 49-61)% of MTC patients on vandetanib and cabozantinib resp. All TKIs were associated with considerable toxicity. Conclusion: The currently studied TKIs show a modest response, while side effects are not negligible. Therefore, we suggest to solely consider TKIs in TC patients with rapid progressive disease, for whom the benefits of treatment outweigh toxicity.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response and toxicity of small-mol. tyrosine kinase inhibitors in patients with thyroid carcinoma: systematic review and meta-anal.)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 104 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:1053832 CAPLUS Full-text

DOCUMENT NUMBER: 163:145772

TITLE: Preparation of heterocyclic modulators of lipid synthesis

INVENTOR(S): Heuer, Timothy Sean; Oslob, Johan D.; Mcdowell, Robert S.; Johnson, Russell; Yang, Hanbiao; Evanchik, Marc; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.

PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA

SOURCE: PCT Int. Appl., 488pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015095767	A1	20150625	WO 2014-US71617	20141219
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2013-61919235	P 20131220

OTHER SOURCE(S): CASREACT 163:145772; MARPAT 163:145772

GI

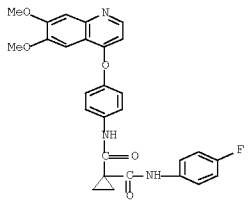
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This invention relates to heterocyclic modulators of lipid synthesis as well as pharmaceutically acceptable salts thereof; to pharmaceutical compns. comprising such compds.; and to methods of treating conditions characterized by dysregulation of a fatty acid synthase pathway by the administration of such compds. and combinations of such compds. and other therapeutic agents. Method of treating a condition characterized by dysregulation of a fatty acid synthase pathway in a subject by administering to the subject a therapeutically effective amount of compound I [LAr = II-IV; Ar = V-IX (wherein Het = 5-6 membered heteroaryl; R1 = H, CN, halo, etc.; R2 = H, halo, alkyl; R3 = H or F; R11 = H or Me); R21 = H, halo, alkyl, etc.; R22 = H, halo, alkyl; R24 = H, CN, alkyl, etc.; R25 = halo, CN, alkyl, etc.], in combination with other therapeutic agent, was claimed. Over three-hundred-eighty compds. I and their heterocyclic analogs were prepared E.g., a multi-step synthesis of X, starting from tert-Bu 4-iodopiperidine-1-carboxylate and 4-bromobenzonitrile, was described. The antiviral activities of the exemplified compds. I were assessed using the HCV1b replicon system (data given).

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of heterocyclic modulators of lipid synthesis useful for treating conditions characterized by dysregulation of a fatty acid synthase pathway)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 105 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:999711 CAPLUS Full-text

DOCUMENT NUMBER: 164:270620

TITLE: Iodide- and glucose-handling gene expression regulated by sorafenib or cabozantinib in papillary thyroid cancer

AUTHOR(S): Ruan, Maomei; Liu, Min; Dong, Qianggang; Chen, Libo

CORPORATE SOURCE: Department of Nuclear Medicine, Sixth People's Hospital, Shanghai Jiao Tong University, Shanghai, 200233, Peop. Rep. China

SOURCE: Journal of Clinical Endocrinology and Metabolism (2015), 100(5), 1771-1779
CODEN: JCEMAZ; ISSN: 0021-972X

DIGITAL OBJECT ID: 10.1210/jc.2014-3023

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

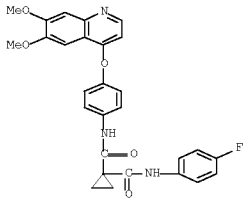
AB Context: The aberrant silencing of iodide-handling genes accompanied by up-regulation of glucose metabolism presents a major challenge for

radioiodine treatment of papillary thyroid cancer (PTC). Objective: This study aimed to evaluate the effect of tyrosine kinase inhibitors on iodide-handling and glucose-handling gene expression in BHP 2-7 cells harboring RET/PTC1 rearrangement. Main Outcome Measures: In this in vitro study, the effects of sorafenib or cabozantinib on cell growth, cycles, and apoptosis were investigated by cell proliferation assay, cell cycle anal., and Annexin V-FITC apoptosis assay, resp. The effect of both agents on signal transduction pathways was evaluated using the Western blot. Quant. real-time PCR, Western blot, immunofluorescence, and radioisotope uptake assays were used to assess iodide-handling and glucose-handling gene expression. Results: Both compds. inhibited cell proliferation in a time-dependent and dose-dependent manner and caused cell cycle arrest in the G0/G1 phase. Sorafenib blocked RET, AKT, and ERK1/2 phosphorylation, whereas cabozantinib blocked RET and AKT phosphorylation. The restoration of iodide-handling gene expression and inhibition of glucose transporter 1 and 3 expression could be induced by either drug. The robust expression of sodium/iodide symporter induced by either agent was confirmed, and 125I uptake was correspondingly enhanced. 18F-fluorodeoxyglucose accumulation was significantly decreased after treatment by either sorafenib or cabozantinib. Conclusions: Sorafenib and cabozantinib had marked effects on cell proliferation, cell cycle arrest, and signal transduction pathways in PTC cells harboring RET/PTC1 rearrangement. Both agents could be potentially used to enhance the expression of iodide-handling genes and inhibit the expression of glucose transporter genes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of tyrosine kinase inhibitors including sorafenib and cabozantinib effect iodide- and glucose-handling gene expression in human papillary thyroid cancer HP 2-7 cells)

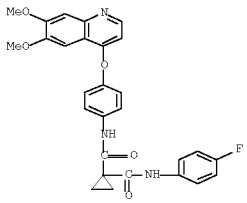
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 107 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:960349 CAPLUS Full-text

DOCUMENT NUMBER: 164:270197

TITLE: Cabozantinib as a new drug for treating metastatic medullary thyroid cancer

AUTHOR(S): Chen, Hui-ling; Zhang, Zhi-ye; Yang, Yan-biao

CORPORATE SOURCE: Department of Pharmacy, Lanzhou City First People's Hospital, Lanzhou, 730050, Peop. Rep. China

SOURCE: Zhongguo Yaofang (2014), 25(29), 2766-2769
CODEN: ZYHAA4; ISSN: 1001-0408

DIGITAL OBJECT ID: 10.6039/j.issn.1001-0408.2014.29.27

PUBLISHER: Zhongguo Yaofang Zazhishe

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Chinese

AB A review with 12 refs. is given on the cabozantinib as a new drug for treating metastatic medullary thyroid cancer. The topic discussed include:: (1) clin. pharmacol. research of cabozantinib(action mechanism and pharmacol. effects), (2) clin. research of cabozantinib, (3) adaptation disease and dosage and administration of cabozantinib, (4) drug interactions with cytochrome P 450 and p-glycoprotein, (5) attention and safety evaluation of cabozantinib, (6) administration for special population.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as a new drug for treating metastatic medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

L8 ANSWER 106 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:981422 CAPLUS Full-text

DOCUMENT NUMBER: 163:88178

TITLE: Methods of selecting treatment regimens of cancer with chemotherapy plus VEGF signaling inhibitors using the predictive potential of serum protein and tumor gene expression

INVENTOR(S): Barry, Simon T.; Critchlow, Susan E.; Pommier, Aurelien J.C.

PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited

SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015082880	A1	20150611	WO 2014-GB53485	20141125

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

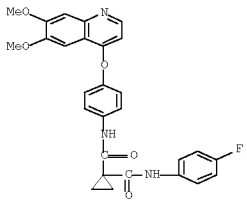
PRIORITY APPLN. INFO.: US 2013-61910652 P 20131202

AB The present invention is directed to, inter alia, the predictive potential of serum protein and tumor gene expression in patients with metastatic colorectal cancer (mCRC) receiving either chemotherapy plus placebo or chemotherapy plus the VEGF signaling inhibitor cediranib, sunitinib, sorafenib, pazopanib, tivozanib, vandetanib, soraninib, axitinib, cabozantinib, bevacizumab, aflibercept or ramucirumab. The present invention, in addition, provides for patient selection methods, as well as kits, that may be used in determining suitable cancer treatment regimens in subjects with cancer, with particular reference to whether the subject will gain benefit from treatment with VEGF signaling inhibitors.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of selecting treatment regimens of cancer with chemotherapy plus VEGF signaling inhibitors using the predictive potential of serum protein and tumor gene expression)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 108 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:948166 CAPLUS Full-text

DOCUMENT NUMBER: 164:367374

TITLE: Update on Cardiovascular Safety of Tyrosine Kinase Inhibitors: With a Special Focus on QT Interval, Left Ventricular Dysfunction and Overall Risk/Benefit

AUTHOR(S): Shah, Rashmi R.; Morganroth, Joel

CORPORATE SOURCE: Rashmi Shah Consultancy Ltd, Buckinghamshire, SL9 7JA, UK

SOURCE: Drug Safety (2015), 38(8), 693-710
CODEN: DRSAEA; ISSN: 0114-5916

DIGITAL OBJECT ID: 10.1007/s40264-015-0300-1

PUBLISHER: Springer International Publishing AG

DOCUMENT TYPE: Journal; General Review; (online computer file)

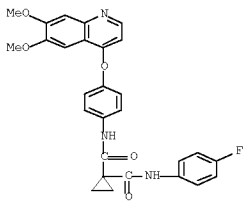
LANGUAGE: English

AB We previously reviewed the cardiovascular safety of 16 tyrosine kinase inhibitors (TKIs), approved for use in oncol. as of 30 Sept. 2012. Since then, the indications for some of them have been widened and an addnl. nine TKIs have also been approved as of 30 Apr. 2015. Eight of these nine are indicated for use in oncol. and one (nintedanib) for idiopathic pulmonary fibrosis. This report is an update on the cardiovascular safety of those 16 TKIs, including the post-marketing data concerning their pro-arrhythmic effects, and reviews the cardiovascular safety of the nine new TKIs approved since (afatinib, cabozantinib, ceritinib, dabrafenib, ibrutinib, lenvatinib, nintedanib, ponatinib, and trametinib). As before, we focus on specific aspects of cardiovascular safety, namely their potential to induce QT interval prolongation, left ventricular (LV) dysfunction and hypertension but now also summarise the risks of arterial thromboembolic events (ATEs) associated with these agents. Of the newer TKIs, cabozantinib and ceritinib have been shown to induce a mild to moderate degree of QTc interval prolongation while cardiac dysfunction has been reported with the use of afatinib, dabrafenib, lenvatinib, ponatinib and trametinib. The label for axitinib was revised to include a new association with cardiac dysfunction. Hypertension is associated with cabozantinib, lenvatinib, nintedanib, ponatinib and trametinib. Ponatinib, within 10 mo of its approval in Dec. 2012, required voluntary (temporary) suspension of its marketing until significant safety revisions (restricted indication, addnl. warnings and precautions about the risk of arterial occlusion and thromboembolic events and amended dose) were made to its label. Compared with the previous 16 TKIs,

more of the recently introduced TKIs are associated with the risk of LV dysfunction, and fewer with QT prolongation. Available data on morbidity and mortality associated with TKIs, together with post-marketing experience with lapatinib and ponatinib, emphasize the need for effective pharmacovigilance and ongoing re-assessment of their risk/benefit after approval of these novel agents. If not adequately managed, these cardiovascular effects significantly decrease the quality of life and increase the morbidity and mortality in a population already at high risk. Evidence accumulated over the last decade suggests that their clin. benefit, although worthwhile, is modest and extends only to progression-free survival and complete response without any effect on overall survival. During uncontrolled use in routine clin. practice, their risk/benefit is likely to be inferior to that perceived from highly controlled clin. trials.

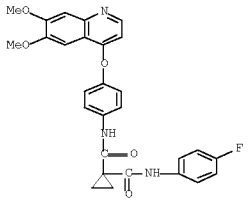
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(update on cardiovascular safety of tyrosine kinase inhibitors with special focus on QT interval, left ventricular dysfunction and overall risk/benefit)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

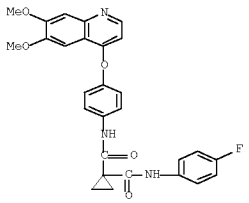
L8 ANSWER 109 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:920388 CAPLUS Full-text
DOCUMENT NUMBER: 164:271039
TITLE: SnapShot: Kinase Inhibitors II
AUTHOR(S): Wang, Jinhua; Gray, Nathanael S.
CORPORATE SOURCE: Department of Cancer Biology, Dana-Farber Cancer Institute, Boston, MA, 02215, USA
SOURCE: Molecular Cell (2015), 58(4), 710-710.e1
CODEN: MOCEFL; ISSN: 1097-2765
DIGITAL OBJECT ID: 10.1016/j.molcel.2015.05.002
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Selective small-mol. inhibitors of protein kinases can serve as powerful tools to elucidate biol. function. Efforts to develop potential drug candidates have yielded a wealth of kinase inhibitors. However, selecting the optimal kinase inhibitor for a particular application can be challenging. While the optimal inhibitor will be application specific, we have attempted to summarize some of the best reported inhibitors for various kinases.
IT 849217-68-1 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discussion on small-mol. of kinases inhibitors II)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

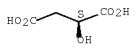
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

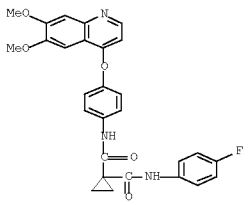


L8 ANSWER 110 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:894377 CAPLUS Full-text
DOCUMENT NUMBER: 163:1020
TITLE: Compositions and methods for diagnosing, evaluating and treating cancer by means of the DNA methylation status
INVENTOR(S): Clement, Kendell; Getz, Gad; Landau, Dan-Avi; Meissner, Alexander; Wu, Catherine Ju-Ying
PATENT ASSIGNEE(S): The Broad Institute Inc., USA; Dana-Farber Cancer Institute, Inc.; The General Hospital Corporation; President and Fellows of Harvard College
SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015077717	A1	20150528	WO 2014-US67146	20141124

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61908316 P 20131125
AB The present invention relates to methods of detg. a cancer treatment prognosis for a subject in need thereof by evaluating epigenetic and genetic changes within a tumor sample from the subject. The present invention further provides methods of treating cancer in a subject by evaluating epigenetic and genetic changes within a tumor sample from the subject, in addition, the present invention provides methods of screening test agents to identify agents that decrease tumor cell plasticity.
IT 849217-68-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for diagnosing, evaluating and treating cancer by means of the DNA methylation status)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 111 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:893490 CAPLUS Full-text
DOCUMENT NUMBER: 163:51687
TITLE: Process for the preparation of cabozantinib salt and its crystal form
INVENTOR(S): Shen, Anxiong; Tang, Dongjun; Kou, Jingping
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 19pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104649969	A	20150527	CN 2014-10676653	20141121

PRIORITY APPLN. INFO.: CN 2013-10596247 A 20131122

AB The invention relates to the cabozantinib L-malate crystal form A2, which has absorption peaks at 9.33°, 11.75°, 13.44°, 15.16°, 19.72°, 23.14°, and 25.92° determined by X-ray powder diffraction at 2θ. The invention also relates to cabozantinib hydrobromide crystal form I, which has absorption peaks at 8.68°, 13.01°, 7.45°, 19.52°, 20.05°, 21.71°, 23.29°, and 26.28° determined by X-ray powder diffraction at 2θ.

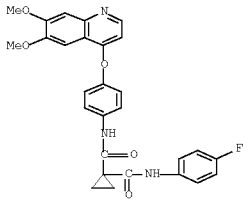
IT 1140909-48-3P 1786398-76-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of cabozantinib salt and its crystal form)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

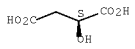
CRN 849217-68-1
CMF C28 H24 F N3 O5



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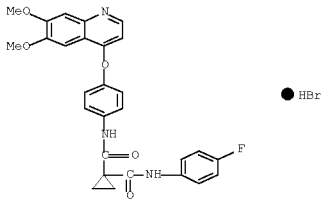
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



RN 1786398-76-2 CAPLUS

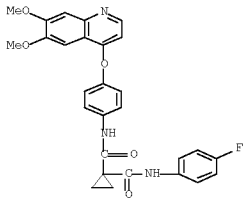
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrobromide (1:1) (CA INDEX NAME)



IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of cabozantinib salt and its crystal form)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

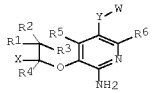


L8 ANSWER 112 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:893241 CAPLUS Full-text
DOCUMENT NUMBER: 163:66113
TITLE: Aminopyridine compounds as protein kinase receptor inhibitors and their preparation, pharmaceutical compositions and use in the treatment of proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Liang; Wang, Tingjin
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 109pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104650049	A	20150527	CN 2014-10429046	20140827

PRIORITY APPLN. INFO.: CN 2013-10383121 A 20130828
CN 2014-10144178 A 20140410

OTHER SOURCE(S): MARPAT 163:66113
GI



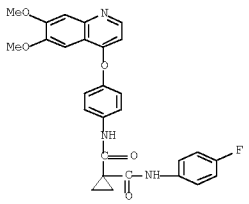
I

AB The invention relates to aminopyridine compds. of formula I, their pharmaceutically acceptable salts, and pharmaceutical formulations, which is used for regulating protein kinase activity, and adjusting signal response within cells or between cells. The invention also relates to compds. I and their stereoisomer, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts or prodrugs which are used in treating mammal, particularly to human hyperproliferative disorders. The pharmaceutical compns. includes the title compds., pharmaceutically acceptable carriers, excipients, diluents, adjuvants, and/or mediums, and other treating agents. The pharmaceutical compns. are used in preparing medicines for preventing, handling, treating or relieving proliferative disorders such as metastatic cancer, colon cancer, gastric adenocarcinoma, bladder cancer, breast cancer, kidney cancer, liver cancer, lung cancer, thyroid cancer, head and neck cancer, prostate cancer, pancreatic cancer, central nervous system cancer, spongioblastoma, bone marrow hyperplasia, atherosclerosis or pulmonary fibrosis. Compds. of formula I wherein R1- R6 are independently H, D or F; X, Y are independently (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl; W is C3-8 cycloalkyl, -(C1-4 alkylene)-(C3-8 cycloalkyl), C3-7 heterocyclyl or -(C1-4 alkylene)-(C3-7 heterocyclyl), etc.; and their stereoisomer, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts or prodrugs as protein kinase receptor inhibitors useful in the treatment of proliferative disorders thereof, are claimed. Compds. of formula I were prepared by using condensation, reduction, and cross-coupling as the key steps. All the invention compds. were evaluated for their protein kinase inhibitory activity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of aminopyridine compds. as protein kinase receptor inhibitors useful in the treatment of proliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

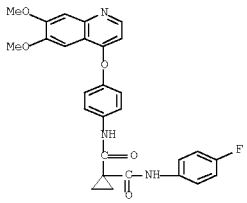
L8 ANSWER 113 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:884680 CAPLUS Full-text
TITLE: Comprehensive transcriptomic analysis of molecularly targeted drugs in cancer for target pathway evaluation
AUTHOR(S): Mashima, Tetsuo; Ushijima, Masaru; Matsuura, Masaaki; Tsukahara, Satomi; Kunimasa, Kazuhiro; Furuno, Aki; Saito, Sakae; Kitamura, Masami; Soma-Nagae, Taeko; Seimiya, Hiroyuki; Dan, Shingo; Yamori, Takao; Tomida, Akihiro
CORPORATE SOURCE: Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo, Japan
SOURCE: Cancer Science (2015), 106(7), 909-920
CODEN: CSACCM; ISSN: 1349-7006
DIGITAL OBJECT ID: 10.1111/cas.12682
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Targeted therapy is a rational and promising strategy for the treatment of advanced cancer. For the development of clin. agents targeting oncogenic signaling pathways, it is important to define the specificity of compds. to the target mol. pathway. Genome-wide transcriptomic anal. is an unbiased approach to evaluate the compound mode of action, but it is still unknown whether the anal. could be widely applicable to classify molecularly targeted anticancer agents. We comprehensively obtained and analyzed 129 transcriptomic datasets of cancer cells treated with 83 anticancer drugs or related agents, covering most clin. used, molecularly targeted drugs alongside promising inhibitors of mol. cancer targets. Hierarchical clustering and principal component anal. revealed that compds. targeting

similar target mols. or pathways were clustered together. These results confirmed that the gene signatures of these drugs reflected their modes of action. Of note, inhibitors of oncogenic kinase pathways formed a large unique cluster, showing that these agents affect a shared mol. pathway distinct from classical antitumor agents and other classes of agents. The gene signature anal. further classified kinome-targeting agents depending on their target signaling pathways, and we identified target pathway-selective signature gene sets. The gene expression anal. was also valuable in uncovering unexpected target pathways of some anticancer agents. These results indicate that comprehensive transcriptomic anal. with our database (http://scads.jfcr.or.jp/db/cs/) is a powerful strategy to validate and re-evaluate the target pathways of anticancer compds.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comprehensive transcriptomic anal. of molecularly targeted drugs in cancer for target pathway evaluation)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 114 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:866343 CAPLUS Full-text
DOCUMENT NUMBER: 163:1013
TITLE: mTOR protein kinase inhibitors for enhancing the immune response for treatment of diseases such as cancer
INVENTOR(S): Mannick, Joan; Glass, David Jonathan; Murphy, Leon
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 149pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015073644	A1	20150521	WO 2014-US65408	20141113
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150140036	A1	20150521	US 2014-14540867	20141113

PRIORITY APPLN. INFO.:

US 2013-61903636	P	20131113
US 2014-62027121	P	20140721
US 2014-62052629	P	20140919
US 2014-62076142	P	20141106

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

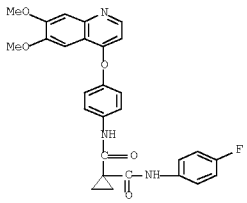
AB The present invention relates, in part, to compns. and methods for enhancement of an immune response by partial mTOR inhibition, e.g., with low, immune enhancing, doses of an mTOR inhibitor, such as RAD001 or rapamycin. In an embodiment, the subject has cancer and the method comprises promoting the subject's immune response to treat cancer.

IT 1140909-48-3, Cabozantinib-S-Malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mTOR protein kinase inhibitors for enhancing the immune response for treatment of diseases such as cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

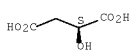
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



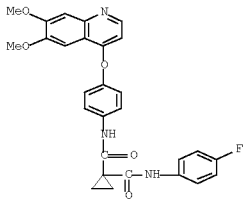
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 115 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:847958 CAPLUS Full-text
DOCUMENT NUMBER: 164:260451
TITLE: Cabozantinib: A MET, RET, and VEGFR2 Tyrosine Kinase Inhibitor
AUTHOR(S): Gruellich, Carsten
CORPORATE SOURCE: Department of Medical Oncology, National Center for Tumor Diseases, Heidelberg University Medical Center, Heidelberg, 69120, Germany
SOURCE: Recent Results in Cancer Research (2014), 201(Small Molecules in Oncology), 207-214
CODEN: RRCRBU; ISSN: 2197-6767
DIGITAL OBJECT ID: 10.1007/978-3-642-54490-3_12
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib is a receptor tyrosine kinase inhibitor with activity against MET, VEGFR2, FLT3, c-KIT, and RET. Activity of cabozantinib toward a broad range of tumor models could be detected in several preclin. studies. Of note, cabozantinib decreases metastasis potential and tumor invasiveness when compared with placebo or agents that target VEGFR and have no activity against MET. Clin. phase I and II studies with cabozantinib have been conducted in various malignancies including medullary thyroid cancer (MTC), NSCLC, breast, ovarian, pancreatic, and prostate cancer. In MTC, gain of function mutations of RET are central for tumorigenesis. Hereditary forms of MTC (MEN II) are caused by germline mutations of RET, in sporadic MTC in up to 50 % of cases RET mutations occur. Addnl., activating mol. changes in VEGFR and MET pathways have also been implicated in MTC progression. Clin. responses with cabozantinib in MTC could be observed in early clin. trials, and following confirmation of clin. benefit in a randomized phase III trial, cabozantinib gained FDA approval for first-line treatment of advanced MTC in 2012. In prostate cancer models, MET expression increases with androgen ablation and clin. progression of bone and lymph node metastasis. A phase II trial with cabozantinib also showed very promising response rates in patients with metastatic prostate cancer. Therefore, randomized phase III studies are currently ongoing to validate the efficacy of cabozantinib in heavily pretreated prostate cancer patients.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as MET, RET, and VEGFR2 tyrosine kinase inhibitor)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

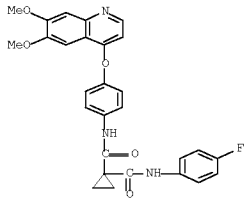


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L8 ANSWER 116 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:827243 CAPLUS Full-text
DOCUMENT NUMBER: 162:650141
TITLE: Methods using TIE2 kinase inhibitors for the treatment of cancer
INVENTOR(S): Flynn, Daniel L.; Kaufman, Michael D.; Smith, Bryan; Rudoltz, Marc S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 121pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

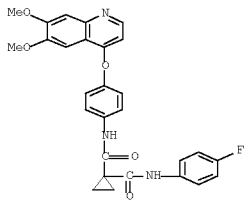
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015069266	A1	20150514	WO 2013-US69005	20131107
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,				

SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: WO 2013-US69005 20131107
AB The present invention relates to methods using TIE2 kinase inhibitors for the treatment of tumor growth, invasiveness, intravasation, dissemination, metastasis, and immunosuppression. Specifically, the invention relates to methods of using 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea and salts thereof.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods using TIE2 kinase inhibitors for the treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 117 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:821056 CAPLUS Full-text
DOCUMENT NUMBER: 164:219602
TITLE: Pharmacological Inhibition of KIT Activates MET Signaling in Gastrointestinal Stromal Tumors
AUTHOR(S): Cohen, Noah A.; Zeng, Shan; Seifert, Adrian M.; Kim, Teresa S.; Sorenson, Eric C.; Greer, Jonathan B.; Beckman, Michael J.; Santamaria-Barria, Juan A.; Crawley, Megan H.; Green, Benjamin L.; Rossi, Ferdinand; Besmer, Peter; Antonescu, Cristina R.; DeMatteo, Ronald P.
CORPORATE SOURCE: Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Cancer Research (2015), 75(10), 2061-2070
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-14-2564
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB These findings offer a preclin. rationale to immediately reposition the MET kinase inhibitor cabozantinib for clin. evaluation in treatment of gastrointestinal stromal tumors that are either sensitive or resistant to imatinib, the kinase inhibitor used to treat this type of sarcoma. Gastrointestinal stromal tumors (GIST) are the most common adult sarcomas and the oncogenic driver is usually a KIT or PDGFRA mutation. Although GISTs are often initially sensitive to imatinib or other tyrosine kinase inhibitors, resistance generally develops, necessitating backup strategies for therapy. In this study, we determined that a subset of human GIST specimens that acquired imatinib resistance acquired expression of activated forms of the MET oncogene. MET activation also developed after imatinib therapy in a mouse model of GIST (KitV558del/+ mice), where it was associated with increased tumor hypoxia. MET activation also occurred in imatinib-sensitive human GIST cell lines after imatinib treatment in vitro. MET inhibition by crizotinib or RNA interference was cytotoxic to an imatinib-resistant human GIST cell population. Moreover, combining crizotinib and imatinib was more effective than imatinib alone in imatinib-sensitive GIST models. Finally, cabozantinib, a dual MET and KIT small-mol. inhibitor, was markedly more effective than imatinib in multiple preclin. models of imatinib-sensitive and imatinib-resistant GIST. Collectively, our findings showed that activation of compensatory MET signaling by KIT inhibition may contribute to tumor resistance. Furthermore, our work offered a preclin. proof of concept for MET inhibition by cabozantinib as an effective strategy for GIST treatment. Cancer Res; 75(10); 2061-70. ©2015 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. inhibition of KIT activates MET signaling in gastrointestinal stromal tumors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

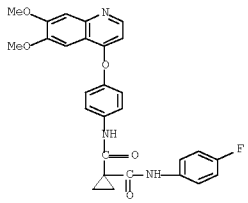


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 118 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:739043 CAPLUS Full-text
DOCUMENT NUMBER: 162:567725
TITLE: Solid particulate formulations of tyrosine derivatives
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: PCT Int. Appl., 20pp.; Chemical Indexing Equivalent to 162:567667 (US)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015061288	A1	20150430	WO 2014-US61527	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150112116	A1	20150423	US 2013-14062194	20131024

PRIORITY APPLN. INFO.: US 2013-61894279 P 20131022
US 2013-14062194 A 20131024
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Provided are methods comprising providing a tyrosine deriv. such as α-methyltyrosine, and a solid particulate material (and, optionally, melanin) and applying force to said tyrosine derivative and said solid particulate material for a time and under conditions effective to impregnate at least one of said tyrosine derivative and said solid particulate material with the other of said tyrosine derivative and said solid particulate material.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid particulate formulations of tyrosine derivs.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 119 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:734279 CAPLUS Full-text
DOCUMENT NUMBER: 162:594407
TITLE: High-speed centrifugal mixing devices for uses in pharmaceuticals
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015061256	A1	20150430	WO 2014-US61481	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150110735	A1	20150423	US 2013-14059837	20131022

PRIORITY APPLN. INFO.: US 2013-14059837 A 20131022
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A centrifugal mixing device can include a shaft assembly that is operably coupled to a motor such that the motor rotates the shaft assembly about a first axis. The devices can further include a turret that is rotatably coupled to the shaft assembly such that the turret rotates about the first axis relative to the shaft assembly. The turret can include a first support,

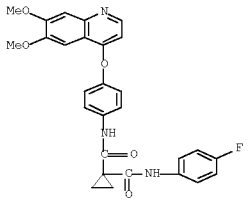
a first canister rotatably coupled to the first support such that the first canister rotates about a second axis, and a second canister rotatably coupled to the first support such that the second canister rotates about a third axis. The turret is configured to rotate about the first axis in a first rotational direction and each of the first and second canisters is configured to rotate about the second and third axes, resp., in a second rotational direction that is opposite the first rotational direction. The centrifugal mixing device consists of the canisters comprising at least 2 different particulate materials. The particulate materials comprises an active pharmaceutical ingredient.

IT 849217-68-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-speed centrifugal mixing devices for uses in pharmaceuticals)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 120 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:694096 CAPLUS Full-text

DOCUMENT NUMBER: 163:240819

TITLE: New therapies for dedifferentiated papillary thyroid cancer

AUTHOR(S): Fallahi, Poupak; Mazzi, Valeria; Vita, Roberto; Ferrari, Silvia Martina; Materazzi, Gabriele; Galleri, David; Benvenga, Salvatore; Miccoli, Paolo; Antonelli, Alessandro

CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56126, Italy

SOURCE: International Journal of Molecular Sciences (2015), 16(3), 6153-6182
CODEN: IJMCFK; ISSN: 1422-0067

DIGITAL OBJECT ID: 10.3390/ijms16036153

PUBLISHER: MDPI AG

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

SOURCE: U.S. Pat. Appl. Publ., 15pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150110735	A1	20150423	US 2013-14059837	20131022
WO 2015061256	A1	20150430	WO 2014-US61481	20141021

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-14059837 A 20131022

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A centrifugal mixing device can include a shaft assembly that is operably coupled to a motor such that the motor rotates the shaft assembly about a first axis. The devices can further include a turret that is rotatably coupled to the shaft assembly such that the turret rotates about the first axis relative to the shaft assembly. The turret can include a first support, a first canister rotatably coupled to the first support such that the first canister rotates about a second axis, and a second canister rotatably coupled to the first support such that the second canister rotates about a third axis. The turret is configured to rotate about the first axis in a first rotational direction and each of the first and second canisters is configured to rotate about the second and third axes, resp., in a second rotational direction that is opposite the first rotational direction. The centrifugal mixing device consists of the canisters comprising at least 2 different particulate materials. The particulate materials comprises an active pharmaceutical ingredient.

IT 849217-68-1, Cabozantinib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-speed centrifugal mixing devices for uses in pharmaceuticals)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

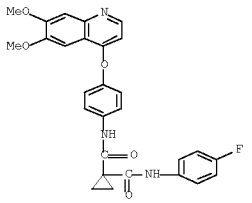
AB The no. of thyroid cancers is increasing. Std. treatment usually includes primary surgery, TSH suppressive therapy, and ablation of the thyroid remnant with radioactive iodine (RAI). Despite the generally good prognosis of thyroid carcinoma, about 5% of patients will develop metastatic disease, which fails to respond to RAI, exhibiting a more aggressive behavior. The lack of specific, effective and well-tolerated drugs, the scarcity of data about the association of multi-targeting drugs, and the limited role of radioiodine for dedifferentiated thyroid cancer, call for further efforts in the field of new drugs development. Rearranged during transfection (RET)/papillary thyroid carcinoma gene rearrangements, BRAF (B-RAF proto-oncogene, serine/threonine kinase) gene mutations, RAS (rat sarcoma) mutations, and vascular endothelial growth factor receptor 2 angiogenesis pathways are some of the known pathways playing a crucial role in the development of thyroid cancer. Targeted novel compds. have been demonstrated to induce clin. responses and stabilization of disease. Sorafenib has been approved for differentiated thyroid cancer refractory to RAI.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discussion on new therapies for dedifferentiated papillary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 178 THERE ARE 178 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 121 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

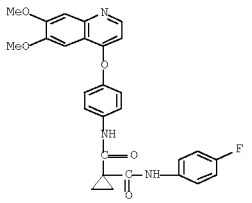
ACCESSION NUMBER: 2015:691735 CAPLUS Full-text

DOCUMENT NUMBER: 162:567753

TITLE: High-speed centrifugal mixing devices for uses in pharmaceuticals

INVENTOR(S): Hoffman, Steven

PATENT ASSIGNEE(S): Tyme, Inc., USA



L8 ANSWER 122 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:691420 CAPLUS Full-text

DOCUMENT NUMBER: 162:567667

TITLE: Solid particulate formulations of tyrosine derivatives

INVENTOR(S): Hoffman, Steven

PATENT ASSIGNEE(S): Tyme, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 6pp.; Chemical Indexing Equivalent to 162:567725 (WO)
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150112116	A1	20150423	US 2013-14062194	20131024
WO 2015061288	A1	20150430	WO 2014-US61527	20141021

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

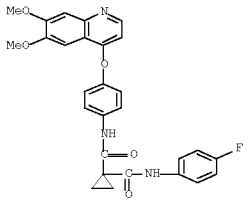
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61894279 P 20131022
US 2013-14062194 A 20131024

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided are methods comprising providing a tyrosine deriv. such as α-methyltyrosine, and a solid particulate material (and, optionally, melanin) and applying force to said tyrosine derivative and said solid particulate material for a time and under conditions effective to impregnate at least one of said tyrosine derivative and said solid particulate material

with the other of said tyrosine derivative and said solid particulate material.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid particulate formulations of tyrosine derivs.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



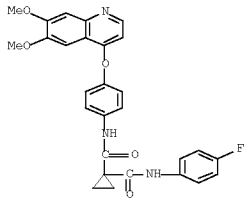
L8 ANSWER 123 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:656704 CAPLUS Full-text
DOCUMENT NUMBER: 162:487306
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Institut de Recerca Biomedica (IRB Barcelona), Spain; Institucio Catalana de Recerca i Estudis Avancats
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015052583	A2	20150416	WO 2014-IB2675	20141007
WO 2015052583	A3	20150723		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2926894	A1	20150416	CA 2014-2926894	20141007
PRIORITY APPLN. INFO.:			US 2013-61888984 P	20131009
			WO 2014-IB2675 W	20141007

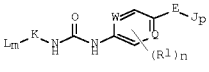
AB The present invention relates to a method for the prognosis of bone metastasis in HER2+ breast cancer, which comprises determining if the MAF gene is amplified in a primary tumor sample. Likewise, the present invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the MAF gene expression level, amplification or translocation. The present invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The present invention also relates to a c-Maf inhibitor as therapeutic agent for use in the treatment of HER2+ breast cancer metastasis. The present invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the present invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for determining prognosis of bone metastasis in HER2+ breast cancer
and use of c-Maf inhibitor as therapeutic agent)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



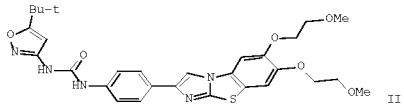
L8 ANSWER 124 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:639512 CAPLUS Full-text
DOCUMENT NUMBER: 162:590248
TITLE: Preparation of substituted urea derivatives for treating FLT3 kinase mediated or induced diseases
INVENTOR(S): Zheng, Changchun; Liu, Bing; Zhang, Weihong; Zhang, Yingjun; Long, Bohua
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 69pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104513257	A	20150415	CN 2014-10498232	20140925
CN 104513258	A	20150415	CN 2014-10498181	20140925
PRIORITY APPLN. INFO.:			CN 2013-10445435 A	20130926
			CN 2014-10108087 A	20140322

OTHER SOURCE(S): CASREACT 162:590248; MARPAT 162:590248
GI

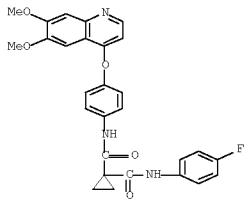


I



II

AB This invention provides substituted urea derivs. I [wherein K = 5- or 6-membered heteroaryl; Q and W = independently CH or N; L = independently NH2, NO2, alkylthio, alkyl, etc.; R1 = independently H, F, Cl, Br, I, etc.; E = bicyclic or tricyclic heteroaryl; J = G-(CH2)q-R; G = independently O, S, SO, SO2, CO, etc.; R = independently H, alkoxy, alkyl, alkenyl, etc.; m = 1-4; n = 0-4; p = 2-4; q = 1-4], stereoisomers, geometrical isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, esters, pharmaceutically acceptable salts, or prodrugs for treating FLT3 kinase mediated or induced diseases, such as autoimmune diseases, inflammatory diseases and proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 6.0 nM against FLT3 kinase.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. for treating FLT3 kinase mediated or induced diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



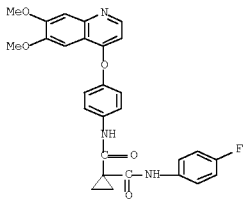
L8 ANSWER 125 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:613471 CAPLUS Full-text
DOCUMENT NUMBER: 162:532738
TITLE: High drug loading system to co-deliver anticancer drugs and nucleic acids for cancer therapy
INVENTOR(S): Cheng, Gang; Tang, Qiong; Cao, Bin
PATENT ASSIGNEE(S): The University of Akron, USA
SOURCE: U.S. Pat. Appl. Publ., 10pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150099005	A1	20150409	US 2014-14510442	20141009
PRIORITY APPLN. INFO.:			US 2013-61888709 P	20131009

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A high drug loading system is described comprising of at least one anticancer drug; at least one peptide; and at least one nucleic acid.
IT 1140909-48-3, Cabozantinib-S-malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high drug loading system to co-deliver anticancer drugs and nucleic acids for cancer therapy)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

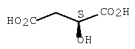
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



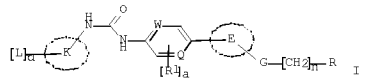
L8 ANSWER 126 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:560353 CAPLUS Full-text
DOCUMENT NUMBER: 162:488682
TITLE: Preparation of substituted urea derivatives for modulating the FLT3 kinase activity and inhibiting FLT3-ITD
INVENTOR(S): Cheng, Changchung; Liu, Bing; Zhang, Yingjun; Long, Bohua; Zhang, Weihong
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015043492	A1	20150402	WO 2014-CN87469	20140925

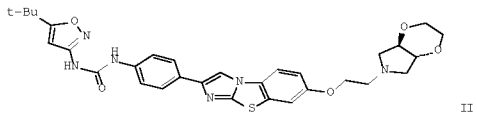
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CN 104513259	A	20150415	CN 2014-10498216	20140925
CN 104513252	A	20150415	CN 2014-10499464	20140925

PRIORITY APPLN. INFO.: CN 2013-10445605 A 20130926
CN 2014-10107854 A 20140322
OTHER SOURCE(S): CASREACT 162:488682; MARPAT 162:488682
GI

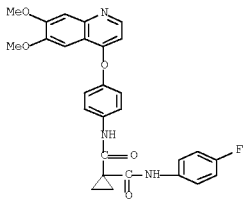


I



II

AB The title compds. I [each of Q and W = (independently) CH or N; G = O, S, C(O), etc.; R = alkoxy, alkyl, (un)substituted amino, etc.; ring K = 5-6 membered heteroaryl group, of which at least two ring members are heteroatoms independently selected from O, S, NR4 and N; each L = (independently) amino, nitro, alkylthio, etc.; ring E = bicyclic or tricyclic heteroarylene; R1 = H, halo, haloalkyl, etc.; R4 = H, alkyl, cycloalkyl, etc.; a = 0-4; d, n = 1-4; with the provisos] which are useful in modulating the FLT3 kinase activity, inhibiting FLT3-ITD, and treating the diseases mediated by FLT3 kinase or caused by FLT3-ITD, were prepared and claimed. E.g., a multi-step synthesis of II, starting from (4aS,7aS)-hexahydro-2H-[1,4]dioxino[2,3-c]pyrrole and 2-chloroethanol, was described. Exemplified compds. I were tested for FLT3 kinase inhibition (data given for representative compds. I). Pharmaceutical compns. comprising compound I, alone or in combination with other therapeutic agents, were disclosed.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. for modulating the FLT3 kinase activity and inhibiting FLT3-ITD)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

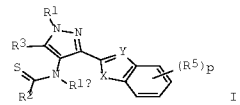


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

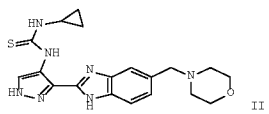
L8 ANSWER 127 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:527604 CAPLUS Full-text
DOCUMENT NUMBER: 162:475187
TITLE: Preparation of pyrazole derivatives as protein kinase over expression inhibitors
INVENTOR(S): Zhang, Jiancun; Liu, Bing; Zhang, Yingjun; Nie, Linlin; Yang, Xueqi
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 80pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104447701	A	20150325	CN 2014-10471458	20140916

PRIORITY APPLN. INFO.: CN 2013-10426478 A 20130917
CN 2014-10109414 A 20140321
OTHER SOURCE(S): MARPAT 162:475187
GI

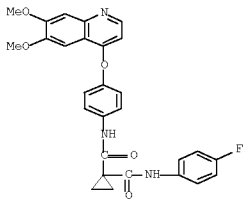


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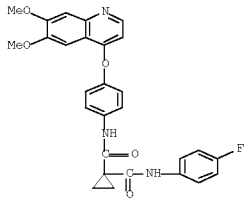


II

AB The title compds. with general formula I [wherein R1 and R1a are independently H or C1-4 alkyl; R2 is alkyl amino, aryl, heteroaryl, etc.; X is CR4aR4 or NR6; Y is CR4a or N; R3 is H, F, Cl, etc.; R3 is H, F, Cl, Br, etc.; R5 is H, alkyl, alkenyl, alkynyl, etc.; p = 1 -4] or isomers, N-oxide, hydrates, solvates, metabolites, esters, prodrugs, or pharmaceutically acceptable salts there of were prepared as protein kinase over expression inhibitors. For example, compound II was prepared in a multi-step synthesis. The title substituted pyrazole derivative for inhibiting protein kinase over expression, or stereoisomer, geometric isomer, tautomer, oxynitride, solvate, hydrate, metabolite, ester, pharmaceutically acceptable salt or prodrug thereof, pharmaceutical compns. containing these compds. as active ingredients, and the application of these compds. or pharmaceutical compns. in preparing the drugs for preventing, treating of reducing cell growth disorders. (assay data given).
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of pyrazolylaminopyrimidine derivs. as aurora kinase inhibitor useful in the treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 128 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:494404 CAPLUS Full-text
DOCUMENT NUMBER: 162:570128
TITLE: Dermatologic adverse events in pediatric patients receiving targeted anticancer therapies: A pooled analysis
AUTHOR(S): Belum, Viswanath Reddy; Washington, Courtney; Pratilas, Christine A.; Sibaud, Vincent; Boralevi, Franck; Lacouture, Mario E.
CORPORATE SOURCE: Department of Dermatology, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Pediatric Blood & Cancer (2015), 62(5), 798-806
CODEN: PBCEAQ; ISSN: 1545-5017
DIGITAL OBJECT ID: 10.1002/pbc.25429
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background : The dermatol. adverse events (AEs) of various molecularly targeted therapies are well-described in adult cancer patients. Little has been reported on the incidence and clin. presentation of such AEs in pediatric patients with cancer. To address this gap, we analyzed the dermatol. AEs reported across clin. trials of targeted anticancer therapies in pediatric patients. Procedures : We conducted an electronic literature search (PubMed, American Society of Clin. Oncol. annual meetings' abstrs., , NCI's Pediatric Oncol. Branch webpage) to identify clin. trials involving targeted anticancer therapies that reported dermatol. AEs in their safety data. Studies were limited to the pediatric population, monotherapy trials (oncol.), and English language publications. Results : Pooled data from 19 clin. studies investigating 11 targeted anticancer agents (alemtuzumab, rituximab, imatinib, dasatinib, erlotinib, vandetanib, sorafenib, cabozantinib, pazopanib, everolimus, and temsirolimus) were analyzed. The most frequently encountered dermatol. AEs were rash (127/660; 19%), xerosis (18/100; 18%), mucositis (68/402; 17%), and pruritus (12/169; 7%). Other AEs included pigmentary abnormalities of the skin/hair (13%), hair disorders (trichomegaly, hypertrichosis, alopecia, and madarosis; 14%), urticaria (7%), palmoplantar erythrodysesthesia (7%), erythema, acne, purpura, skin fissures, other 'unknown skin changes', exanthem, infection, flushing, telangiectasia, and photosensitivity. Conclusion : This study describes the dermatol. manifestations of targeted anticancer therapy-related AEs in the pediatric population. Since these AEs are often associated with significant morbidity, it is imperative that pediatric oncologists be familiar with their recognition and management, to avoid unnecessary dose modifications and/or termination, and to prevent impairments in patients' quality of life. Pediatr Blood Cancer 2015;62:798-806. © 2015 Wiley Periodicals, Inc.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dermatol. adverse events in pediatric patients receiving targeted anticancer therapies)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

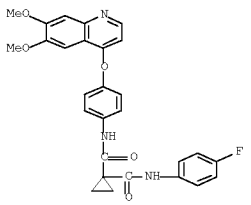


REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 129 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:460229 CAPLUS full-text
DOCUMENT NUMBER: 162:398722
TITLE: Anti-human angiopoietin 2 antibody for enhancing efficacy of antitumor agent and for combination cancer therapy
INVENTOR(S): Kim, Kyung Eun; Han, Sang Yeul; Koh, Gou Young; Lee, Hyo Seon; Kim, Chan
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd, S. Korea; Korea Advanced Institute of Science and Technology
SOURCE: Eur. Pat. Appl., 66pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2848631	A1	20150318	EP 2014-178842	20140729
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015032075	A	20150325	KR 2013-112089	20130917
US 20150079112	A1	20150319	US 2014-14446199	20140729
PRIORITY APPLN. INFO.:			KR 2013-112089 A	20130917

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method of preventing or treating cancer using an anti-Ang2 antibody or an antigen-binding fragment thereof that specifically binds to an angiogenesis-inducing factor Angiopoietin-2 (Ang2) and complexes to a Tie2 receptor while bound with Ang2.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human angiopoietin 2 antibody for enhancing efficacy of antitumor agent and for combination cancer therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

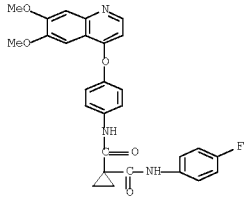


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 130 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:458209 CAPLUS full-text
DOCUMENT NUMBER: 162:447668
TITLE: Anti-human VSTM5 antibodies, fragments and conjugates for therapy and diagnosis of cancer, infection and immune disease
INVENTOR(S): Levine, Zurit; Rotman, Galit; Dassa, Liat; Levy, Ofer; Cojocaru, Gad S.; Toporik, Amir; Kliger, Yossef; Pow, Andrew; Liang, Spencer
PATENT ASSIGNEE(S): Compugen Ltd., Israel
SOURCE: PCT Int. Appl., 490pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015037005	A1	20150319	WO 2014-IL50814	20140911
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2922805	A1	20150319	CA 2014-2922805	20140911
AU 2014319921	A1	20160317	AU 2014-319921	20140911
PRIORITY APPLN. INFO.:			US 2013-61876324 P	20130911
			WO 2014-IL50814 W	20140911

AB The present invention relates to VSTM5-specific antibodies, antibody fragments, and VSTM5 polypeptides, conjugates and compns. comprising same, for modulating (antagonizing or agonizing) one or more of the effects of VSTM5 expression on immunity. More specifically, the present invention relates to VSTM5-specific antibodies, antibody fragments, and VSTM5 polypeptides, conjugates and compns. comprising same for treating and aiding in the diagnosis of cancer, infectious diseases and immune related diseases, e.g., those associated with aberrant (higher or lower than normal) VSTM5 expression by diseased and/or immune cells and/or aberrant (increased or reduced) VSTM5-mediated effects on immunity.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human VSTM5 antibodies, fragments and conjugates for therapy and diagnosis of cancer, infection and immune disease)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



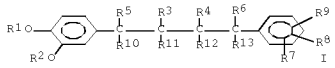
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

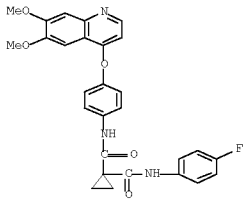
L8 ANSWER 131 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:423197 CAPLUS Full-text
DOCUMENT NUMBER: 162:419539
TITLE: Cancer therapy using dual kinase inhibitors such as catecholic butanes
INVENTOR(S): White, Thomas F.; Hoth, Daniel
PATENT ASSIGNEE(S): Triact Therapeutic, Inc., USA
SOURCE: PCT Int. Appl., 76pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015035410	A1	20150312	WO 2014-US54832	20140909
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2923667	A1	20150312	CA 2014-2923667	20140909
US 20150071919	A1	20150312	US 2014-14481837	20140909

PRIORITY APPLN. INFO.: US 2013-61875502 P 20130909
WO 2014-US54832 W 20140909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 162:419539
GI



AB The application relates to methods for treating a proliferative disorder by administering to a subject a pharmaceutical composition of a dual kinase inhibitor e.g. catecholic butanes of formula I [R1, R2 = independently H, lower alkyl, lower acyl; R3 - R6, R10 - R13 = independently H, lower alkyl; R7 - R9 = independently H, OH, lower alkoxy, lower acyloxy]. Patients to be treated include those that have been treated with Tarceva or other therapeutic compds. and relapsed or are resistant to treatment. The compds. described herein may exhibit a synergistic effect when administered with another agent.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer therapy using a dual kinase inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

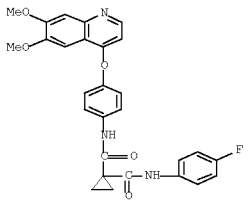


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 132 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:422447 CAPLUS Full-text
DOCUMENT NUMBER: 162:371151
TITLE: Combination therapy for the treatment of cancer using c-met inhibitor and c-myc inhibitor
INVENTOR(S): Lee, Ji Min; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 83pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150071932	A1	20150312	US 2014-14481509	20140909
KR 2015029175	A	20150318	KR 2013-107995	20130909

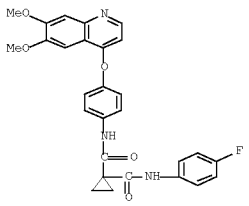
PRIORITY APPLN. INFO.: KR 2013-107995 A 20130909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 162:371151
AB The invention relates to a method of preventing and/or treating a cancer including co-administering a c-Met inhibitor and a c-Myc Inhibitor to a subject in need thereof. The invention relates to a pharmaceutical composition comprising a c-Met inhibitor and a c-Myc inhibitor. The inhibitor comprises at least one selected from the group consisting of an antibody, an antigen-binding fragment thereof, aptamers, siRNA, shRNA, microRNA, or a small mol. The invention relates to a kit comprising a pharmaceutically effective amount of a c-Met inhibitor as an active ingredient, and a second pharmaceutical composition comprising a pharmaceutically effective amount of a c-Myc inhibitor as an active ingredient, packaged together.
IT 849217-68-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for the treatment of cancer using c-met inhibitor and c-myc inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 133 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:422412 CAPLUS Full-text
DOCUMENT NUMBER: 162:423721
TITLE: Combination cancer therapy using c-met inhibitor and β-catenin inhibitor
INVENTOR(S): Lee, Ji Min; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 98pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150071930	A1	20150312	US 2014-14480174	20140908
KR 2015028652	A	20150316	KR 2013-107568	20130906

PRIORITY APPLN. INFO.: KR 2013-107568 A 20130906
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose a method of preventing and/or treating cancer. The method comprises the administration of a c-Met inhibitor and a β-catenin inhibitor. In several examples, an anti-MET receptor antibody in combination with a β-catenin inhibitor are shown to be effective in inhibiting the proliferation of breast, colon, and renal cancer cells.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy using MET inhibitor and β-catenin inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



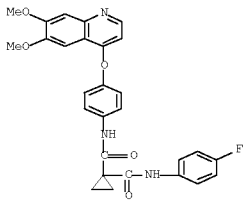
L8 ANSWER 134 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:414572 CAPLUS Full-text
DOCUMENT NUMBER: 162:425170
TITLE: Preparation of substituted pyridine compounds as tyrosine kinase inhibitors for treating proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Liang; Wang, Tingjin
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 142pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

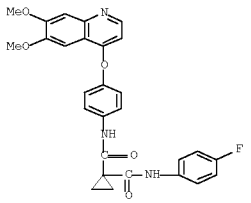
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015034729	A1	20150312	WO 2014-US53017	20140827
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS,				

SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2013-61873963 P 20130905
OTHER SOURCE(S): CASREACT 162:425170; MARPAT 162:425170
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

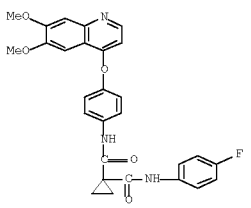
AB The present invention provides novel substituted pyridine compds. of general formula I (wherein each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; each of X and Y is independently C6-10aryl or 5-10 membered heteroaryl, both optionally substituted; W is C3-8cycloalkyl, -(C1-4-alkylene)(C3-8cycloalkyl), C3-7heterocyclyl or -(C1-4-alkylene)-C3-7heterocyclyl, each optionally substituted), pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 4-step synthesis that involved reaction of intermediate tert-Bu 4-(5-bromopyridin-2-yl)piperazine-1-carboxylate with III, and deprotecting the intermediate formed. The stability of the example compds. in human and rat liver microsomes, their pharmacokinetic profile in rats, and their ALK kinase and c-met kinase inhibitory activities were measured.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyridine compds. as tyrosine kinase inhibitors for treating proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 136 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:359181 CAPLUS Full-text
DOCUMENT NUMBER: 163:714261
TITLE: Patient-Derived Xenografts from Non-Small Cell Lung Cancer Brain Metastases Are Valuable Translational Platforms for the Development of Personalized Targeted Therapy
AUTHOR(S): Lee, Hye Won; Lee, Jung-il; Lee, Se Jeong; Cho, Hyun Jung; Song, Hye Jin; Jeong, Da Eun; Seo, Yun Jee; Shin, Sang; Joung, Je-Gun; Kwon, Yong-Jun; Choi, Yoon-La; Park, Woong-Yang; Lee, Hyun Moo; Seol, Ho Jun; Shim, Young Mog; Joo, Kyeung Min; Nam, Do-Hyun
CORPORATE SOURCE: Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, S. Korea
SOURCE: Clinical Cancer Research (2015), 21(5), 1172-1182
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-14-1589
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: The increasing prevalence of distant metastases from non-small cell lung cancer (NSCLC) indicates an urgent need for novel therapeutic modalities. Brain metastasis is particularly common in NSCLC, with severe adverse effects on clin. prognosis. Although the mol. heterogeneity of NSCLC and availability of various targeted agents suggest personalized therapeutic approaches for such brain metastases, further development of appropriate preclin. models is needed to validate the strategies. Exptl. Design: We established patient-derived xenografts (PDX) using NSCLC brain metastasis surgical samples and elucidated their possible preclin. and clin. implications for personalized treatment. Results: NSCLC brain metastases (n = 34) showed a significantly higher successful PDX establishment rate than primary specimens (n = 64; 74% vs. 23%). PDXs derived from NSCLC brain metastases recapitulated the pathol., genetic, and functional properties of corresponding parental tumors. Furthermore, tumor spheres established in vitro from the xenografts under serum-free conditions maintained their in vivo brain metastatic potential. Differential phenotypic and mol. responses to 20 targeted agents could subsequently be screened in vitro using these NSCLC PDXs derived from brain metastases. Although PDX establishment from primary NSCLCs was significantly influenced by histol. subtype, clin. aggressiveness, and genetic alteration status, the brain metastases exhibited consistently adequate in vivo tumor take rate and in vitro tumor sphere formation capacity, regardless of clin. and mol. conditions. Conclusions: Therefore, PDXs from NSCLC brain metastases may better represent the heterogeneous advanced NSCLC population and could be utilized as preclin. models to meet unmet clin. needs such as drug screening for personalized treatments. Clin Cancer Res; 21(5); 1172-82. ©2014 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(patient-derived xenografts from non-small cell lung cancer brain metastases are valuable translational platforms for the development of personalized targeted therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 137 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:316867 CAPLUS Full-text
DOCUMENT NUMBER: 162:399931
TITLE: Novel crystal form of quinoline compound and preparation method thereof
INVENTOR(S): Tang, Dongjun; Liu, Yanping; Kou, Jingping
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104370811	A	20150225	CN 2014-10399795	20140814

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 135 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:383707 CAPLUS Full-text
DOCUMENT NUMBER: 162:337080
TITLE: Gene expression signatures predictive of subject response to a multi-kinase inhibitor and methods of using the same
INVENTOR(S): Guo, Sheng; Chen, Dawei; Zhang, Juan; Cai, Jie; Li, Henry Qixiang
PATENT ASSIGNEE(S): Crown Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015031604	A1	20150305	WO 2014-US53142	20140828

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

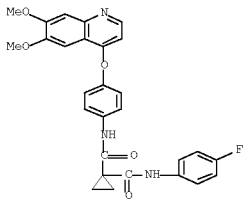
PRIORITY APPLN. INFO.: WO 2013-CN82487 A 20130828
AB Gene expression signature predictive of cancer patient response to multi-kinase inhibitor is disclosed. Also disclosed are methods predicting the efficacy of the multi-kinase inhibitor for treating cancer in a patient. Also disclosed are methods for distinguishing responders from non-responders to a multi-kinase inhibitor in treating cancer. Also disclosed are methods for treating a cancer patient with a multi-kinase inhibitor.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene expression signature predictive of subject response to a multi-kinase inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

PRIORITY APPLN. INFO.: CN 2013-10356174 A 20130815

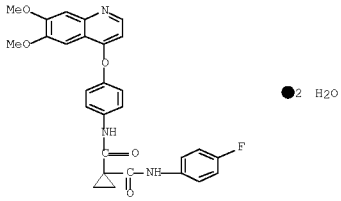
AB The present invention relates to a novel crystal form of quinoline compd. N-(4-{[6,7-dimethoxyquinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarbonamide and preparation method thereof, and belongs to medicinal chemical field. The crystal form is basically pure crystal form I or crystal form II. In the X-ray powder diffraction pattern of crystal form I, there are peaks at 2θ angles of about 11.9, 12.9, 14.4, 16.0, 22.1 and 26.0 degrees. In the X-ray powder diffraction pattern of crystal form II, there are peaks at 2θ angles of about 11.6, 14.1, 18.5, 21.1, 22.2, 23.2, 24.1 and 29.0 degrees. The novel crystal form possesses good stability and mobility, which is conducive to operate in storage, transfer and production, and the novel crystal form can be used for preparing pharmaceutically acceptable salt thereof for application in pharmaceutics.

IT 849217-68-1 1669412-61-6 1669412-63-8
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal forms of quinoline compound by using three-component coupling and/or condensation as the key steps)

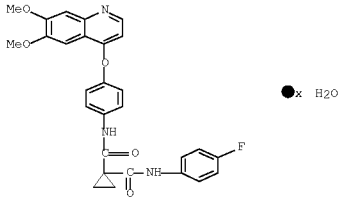
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1669412-61-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrate (1:2) (CA INDEX NAME)



RN 1669412-63-8 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrate (1:?) (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

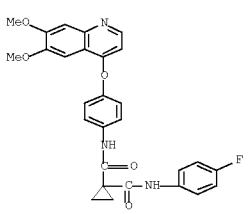
L8 ANSWER 138 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:312826 CAPLUS Full-text
DOCUMENT NUMBER: 163:407215
TITLE: Treating medullary thyroid cancer in the age of targeted therapy
AUTHOR(S): Cabanillas, Maria E.; Hu, Mimi I.; Jimenez, Camilo; Grubbs, Elizabeth G.; Cote, Gilbert J.
CORPORATE SOURCE: Department of Endocrine Neoplasia & Hormonal Disorders, Unit 1461, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX, 77030, USA
SOURCE: International Journal of Endocrine Oncology (2014), 1(2), 203-216
CODEN: IJEOBC; ISSN: 2045-0869

DIGITAL OBJECT ID: 10.2217/ije.14.26
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor deriving from the thyroid parafollicular cell. Thyroidectomy continues to serve as the primary initial treatment for this cancer. Because standard cytotoxic chemotherapy has proven ineffective, reoperation and external beam radiation therapy had been the only tools to treat recurrences or distant disease. The discovery that aberrant activation of RET, a receptor tyrosine kinase, is a primary driver of MTC tumorigenesis led to clin. trials using RET-targeting tyrosine kinase inhibitors. The successes of those trials led to the approval of vandetanib and cabozantinib for treating patients with progressive or symptomatic MTC. The availability of these drugs, along with addnl. targeted therapies in development, requires a thoughtful reconsideration of the approach to treating patients with unresectable locally advanced and/or metastatic progressive MTC.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating medullary thyroid cancer in age of targeted therapy)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

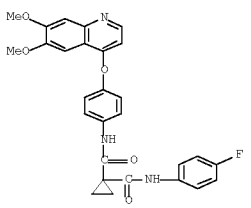
L8 ANSWER 139 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:312823 CAPLUS Full-text
DOCUMENT NUMBER: 163:437839
TITLE: Protein kinase inhibitor therapy in advanced thyroid cancer: ethical challenges and potential solutions
AUTHOR(S): Bible, Keith C.; Ain, Kenneth B.; Rosenthal, M. Sara
CORPORATE SOURCE: Mayo Clinic, Division of Medical Oncology, Rochester, MN, USA
SOURCE: International Journal of Endocrine Oncology (2014), 1(2), 145-151
CODEN: IJEOBC; ISSN: 2045-0869

DIGITAL OBJECT ID: 10.2217/ije.14.24
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB Protein kinase inhibitors (PKIs) have emerged as highly promising therapies in progressive metastatic radioiodine-refractory differentiated thyroid cancer and in medullary thyroid cancer; two were recently approved in the USA for use in medullary thyroid cancer (vandetanib, cabozantinib), and another for use in progressive metastatic radioiodine-refractory differentiated thyroid cancer (sorafenib). Although more than 90% of thyroid cancer patients fare well in response to conventional treatment, PKI therapy has the potential to provide benefit. Nonetheless, PKIs produce numerous side effects, may worsen quality of life, may hasten mortality (by 1-2%), require discerning clin. acumen, are not yet proven to improve thyroid cancer survival and are very costly. This raises questions about who should prescribe PKIs, and about whether their use in thyroid cancer is truly beneficent and ethically justified. Restraint should be exercised in their use in thyroid cancer, with potential risks and benefits carefully weighed and solns. devised to help ameliorate many of the problems associated with their use.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein kinase inhibitor therapy in advanced thyroid cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 140 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:293134 CAPLUS Full-text
DOCUMENT NUMBER: 162:337073
TITLE: 1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy
INVENTOR(S): Jefford, Charles William; Hoessli, Daniel

PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 69pp.; Chemical Indexing Equivalent to 162:337069 (GB)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015022497	A1	20150219	WO 2014-GB52392	20140805
GB 2517199	A	20150218	GB 2013-14639	20130815

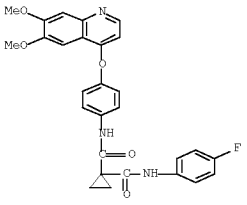
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2013-14639 A 20130815
OTHER SOURCE(S): MARPAT 162:337070

AB The invention provides 1,2,4-trioxane compds. or pharmaceutically acceptable salts, esters, solvates, tautomers, stereoisomers thereof, for use as adjuvants for tyrosine kinase inhibitors in the treatment of cancer. Preferably the tyrosine kinase inhibitor is selected from imatinib, gefitinib, erlotinib, lapatinib, canertinib, vatalanib, sorafenib or genistein. The cancer may be selected from lymphoma, breast cancer, leukemia, gastrointestinal tumors, nonsmall cell lung cancer, melanoma, renal carcinoma, multiple myeloma, kidney cancer, colon cancer, pancreatic cancer, lung cancer, ovarian cancer and prostate cancer.

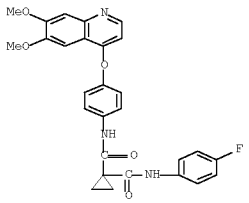
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 142 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:283246 CAPLUS Full-text
DOCUMENT NUMBER: 163:418637
TITLE: Cabozantinib reverses multidrug resistance of human hepatoma HepG2/adr cells by modulating the function of P-glycoprotein
AUTHOR(S): Xiang, Qing-feng; Zhang, Dong-mei; Wang, Jing-nan; Zhang, Hong-wu; Zheng, Zhe-yu; Yu, Da-cheng; Li, Ying-jie; Xu, Jun; Chen, Ya-jin; Shang, Chang-zhen
CORPORATE SOURCE: Department of Hepatopancreatobiliary Surgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Peop. Rep. China
SOURCE: Liver International (2015), 35(3), 1010-1023
CODEN: LIINCM; ISSN: 1478-3223
DIGITAL OBJECT ID: 10.1111/liv.12524
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 141 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:283370 CAPLUS Full-text
DOCUMENT NUMBER: 163:438161
TITLE: Is there an antiandrogen withdrawal syndrome with enzalutamide?
AUTHOR(S): Rodriguez-Vida, Alejo; Bianchini, Diletta; Van Hemelrijck, Mieke; Hughes, Simon; Malik, Zafar; Powles, Thomas; Bahl, Amit; Rudman, Sarah; Payne, Heather; de Bono, Johann; Chowdhury, Simon
CORPORATE SOURCE: Great Maze Pond, Guy's and St Thomas' NHS Foundation Trust, London, UK
SOURCE: BJU International (2015), 115(3), 373-380
CODEN: BJINFO; ISSN: 1464-410X
DIGITAL OBJECT ID: 10.1111/bju.12826
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Objective : To examine prostate-specific antigen (PSA) levels after enzalutamide discontinuation to assess whether an antiandrogen withdrawal syndrome (AAWS) exists with enzalutamide. Methods : We retrospectively identified 30 consecutive patients with metastatic prostate cancer who were treated with enzalutamide after docetaxel. Post-discontinuation PSA results were available for all patients and were determined at 2-weekly intervals until starting further anticancer systemic therapy. PSA withdrawal response was defined as a PSA decline by ≥50% from the last on-treatment PSA, with a confirmed decrease ≥3 wk later. Patient characteristics were evaluated in relation to the AAWS using univariate logistic regression anal. Results : The median (range) patient age was 70.5 (56-86) years and the median (range) follow-up was 9.0 (0.5-16) months. The most common metastatic sites were the bone (86.7%) and lymph nodes (66.7%). Most patients (70%) had previously received abiraterone and 12 patients (40%) had also received cabazitaxel. The median (range) treatment duration with enzalutamide was 3.68 (1.12-21.39) months. PSA levels after enzalutamide withdrawal were monitored for a median (range) time of 35 (10-120) days. Only one patient (3.3%) had a confirmed PSA response ≥50% after enzalutamide discontinuation. One patient (3.3%) had a confirmed PSA response of between 30 and 50% and another patient (3.3%) had an unconfirmed PSA response of between 30 and 50%. The median overall survival was 15.5 mo (95% CI 8.1-24.7). None of the factors analyzed in the univariate anal. were significant predictors of PSA decline after enzalutamide discontinuation. Conclusions : This retrospective study provides the first evidence that enzalutamide may have an AAWS in a minority of patients with metastatic castration-resistant prostate cancer. Further studies are needed to confirm the existence of an enzalutamide AAWS and to assess its relevance in prostate cancer management.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiandrogen withdrawal syndrome with enzalutamide)

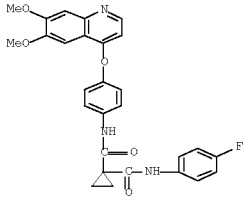
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

L8 ANSWER 140 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:283370 CAPLUS Full-text
DOCUMENT NUMBER: 163:438161
TITLE: Is there an antiandrogen withdrawal syndrome with enzalutamide?
AUTHOR(S): Rodriguez-Vida, Alejo; Bianchini, Diletta; Van Hemelrijck, Mieke; Hughes, Simon; Malik, Zafar; Powles, Thomas; Bahl, Amit; Rudman, Sarah; Payne, Heather; de Bono, Johann; Chowdhury, Simon
CORPORATE SOURCE: Great Maze Pond, Guy's and St Thomas' NHS Foundation Trust, London, UK
SOURCE: BJU International (2015), 115(3), 373-380
CODEN: BJINFO; ISSN: 1464-410X
DIGITAL OBJECT ID: 10.1111/bju.12826
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Objective : To examine prostate-specific antigen (PSA) levels after enzalutamide discontinuation to assess whether an antiandrogen withdrawal syndrome (AAWS) exists with enzalutamide. Methods : We retrospectively identified 30 consecutive patients with metastatic prostate cancer who were treated with enzalutamide after docetaxel. Post-discontinuation PSA results were available for all patients and were determined at 2-weekly intervals until starting further anticancer systemic therapy. PSA withdrawal response was defined as a PSA decline by ≥50% from the last on-treatment PSA, with a confirmed decrease ≥3 wk later. Patient characteristics were evaluated in relation to the AAWS using univariate logistic regression anal. Results : The median (range) patient age was 70.5 (56-86) years and the median (range) follow-up was 9.0 (0.5-16) months. The most common metastatic sites were the bone (86.7%) and lymph nodes (66.7%). Most patients (70%) had previously received abiraterone and 12 patients (40%) had also received cabazitaxel. The median (range) treatment duration with enzalutamide was 3.68 (1.12-21.39) months. PSA levels after enzalutamide withdrawal were monitored for a median (range) time of 35 (10-120) days. Only one patient (3.3%) had a confirmed PSA response ≥50% after enzalutamide discontinuation. One patient (3.3%) had a confirmed PSA response of between 30 and 50% and another patient (3.3%) had an unconfirmed PSA response of between 30 and 50%. The median overall survival was 15.5 mo (95% CI 8.1-24.7). None of the factors analyzed in the univariate anal. were significant predictors of PSA decline after enzalutamide discontinuation. Conclusions : This retrospective study provides the first evidence that enzalutamide may have an AAWS in a minority of patients with metastatic castration-resistant prostate cancer. Further studies are needed to confirm the existence of an enzalutamide AAWS and to assess its relevance in prostate cancer management.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiandrogen withdrawal syndrome with enzalutamide)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



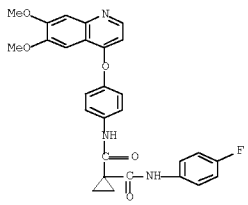
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 143 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:281739 CAPLUS Full-text
DOCUMENT NUMBER: 162:337069
TITLE: 1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy
INVENTOR(S): Jefford, Charles William; Hoessli, Daniel Christian
PATENT ASSIGNEE(S): Switz.
SOURCE: Brit. UK Pat. Appl., 66pp.; Chemical Indexing Equivalent to 162:337073 (WO)
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2517199	A	20150218	GB 2013-14639	20130815
WO 2015022497	A1	20150219	WO 2014-GB52392	20140805

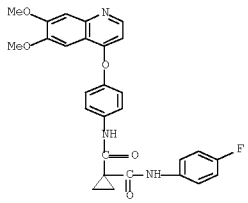
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2013-14639 A 20130815
AB The invention provides 1,2,4-trioxane compds. or pharmaceutically acceptable salts, esters, solvates, tautomers, stereoisomers thereof, for use as adjuvants for tyrosine kinase inhibitors in the treatment of cancer. Preferably the tyrosine kinase inhibitor is selected from imatinib, gefitinib, erlotinib, lapatinib, canertinib, vatalanib, sorafenib or genistein. The cancer may be selected from lymphoma, breast cancer, leukemia, gastrointestinal tumors, nonsmall cell lung cancer, melanoma, renal carcinoma, multiple myeloma, kidney cancer, colon cancer, pancreatic cancer, lung cancer, ovarian cancer and prostate cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



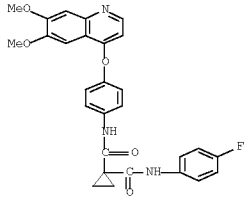
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 145 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:232900 CAPLUS Full-text
DOCUMENT NUMBER: 163:340057
TITLE: Potent antitumor activity of cabozantinib, a c-MET and VEGFR2 inhibitor, in a colorectal cancer patient-derived tumor explant model
AUTHOR(S): Song, Eun-Kee; Tai, W. M.; Messersmith, Wells A.; Bagby, Stacey; Purkey, Alicia; Quackenbush, Kevin S.; Pitts, Todd M.; Wang, Guoliang; Blatchford, Patrick; Yahn, Rachel; Kaplan, Jeffrey; Tan, Aik Choon; Atreya, Chloe E.; Eckhardt, Gail; Kelley, Robin K.; Venook, Alan; Kwak, Eunice L.; Ryan, David; Arcaroli, John J.
CORPORATE SOURCE: Division of Medical Oncology, University of Colorado Denver and University of Colorado Cancer Center, Aurora, CO, USA
SOURCE: International Journal of Cancer (2015), 136(8), 1967-1975
CODEN: IJCNAW; ISSN: 0020-7136
DIGITAL OBJECT ID: 10.1002/ijc.29225
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Antiangiogenic therapy is commonly used for the treatment of colorectal cancer (CRC). Although patients derive some clin. benefit, treatment resistance inevitably occurs. The MET signaling pathway has been proposed to be a major contributor of resistance to antiangiogenic therapy. MET is upregulated in response to vascular endothelial growth factor pathway inhibition and plays an essential role in tumorigenesis and progression of tumors. In this study, we set out to determine the efficacy of cabozantinib in a preclin. CRC patient-derived tumor xenograft model. We demonstrate potent inhibitory effects on tumor growth in 80% of tumors treated. The greatest antitumor effects were observed in tumors that possess a mutation in the PIK3CA gene. The underlying antitumor mechanisms of cabozantinib consisted of inhibition of angiogenesis and Akt activation and significantly decreased expression of genes involved in the PI3K pathway. These findings support further evaluation of cabozantinib in patients with CRC. PIK3CA mutation as a predictive biomarker of sensitivity is intriguing and warrants further elucidation. A clin. trial of cabozantinib in refractory metastatic CRC is being activated.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VEGFR2 and c-Met inhibitor, cabozantinib show antitumor activity in xenograft mouse model of colorectal cancer especially with PIK3CA mutation via inhibiting angiogenesis, Akt activation and lowering expression of PI3K pathway genes)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 144 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:258957 CAPLUS Full-text
DOCUMENT NUMBER: 162:370540
TITLE: Design and Optimization of a Series of 1-Sulfonylpyrazolo[4,3-b]pyridines as Selective c-Met Inhibitors
AUTHOR(S): Ma, Yuchi; Sun, Guangqiang; Chen, Danqi; Peng, Xia; Chen, Yue-Lei; Su, Yi; Ji, Yinchun; Liang, Jin; Wang, Xin; Chen, Lin; Ding, Jian; Xiong, Bing; Ai, Jing; Geng, Meiyu; Shen, Jingkang
CORPORATE SOURCE: Department of Medicinal Chemistry, State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 201203, Peop. Rep. China
SOURCE: Journal of Medicinal Chemistry (2015), 58(5), 2513-2529
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/jm502018y
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 162:370540
AB C-Met has emerged as an attractive target for targeted cancer therapy because of its abnormal activation in many cancer cells. To identify high potent and selective c-Met inhibitors, we started with profiling the potency and in vitro metabolic stability of a reported hit 7. By rational design, a novel sulfonylpyrazolo[4,3-b]pyridine 9 with improved DMPK properties was discovered. Further elaboration of π-π stacking interactions and solvent accessible polar moieties led to a series of highly potent and selective type I c-Met inhibitors. On the basis of in vitro and in vivo pharmacol. and pharmacokinetics studies, compound 46 was selected as a preclin. candidate for further anticancer drug development.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design and optimization of a series of 1-sulfonylpyrazolo[4,3-b]pyridines as selective c-Met inhibitors)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

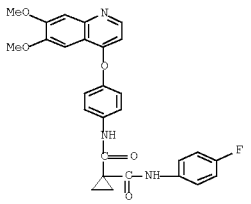
L8 ANSWER 146 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:226654 CAPLUS Full-text
DOCUMENT NUMBER: 163:214328
TITLE: Dual effects of a targeted small-molecule inhibitor (cabozantinib) on immune-mediated killing of tumor cells and immune tumor microenvironment permissiveness when combined with a cancer vaccine
AUTHOR(S): Kwilas, Anna R.; Ardiani, Andressa; Donahue, Renee N.; Aftab, Dana T.; Hodge, James W.
CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Translational Medicine (2014), 12, 294/1-294/15, 15 pp.

CODEN: JTMOBV; ISSN: 1479-5876
DIGITAL OBJECT ID: 10.1186/s12967-014-0294-y
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background: Growing awareness of the complexity of carcinogenesis has made multimodal therapies for cancer increasingly compelling and relevant. In recent years, immunotherapy has gained acceptance as an active therapeutic approach to cancer treatment, even though cancer is widely considered an immunosuppressive disease. Combining immunotherapy with targeted agents that have immunomodulatory capabilities could significantly improve its efficacy. Methods: We evaluated the ability of cabozantinib, a receptor tyrosine kinase inhibitor, to modulate the immune system in vivo as well as alter the phenotype of tumor cells in vitro in order to determine if this inhibitor could act synergistically with a cancer vaccine. Results: Our studies indicated that cabozantinib altered the phenotype of MC38-CEA murine tumor cells, rendering them more sensitive to immune-mediated killing. Cabozantinib also altered the frequency of immune sub-populations in the periphery as well as in the tumor microenvironment, which generated a more permissive immune environment. When cabozantinib was combined with a poxviral-based cancer vaccine targeting a self-antigen, the combination significantly reduced the function of regulatory T cells and increased cytokine production from effector T cells in response to the antigen. These alterations to the immune landscape, along with direct modification of tumor cells, led to markedly improved antitumor efficacy. Conclusions: These studies support the clin. combination of cabozantinib with immunotherapy for the treatment of cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual role of targeted small mol. inhibitor cabozantinib combined with cancer vaccine on immune mediated killing of tumor cells and immune tumor microenvironment permissiveness)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

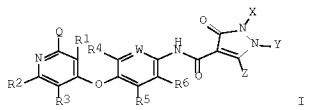


REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

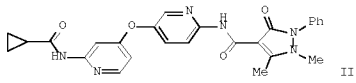
L8 ANSWER 147 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:213358 CAPLUS Full-text
DOCUMENT NUMBER: 162:245319
TITLE: Preparation of pyrazolone compounds that are protein tyrosine kinase activity modulators useful in treatment of proliferative and other diseases
INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150037280	A1	20150205	US 2013-13945924	20130719
US 8975282	B2	20150310		
US 20150050239	A1	20150219	US 2013-13945925	20130719
US 8969388	B2	20150303		
US 20150141463	A1	20150521	US 2015-14601207	20150120

PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
US 2013-13945924 A3 20130719
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 162:245319; MARPAT 162:245319
GI



I

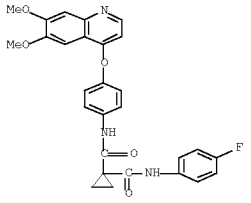


II

AB The invention provides novel substituted pyrazolone compds. of formula I [each of R1-R7 is independently H, F, Cl, (C1-C6)alkyl, (C1-C6)haloalkyl, etc.; each of X, Y and Z is independently H, (C1-C6)alkyl, (C6-C10)aryl, etc.; W is CR7 or N; Q as defined in the disclosure], pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The example compound II was prepared in two-step synthesis (procedure shown) was tested in multiple bioassay for activity in modulation of protein tyrosine kinase, pharmacokinetics and metabolic stability, as well as for antiproliferative activity. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyrazolone compds. that are protein tyrosine kinase activity modulators useful in treatment of proliferative and other diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 148 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:210763 CAPLUS Full-text
DOCUMENT NUMBER: 162:283487
TITLE: Dielectrophoresis methods for determining a property of a plurality of cancer cells to determine drug efficacy and/or resistance
INVENTOR(S): Schmelz, Eva M.; Elvington, Elizabeth S.; Salmanzadeh, Alireza; Sano, Mike; Roberts, Paul C.; Davalos, Rafael V.
PATENT ASSIGNEE(S): Virginia Tech Intellectual Properties, Inc., USA
SOURCE: PCT Int. Appl., 82pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015017729	A1	20150205	WO 2014-US49296	20140731
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20100224493	A1	20100909	US 2010-720406	20100309
US 8968542	B2	20150303		
US 20120085649	A1	20120412	US 2011-13269286	20111007

PRIORITY APPLN. INFO.: US 2010-720406 A2 20100309
US 2011-13269286 A2 20111007
US 2013-61860309 P 20130731
US 2009-61158553 P 20090309
US 2009-61252942 P 20091019
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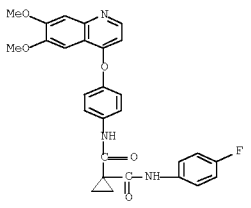
AB Provided are dielectrophoresis (DEP) devices and methods that allow cell sorting to identify, isolate, and/or sep. cells of interest based on elec. and phys. properties of the cells. Particularly, provided are systems and methods for manipulating particles suspended in a fluid, e.g., cells, micro- or nano-particles, using their elec. signatures. Such methods can be performed using DEP, iDEP, and/or cDEP (contactless dielectrophoresis, where direct contact between the electrodes and the sample is avoided). Typically, an elec. field is induced in a sample comprising the target particles and/or cells, such as cancer cells, and the spatial distribution of cells is measured to identify one or more characteristics or properties of the cancer cells. The identified characteristics of the sorted cells can be used to determine drug efficacy and/or resistance with respect to the cells.

IT 1140909-48-3, Cabozantinib-S-Malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dielectrophoresis methods for determining a property of a plurality of cancer cells to determine drug efficacy and/or resistance)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

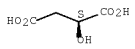
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 149 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:203193 CAPLUS Full-text
DOCUMENT NUMBER: 162:294277
TITLE: Methods of treating a cancer through targeted disruption of alpha connexin 43-zonula occludens-1 (zo-1) interaction
INVENTOR(S): Gourdie, Robert G.; Sheng, Zhi
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 152pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015017034	A1	20150205	WO 2014-US42528	20140616

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2013-61861686 P 20130802

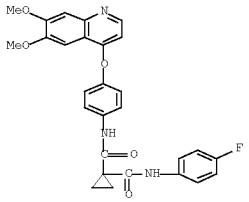
AB The present disclosure describes methods of treating a cancer based on the targeted disruption of alpha connexin 43-zonula occludens-1 (ZO-1) interaction. The methods may include administering to a subject an effective amount of a composition comprising a peptide with a contiguous sequence of amino acids representing a portion of the C-terminus of an alpha connexin protein or conservative variant thereof, wherein said C-terminus includes the sequence up to the transmembrane domain, optionally in combination with administration of a chemotherapeutic agent. In embodiments, the cancer is glioma and the chemotherapeutic agent is temozolomide. The methods may also include administration of vectors encoding the peptide or host cells comprising the vectors. Also described are compns. for treating a cancer comprising one or more peptides, nucleic acids, vectors, and/or host cells, optionally in combination with a chemotherapeutic agent such as temozolomide.

IT 1140909-48-3, Cabozantinib-s-malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of treating cancer through targeted disruption of alpha connexin 43-zonula occludens-1 interaction)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

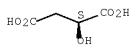
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



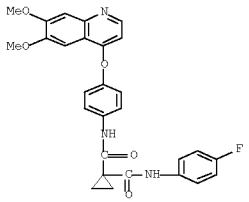
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REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 150 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:173876 CAPLUS Full-text
DOCUMENT NUMBER: 162:320090
TITLE: An LC-MS/MS method for the quantitation of cabozantinib in rat plasma: Application to a pharmacokinetic study
AUTHOR(S): Su, Qinghong; Li, Jian; Ji, Xiwei; Li, Jingyun; Zhou, Tianyan; Lu, Wei; Li, Liang
CORPORATE SOURCE: Department of Pharmaceutics, School of Pharmaceutical Sciences, Peking University Health Science Center, Beijing, 100191, Peop. Rep. China
SOURCE: Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences (2015), 985, 119-123
CODEN: JCBAAI; ISSN: 1570-0232
DIGITAL OBJECT ID: 10.1016/j.jchromb.2015.01.024
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB A simple, rapid and sensitive high-performance liq. chromatog. tandem mass-spectrometric method (LC-MS/MS) for the novel multiple tyrosine kinase inhibitor (TKI) cabozantinib was developed and validated using erlotinib as internal standard (IS). Plasma samples were pre-treated by liquid-liquid extraction with Et acetate. Separation was achieved on a reversed phase C18 column (50 × 2 mm, 5 μm) at ambient temperature using isocratic elution with acetonitrile-water (45:55, volume/volume) containing 5 mM ammonium formate buffer (finally adjusted to apparent pH* = 5.0 with formic acid) at a flow rate of 0.4 mL/min. The analytes were monitored by a triple quadrupole tandem mass spectrometer with electrospray ionization source in the pos. ion mode. Calibration curve was linear (r > 0.99) in a concentration range of 0.5-1000 ng/mL with the lower limit of quantification (LLOQ) of 0.5 ng/mL. Intra- and inter-day accuracy and precision were validated by relative error values (RE) and relative standard deviation values (RSD), resp., which were both lower than the limit of 15%. This method was successfully applied to a pharmacokinetic study of cabozantinib in rats.

IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(LC-MS/MS method for the quantitation of cabozantinib in rat plasma with application to a pharmacokinetic study)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

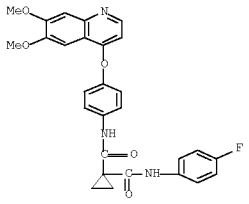


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 151 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:159139 CAPLUS Full-text
DOCUMENT NUMBER: 162:560084
TITLE: Progress in Discovery of KIF5B-RET Kinase Inhibitors for the Treatment of Non-Small-Cell Lung Cancer
AUTHOR(S): Song, Minsoo
CORPORATE SOURCE: New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Taegu, 701 310, S. Korea
SOURCE: Journal of Medicinal Chemistry (2015), 58(9), 3672-3681
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/jm501464c
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

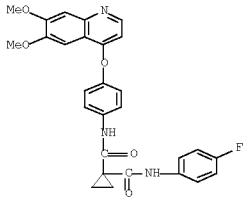
AB A review. A new chimeric fusion transcript of KIF5B (the kinesin family 5B gene) and the RET (Rearranged during Transcription) oncogene, KIF5B-RET, was found in 1-2% of lung adenocarcinomas (LADCs) in late 2011. Several related clin. trials for non-small-cell lung cancer (NSCLC) with KIF5B-RET rearrangements using existing RET inhibitors, such as lenvatinib, vandetanib, sunitinib, ponatinib, cabozantinib, and AUY922, have been swiftly initiated by the discovery of the KIF5B-RET fusion gene. Anti-RET activity and the status of clin. development of these known RET tyrosine kinase inhibitors (TKIs) for KIF5B-RET fusion-pos. NSCLC are discussed. A kinase inhibitor that can target a driver mutation specifically may lead to a superior clin. benefit compared with broad-spectrum kinase inhibitors. In this regard, an anal. of the structure of RET kinase and its complex with known RET inhibitors are also briefly discussed.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progress in discovery of KIF5B-RET kinase inhibitors for the treatment of nonsmall cell lung cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



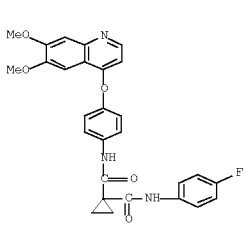
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 152 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:152289 CAPLUS Full-text
DOCUMENT NUMBER: 162:320143
TITLE: Pharmacokinetics and tissue distribution model of cabozantinib in rat determined by UPLC-MS/MS
AUTHOR(S): Wang, Xiangin; Wang, Shuanghu; Lin, Feiyan; Zhang, Qingwei; Chen, HuiLing; Wang, Xianchuan; Wen, Congcong; Ma, Jianshe; Hu, Lufeng
CORPORATE SOURCE: Analytical and Testing Center, Wenzhou Medical University, Wenzhou, 325035, Peop. Rep. China
SOURCE: Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences (2015), 983-984, 125-131
CODEN: JCBAAI; ISSN: 1570-0232
DIGITAL OBJECT ID: 10.1016/j.jchromb.2015.01.020
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib (XL184) is a novel small mol. inhibitor of receptor tyrosine kinases (RTKs) targeted at mesenchymal-epithelial transition factor (MET). To study the pharmacokinetics and tissue distribution in rat, a specific ultra-performance liquid chromatog.-tandem mass spectrometry (UPLC-MS/MS) method was developed with midazolam as internal standard The calibration curves in plasma and tissues were linear in the range of 5-5000 ng/mL (R2 > 0.99). The recoveries were better than 80.4% and matrix effects ranged from 96.9% to 105.1%. Then, the developed UPLC-MS/MS method was applied to determine the concentration of XL184 in blood and tissues. The pharmacokinetics of four different dosages (iv 5, 10 mg/kg and ig 15, 30 mg/kg) revealed that XL184 was eliminated slowly, the t1/2 was longer than 10 h and the absolute bioavailability was 25.6±8.3%. The concentration distribution of XL184 in tissues was liver > lung > kidney > spleen > heart. Based on the concentration-time of XL184 in tissues, a BP-ANN distribution model was developed with good performance, and can be used to predict the concentration of XL184 in tissues.
IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); PKT (Pharmacokinetics); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(XL184; pharmacokinetics and tissue distribution model of cabozantinib in rat determined by UPLC-MS/MS)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



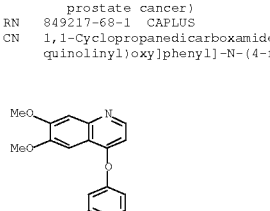
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 153 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:142298 CAPLUS Full-text
DOCUMENT NUMBER: 163:360237
TITLE: QTc interval prolongation with vascular endothelial growth factor receptor tyrosine kinase inhibitors
AUTHOR(S): Ghatalia, P.; Je, Y.; Kaymakcalan, M. D.; Sonpavde, G.; Choueiri, T. K.
CORPORATE SOURCE: Department of Internal Medicine, University of Alabama at Birmingham (UAB), Birmingham, AL, USA
SOURCE: British Journal of Cancer (2015), 112(2), 296-305
CODEN: BJCAAI; ISSN: 0007-0920
DIGITAL OBJECT ID: 10.1038/bjc.2014.564
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Multi-targeted vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) are known to cause cardiac toxicity, but the relative risk (RR) of QTc interval prolongation and serious arrhythmias associated with them are not reported. Methods: We conducted a trial-level meta-anal. of randomized phase II and III trials comparing arms with and without a US Food and Drug Administration-approved VEGFR TKI (sunitinib, sorafenib, pazopanib, axitinib, vandetanib, cabozantinib, ponatinib and regorafenib). A total of 6548 patients from 18 trials were selected. Statistical analyses were conducted to calculate the summary incidence, RR and 95% CIs. Results: The RR for all-grade and high-grade QTc prolongation for the TKI vs no TKI arms was 8.66 (95% CI 4.92-15.2, P<0.001) and 2.69 (95% CI 1.33-5.44, P=0.006), resp., with most of the events being asymptomatic QTc prolongation. Resp., 4.4% and 0.83% of patients exposed to VEGFR TKI had all-grade and high-grade QTc prolongation. On subgroup anal., only sunitinib and vandetanib were associated with a statistically significant risk of QTc prolongation, with higher doses of vandetanib associated with a greater risk. The rate of serious arrhythmias including torsades de pointes did not seem to be higher with high-grade QTc prolongation. The risk of QTc prolongation was independent of the duration of therapy. Conclusions: In the largest study to date, we show that VEGFR TKI can be associated with QTc prolongation. Although most cases were of low clin. significance, it is unclear whether the same applies to patients treated off clin. trials.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on QTc interval prolongation with vascular endothelial growth factor receptor tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

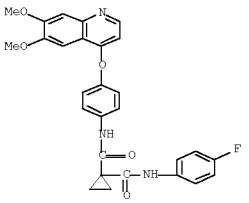
L8 ANSWER 154 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:138904 CAPLUS Full-text
DOCUMENT NUMBER: 163:511501
TITLE: Current role of cabozantinib in metastatic castration-resistant prostate cancer
AUTHOR(S): Fay, Andre P.; Albiges, Laurence; Bellmunt, Joaquim
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02215, USA
SOURCE: Expert Review of Anticancer Therapy (2015), 15(2), 151-156
CODEN: ERATBJ; ISSN: 1473-7140
DIGITAL OBJECT ID: 10.1586/14737140.2015.1003047
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Over 80% of men with castration-resistant prostate cancer have bone metastases. This condition can dramatically impact quality of life and is associated with short-term survival. Consequently, the development of bone-targeted therapies is a relevant topic on prostate cancer management. Hepatocyte growth factor receptor and vascular endothelial growth factor signaling pathways have been identified to play a role in prostate cancer progression and bone metastasis and are potential targets for therapeutic intervention. Early-phase studies have shown encouraging responses in bone metastases and pain control with cabozantinib, a multi-tyrosine kinase inhibitor targeting hepatocyte growth factor receptor and vascular endothelial growth factor receptor. Despite striking responses seen in some patients, preliminary results from a pivotal Phase III study have failed to produce survival benefit. This review encompasses preclin. and clin. data of cabozantinib in metastatic castration-resistant prostate cancer highlighting future research options for this agent.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(current role of cabozantinib in metastatic castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

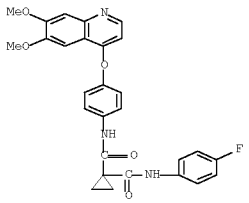
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 155 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:104550 CAPLUS Full-text
DOCUMENT NUMBER: 162:265265
TITLE: Thyroid carcinoma, version 2.2014: featured updates to the NCCN guidelines
AUTHOR(S): Tutele, R. Michael; Haddad, Robert I.; Ball, Douglas W.; Byrd, David; Dickson, Paxton; Duh, Quan-Yang; Ehya, Hormoz; Haymart, Megan; Hoh, Carl; Hunt, Jason P.; Iagaru, Andrei; Kandeel, Fouad; Kopp, Peter; Lamonica, Dominick M.; Lydiatt, William M.; McCaffrey, Judith; Moley, Jeffrey F.; Parks, Lee; Raeburn, Christopher D.; Ridge, John A.; Ringel, Matthew D.; Scheri, Randall P.; Shah, Jatin P.; Sherman, Steven I.; Sturgeon, Cord; Waguespack, Steven G.; Wang, Thomas N.; Wirth, Lori J.; Hoffmann, Karin G.; Hughes, Miranda
CORPORATE SOURCE: Memorial Sloan Kettering Cancer Center, USA
SOURCE: Journal of the National Comprehensive Cancer Network (2014), 12(12), 1671-1680
CODEN: JNCCA4; ISSN: 1540-1405
PUBLISHER: Harborside Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. These NCCN Guidelines Insights focus on some of the major updates to the 2014 NCCN Guidelines for Thyroid Carcinoma. Kinase inhibitor therapy may be used to treat thyroid carcinoma that is symptomatic and/or progressive and not amenable to treatment with radioactive iodine. Sorafenib may be considered for select patients with metastatic differentiated thyroid carcinoma, whereas vandetanib or cabozantinib may be recommended for select patients with metastatic medullary thyroid carcinoma. Other kinase inhibitors may be considered for select patients with either type of thyroid carcinoma. A new section on "Principles of Kinase Inhibitor Therapy in Advanced Thyroid Cancer" was added to the NCCN Guidelines to assist with using these novel targeted agents.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(featured updates to the NCCN guidelines for thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



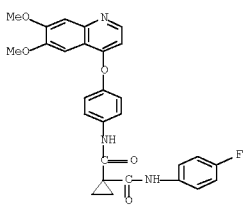
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 157 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:100878 CAPLUS Full-text
DOCUMENT NUMBER: 163:292268
TITLE: Should the Incorporation of Structural Alerts be Restricted in Drug Design? An Analysis of Structure-Toxicity Trends with Aniline-Based Drugs
AUTHOR(S): Kalgutkar, A. S.
CORPORATE SOURCE: Pharmacokinetics, Dynamics and Metabolism Department-New Chemical Entities, Pfizer Worldwide Research and Development, Cambridge, MA, 02139, USA
SOURCE: Current Medicinal Chemistry (2015), 22(4), 438-464
CODEN: CMCHE7; ISSN: 0929-8673
DIGITAL OBJECT ID: 10.2174/0929867321666141112122118
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Certain idiosyncratic adverse drug reactions (IADRs) can be triggered by electrophilic protein-reactive metabolites that are formed in the process of drug metabolism While methodologies (e.g., structural alert concept in drug design, glutathione (GSH) trapping, and protein covalent binding) for examining reactive metabolite (RM) formation are available, predicting the IADR potential applying these parameters remains a significant challenge. The present work examines toxicity trends associated with the aniline structural alert in the top 200 prescribed drugs of 2011 and recently approved (2009-2013) small mol. drugs, in relation with 30 aniline-based drugs withdrawn from com. use or associated with a black box warning for IADRs. The aniline sub-structure was found in several drugs from the toxic, mostprescribed, and recently approved category. RMs resulting from the bioactivation of the aniline alert was also noted in the three categories chosen for comparison. A major discriminator between the toxic drugs and the majority of drugs in the most-prescribed list, however, was the daily dose - drugs most frequented associated with IADRs were the ones with higher daily doses (exceeding hundreds of milligrams). A greater tolerance for IADRs was also noted with certain drugs intended to treat rare, unmet medical needs (e.g., cancer). Overall, the anal. suggests that optimization of pharmacol. potency and pharmacokinetics that would lead to a lower daily dose, and therefore, a lower body burden of parent drug/metabolites, should be taken into consideration in drug discovery.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anal. of structure-toxicity trends with aniline-based drugs)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 156 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:100945 CAPLUS Full-text
DOCUMENT NUMBER: 163:480691
TITLE: Targeting Angiogenesis in Thyroid Cancer
AUTHOR(S): Lkhoyaali, S.; Benhmida, S.; Aitelhaj, M.; Layachi, M.; Abahssain, H.; Ismaili, H. N.; Errihani, H.
CORPORATE SOURCE: Department of Medical Oncology, Mohammed VI University Hospital, Marrakech, Morocco
SOURCE: Current Angiogenesis (2014), 3(2), 107-112
CODEN: CAUNBS; ISSN: 2211-5528
DIGITAL OBJECT ID: 10.2174/2211552802666140716170521
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Thyroid cancers are characterized by a good prognosis but 10 to 15% of patients progress and become refractory to current therapies. Systemic treatment based on chemotherapy in these settings has shown limited efficacy, with response rates not exceeding 25%. At progression, differentiated thyroid cancer is characterized by a high level of expression of vascular endothelial growth factor (VEGF). This high expression of VEGF is associated with an aggressive tumor behavior and a poor clin. outcome.; We will review the recent advances in targeting angiogenesis in the treatment of recurrent and metastatic thyroid carcinoma.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting Angiogenesis in Thyroid Cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

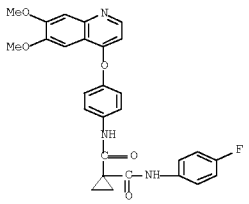
L8 ANSWER 158 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2015:28803 CAPLUS Full-text
DOCUMENT NUMBER: 162:393504
TITLE: Development of therapeutic drug for castration-resistant prostate cancer
AUTHOR(S): Zhou, Xiang-jun; Zhang, Jie
CORPORATE SOURCE: Department of Urology, Renmin Hospital of Wuhan University, Wuhan, 430060, Peop. Rep. China
SOURCE: Shijie Linchuang Yaowu (2014), 35(2), 74-79
CODEN: SLYHAA; ISSN: 1672-9188
PUBLISHER: Shijie Linchuang Yaowu Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 28 ref. is given on development of therapeutic drug for castration-resistant prostate cancer. The treatment of castration-resistant prostate cancer (CRPC) is still a challenge, as there are few effective therapies to lengthen life of patients. Many novel approaches with extended survival benefit currently in development yielded promising results for patients. This review describes the therapeutic drug for CRPC. The therapeutic drug comprises antiandrogen drug such as abiraterone, enzalutamide, orteronel, galeterone; cytotoxic chemotherapy such as docetaxel, cabazitaxel; immunotherapy such as sipuleucel-T,

rilimogene galvacirepvec, ipilimumab; targeting therapy including endothelin-A receptor antagonist such as atrasentan, zibotentan, tyrosine kinase inhibitor such as dasatinib and sorafenib, cabozantinib, anti-angiogenesis agent such as bevacizumab, aflibercept, tasquinimod, clusterin inhibitor such as custirsen, and radium chloride.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of therapeutic drug for castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 159 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:26950 CAPLUS Full-text

DOCUMENT NUMBER: 163:325796

TITLE: Cabozantinib Overcomes Crizotinib Resistance in ROS1 Fusion-Positive Cancer

AUTHOR(S): Katayama, Ryohei; Kobayashi, Yuka; Friboulet, Luc; Lockerman, Elizabeth L.; Koike, Sumie; Shaw, Alice T.; Engelman, Jeffrey A.; Fujita, Naoya

CORPORATE SOURCE: Division of Experimental Chemotherapy, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo, Japan

SOURCE: Clinical Cancer Research (2015), 21(1), 166-174
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-14-1385

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

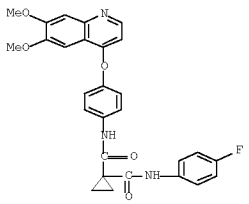
LANGUAGE: English

AB Purpose: ROS1 rearrangement leads to constitutive ROS1 activation with potent transforming activity. In an ongoing phase I trial, the ALK tyrosine kinase inhibitor (TKI) crizotinib shows remarkable initial responses in patients with non-small cell lung cancer (NSCLC) harboring ROS1 fusions; however, cancers eventually develop crizotinib resistance due to acquired mutations such as G2032R in ROS1. Thus, understanding the crizotinib-resistance mechanisms in ROS1-rearranged NSCLC and identification of therapeutic strategies to overcome the resistance are required. Exptl. Design: The sensitivity of CD74-ROS1-transformed Ba/F3 cells to multiple ALK inhibitors was examined Acquired ROS1 inhibitor-resistant mutations in CD74-ROS1 fusion were screened by N-ethyl-N-nitrosourea mutagenesis with Ba/F3 cells. To overcome the resistance mutation, we performed high-throughput drug screening with small-mol. inhibitors and anticancer drugs used in clin. practice or being currently tested in clin. trials. The effect of the identified drug was assessed in the CD74-ROS1-mutant Ba/F3 cells and crizotinib-resistant patient-derived cancer cells (MGH047) harboring G2032R-mutated CD74-ROS1. Results: We identified multiple novel crizotinib-resistance mutations in the ROS1 kinase domain, including the G2032R mutation. As the result of high-throughput drug screening, we found that the cMET/RET/VEGFR inhibitor cabozantinib (XL184) effectively inhibited the survival of CD74-ROS1 wild-type (WT) and resistant mutants harboring Ba/F3 and MGH047 cells. Furthermore, cabozantinib could overcome all the resistance by all newly identified secondary mutations. Conclusions: We developed a comprehensive model of acquired resistance to ROS1 inhibitors in NSCLC with ROS1 rearrangement and identified cabozantinib as a therapeutic strategy to overcome the resistance. Clin Cancer Res; 21(1); 166-74. cpr2014 AACR.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib overcoming crizotinib resistance in ROS1 fusion-pos. cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

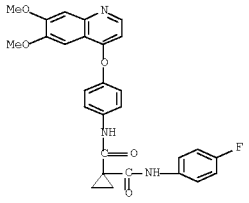


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

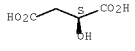
CRN 849217-68-1
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CM 2

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CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L8 ANSWER 160 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2015:21816 CAPLUS Full-text

DOCUMENT NUMBER: 162:172165

TITLE: A Novel Multiple Tyrosine-kinase Targeted Agent to Explore the Future Perspectives of Anti-Angiogenic Therapy for the Treatment of Multiple Solid Tumors: Cabozantinib

AUTHOR(S): Roy, Subhajit; Narang, Bawneet K.; Rastogi, Shiva K.; Rawal, Ravindra K.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Indo-Soviet Friendship College of Pharmacy, Punjab, 142 001, India

SOURCE: Anti-Cancer Agents in Medicinal Chemistry (2015), 15(1), 37-47
CODEN: AAMCE4; ISSN: 1871-5206

DIGITAL OBJECT ID: 10.2174/1871520614666140902153840

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

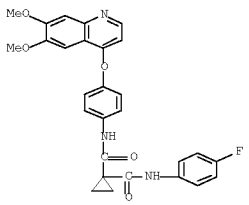
LANGUAGE: English

AB A review. The process of angiogenesis involves the formation of new blood vessels from pre-existing vasculature by the over expression of certain factors leading to the growth and development of all solid tumor types. Hepatocyte growth factor receptor abbreviated as c-Met and vascular endothelial growth factor abbreviated as VEGF are some of the factors responsible for the induction in tumor growth and development. Recently a number of analogs associated with these receptors are under study. US FDA on Nov. 29, 2012 approved a drug named cabozantinib formerly known as XL184 which is being marketed under the trade name of Cometriq for the treatment of Medullary Thyroid Cancer (MTC). Designing of the drug has been done in such a fashion that it can inhibit both VEGFR2 and c-Met simultaneously without over expressing any of the factors leading to the inhibition of angiogenesis. The drug is still under study for the evaluation of its efficacy in cases of many other solid tumor types including breast cancer, castration resistant prostate cancer (CRPC), renal cell carcinoma (RCC), hepatocellular carcinoma (HCC), gastric or gastroesophageal junction cancer, melanoma, small cell lung cancer (SCLC), ovarian cancer and primary peritoneal or fallopian tube carcinoma. This review article consists of preclin. and clin. data of cabozantinib and its efficacy and safety towards various types of solid tumors.

IT 849217-68-1, Cabozantinib 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel multiple tyrosine-kinase targeted agent, cabozantinib to explore future perspectives of anti-angiogenic therapy for treatment of human multiple solid tumors and in mouse models)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

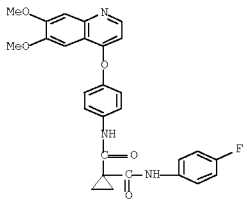


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

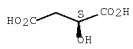
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

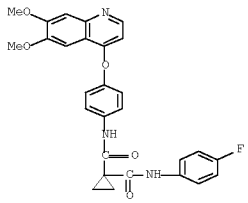
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

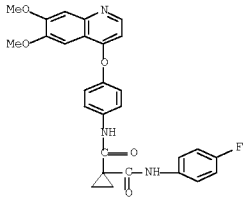


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 161 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2163755 CAPLUS Full-text
DOCUMENT NUMBER: 162:309823
TITLE: Antiangiogenic drugs for castration-resistant prostate cancer: Recent findings
AUTHOR(S): Huang, Dao-guang; Gan, Wei-dong
CORPORATE SOURCE: Department of Urology, Nanjing Drum Tower Hospital, the Affiliated Hospital, School of Medicine, Nanjing University, Nanjing, Jiangsu Province, 210008, Peop. Rep. China
SOURCE: Zhonghua Nankexue Zazhi (2014), 20(10), 932-937
CODEN: ZNZHB5
DIGITAL OBJECT ID: 10.13263/j.cnki.nja.2014.10.014
PUBLISHER: Zhonghua Nankexue Zazhi Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. In the recent years, treatment options for castration-resistant prostate cancer had evolved from conventional antiandrogens and chemotherapy to novel androgen receptor signaling inhibitors, a new generation of taxanes, and immunotherapy. Randomized clin. trials had shown that docetaxel, cabazitaxel, enzalutamide, abiraterone acetate, radium-223, and sipuleucel-T could improve the overall survival of the patients with androgen-independent prostate cancer. However, drug resistance was inevitable and androgen-independent prostate cancer remained a major clin. burden, which urgently called for novel therapeutic options for the improvement of the patients' survival and quality of life. Angiogenesis played a central role in the formation and progression of prostate cancer, and the anti angiogenic targeted therapy was shown in many clin. trials to be an effective therapeutic supplement for advanced prostate cancer beyond surgery and endocrine treatment. The recent findings of antiangiogenic mugs for castration-resistant prostate cancer was reviewed.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiangiogenic drugs for castration-resistant prostate cancer: Recent findings)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 162 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2157654 CAPLUS Full-text
DOCUMENT NUMBER: 162:99756
TITLE: New drug cabozantinib malate for medullary thyroid cancer treatment
AUTHOR(S): Lu, Juanli; Liu, Yang; Sun, Huiping
CORPORATE SOURCE: Department of Pharmacy, General Hospital of Armed Police Forces, Beijing, 100039, Peop. Rep. China
SOURCE: Zhongguo Linchuang Yaoxue Zazhi (2014), 23(1), 58-62
CODEN: ZLYZA5; ISSN: 1007-4406
PUBLISHER: Zhongguo Linchuang Yaoxue Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 21 refs. to introduce the new drug cabozantinib malate for medullary thyroid cancer treatment, including its basic properties, action mechanism, pharmacokinetic parameters, clin. trial, drug interactions, adverse reactions, and comparison on therapeutic effect with vandetanib.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new drug cabozantinib malate for medullary thyroid cancer treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

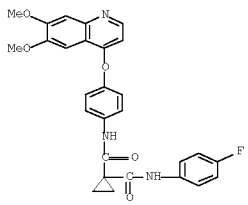


L8 ANSWER 163 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2146461 CAPLUS Full-text
DOCUMENT NUMBER: 162:114047
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 12pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
US 20140378401	A1	20141225	US 2013-14132822	20131218
WO 2014204791	A1	20141224	WO 2014-US42221	20140613

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-13924189 A2 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The ophthalmic drug delivery vehicles provide comfort and compliance; drug solubility, residence time and permeability; and reduce side effects. In addition, the delivery vehicle can be slightly modified to provide an artificial tear formulation. The ophthalmic drug delivery vehicles include 2-12% nonionic surfactant, one or more non-Newtonian high blend viscosity enhancing, non-gelling agents and 0.1-0.90% sodium chloride. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.
IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 164 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2146420 CAPLUS Full-text
DOCUMENT NUMBER: 162:144424
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 924,189.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

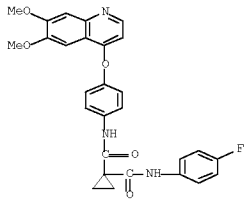
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140378401	A1	20141225	US 2013-14132822	20131218
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		

WO 2014204791 A1 20141224 WO 2014-US42221 20140613
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2013-13924189 A2 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The ophthalmic drug delivery vehicles provide comfort and compliance; drug solubility, residence time and permeability; and reduce side effects. In addition, the delivery vehicle can be slightly modified to provide an artificial tear formulation. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

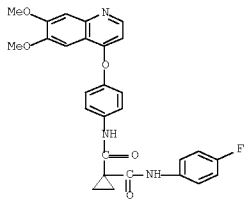


L8 ANSWER 165 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2145974 CAPLUS Full-text
DOCUMENT NUMBER: 163:58679
TITLE: Cabozantinib in chemotherapy-pretreated metastatic castration-resistant prostate cancer: results of a phase II nonrandomized expansion study
AUTHOR(S): Smith, Matthew R.; Sweeney, Christopher J.; Corn, Paul G.; Rathkopf, Dana E.; Smith, David C.; Hussain, Maha; George, Daniel J.; Higano, Celestia S.; Harzstark, Andrea L.; Sartor, A. Oliver; Vogelzang, Nicholas J.; Gordon, Michael S.; de Bono, Johann S.; Haas, Naomi B.; Logothetis, Christopher J.; Elfiky, Aymen; Scheffold, Christian; Laird, A. Douglas; Schimmoller, Frauke; Basch, Ethan M.; Scher, Howard I.
CORPORATE SOURCE: USA
SOURCE: Journal of Clinical Oncology (2014), 32(30), 3391-3399
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2013.54.5954
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose Cabozantinib (XL184), an oral inhibitor of multiple receptor tyrosine kinases such as MET and VEGFR2, was evaluated in a phase II nonrandomized expansion study in castration-resistant prostate cancer (CRPC). Patients and Methods Patients received open-label cabozantinib at daily starting doses of 100 mg or 40 mg until disease progression or unacceptable toxicity. The primary end point was bone scan response, defined as ≥ 30% reduction in bone scan lesion area. Other efficacy end points included overall survival, pain, analgesic use, and biomarkers. Results One hundred forty-four patients sequentially enrolled in either a 100-mg (n = 93) or 40-mg (n = 51) study cohort. Ninety-one patients (63%) had a bone scan response, often by week 6. Treatment resulted in clin. meaningful pain relief (57% of patients) and reduction or discontinuation of narcotic analgesics (55% of patients), as well as improvements in measurable soft tissue disease, circulating tumor cells, and bone biomarkers. Improvements in each of these outcomes were observed in both cohorts: bone scan response in 73% and 45%, resp.; redns. in measurable soft tissue disease in 80% and 79%, resp. Median overall survival was 10.8 mo for the entire population. Most common grade 3 or 4 adverse events were fatigue (22%) and hypertension (14%). Fewer dose redns. because of toxicity were required in the 40-mg group. Conclusion The evidence suggests that cabozantinib has clin. meaningful activity in CRPC. Cabozantinib resulted in improvements in bone scans, pain, analgesic use, measurable soft tissue disease, circulating tumor cells, and bone biomarkers. Taken together, these phase II observations warrant further development of cabozantinib in prostate cancer.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of cabozantinib in chemotherapy-pretreated metastatic castration-resistant prostate cancer patients in phase II nonrandomized expansion study)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 166 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2128221 CAPLUS Full-text
DOCUMENT NUMBER: 162:127174
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: PCT Int. Appl., 57pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014204791	A1	20141224	WO 2014-US42221	20140613
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
US 20140378401	A1	20141225	US 2013-14132822	20131218

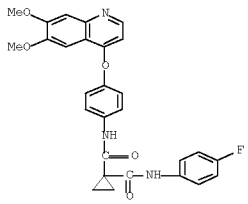
WO 2014204791 W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-13924189 A 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The ophthalmic drug delivery vehicles include 1-15% nonionic surfactant, one or more non-Newtonian high blend viscosity enhancing, non-gelling agents and 0.025-0.90% sodium chloride. Particularly, formulations that have the non-Newtonian characteristics at 37° of creating a viscosity increase in ratio of 3:1 within 1-2 s at the low shear force between blinks and drops within the fraction of a second to the high shear force of each blink, which on dilution maintain a viscosity of ≥10 cPs during each blink and which do not cause excessive stinging or discomfort, are disclosed. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.

IT 849217-68-1 1642298-56-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)

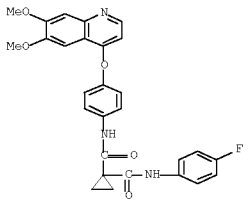
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1642298-56-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, methanesulfonate (1:1) (CA INDEX NAME)

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CRN 849217-68-1
CMF C28 H24 F N3 O5



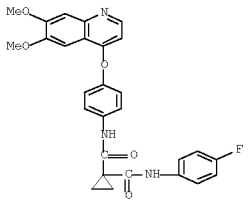
CM 2

CRN 75-75-2
CMF C H4 O3 S



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 167 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2126341 CAPLUS Full-text
DOCUMENT NUMBER: 162:148367
TITLE: Medullary thyroid cancer in the era of tyrosine kinase inhibitors: to treat or not to treat-and with which drug-those are the questions
AUTHOR(S): Cabanillas, Maria E.; Hu, Mimi I.; Jimenez, Camilo
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2014), 99(12), 4390-4396
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2014-2811
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Context: Medullary thyroid cancer (MTC) is a rare form of thyroid cancer comprising approx. 4% of all thyroid cancers. The majority of patients have a relatively good prognosis; however, a subgroup of patients will require systemic therapy. Large phase III randomized trials led to the approval of two drugs-vandetanib and cabozantinib-for progressive or symptomatic MTC. The decision regarding which drug to initiate first is not entirely clear and is a common concern amongst treating physicians. Evidence Acquisition and Synthesis: A review of the literature in English was conducted, and data were summarized and integrated into a decision matrix. Conclusions: The decision regarding which drug to initiate first for progressive MTC should be based on a careful review of the medical history, phys. examination findings, medication list, ECG, laboratory results, and tumor characteristics. It is necessary to consider the relative contraindications when choosing which drug to initiate first.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medullary thyroid cancer in era of tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

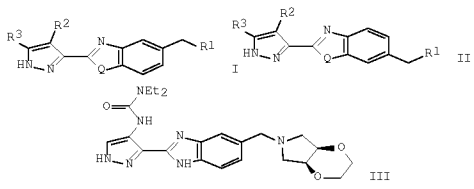


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

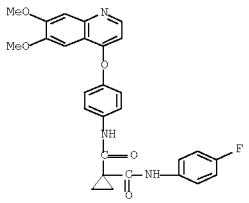
L8 ANSWER 168 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2105568 CAPLUS Full-text
DOCUMENT NUMBER: 162:137867
TITLE: Substituted pyrazole-type deriv. as aurora kinase inhibitor useful in treatment of various diseases and its preparation
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Zhang, Jiquan; Li, Yanping; Yang, Xueqi; Zhang, Jiancun; Zheng, Changchun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 96pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104211692	A	20141217	CN 2014-10245663	20140604
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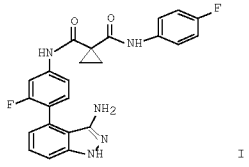
OTHER SOURCE(S): MARPAT 162:137867
GI



AB The invention relates to substituted pyrazole-type deriv. of formula I and II as aurora kinase inhibitor useful in treatment of various diseases and their preparation Compds. I and II, wherein Q is NH or O; R1 is one of morpholinyl, C5-12 bridged bicyclic group, etc.; R2 is R4R4aN-CO-NH, R5R5aCHCONH, or R6OCONH; and R3 is H or C1-6 alkyl; R4 is H, C1-6 alkyl, C3-6 cycloalkyl, etc.; R4a is C1-6 alkyl, C3-6 cycloalkyl, C6-10 aryl, etc.; R5 and R5a are independently H, C3-6 cycloalkyl, etc.; R6 is C1-6 alkyl or C6-10 aryl; their stereoisomer, geometric isomer, tautomer, nitrogen oxide, hydrate, solvate, metabolite, ester, pharmaceutically acceptable salt or prodrug are claimed. Compound III was prepared by multi-step procedure (procedure given). The invention compds. were evaluated for their aurora kinase inhibitor activity. From assay, it was determined that III exhibited the IC50 value of 2.16 nM against aurora A kinase .
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted pyrazole-type derivative as aurora kinase inhibitor
useful in treatment of various diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 169 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2087478 CAPLUS Full-text
DOCUMENT NUMBER: 162:183726
TITLE: Discovery and SAR study of c-Met kinase inhibitors bearing an 3-amino-benzo[d]isoxazole or 3-aminoindazole scaffold
AUTHOR(S): Jiang, Xiaolong; Liu, Hongyan; Song, Zilan; Peng, Xia; Ji, Yinchun; Yao, Qizheng; Geng, Meiyu; Ai, Jing; Zhang, Ao
CORPORATE SOURCE: Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry (2015), 23(3), 564-578
CODEN: BMECEP; ISSN: 0968-0896
DIGITAL OBJECT ID: 10.1016/j.bmc.2014.12.002
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 162:183726
GI



AB A series of 3-amino-benzo[d]isoxazole-/3-aminoindazole-based compds. were designed, synthesized and pharmacol. evaluated as tyrosine kinase c-Met inhibitors. The SAR study was conducted leading to identification of nine compds. with IC50s less than 10 nM against c-Met. Compound I stood out as the most potent c-Met inhibitor displaying potent inhibitory effects both at enzymic (IC50 = 1.8 nM) and cellular (IC50 = 0.18 μM on EBC-1 cells) levels. In addition, I had a relatively good selectivity compared to a panel of the inhouse 14 RTKs.

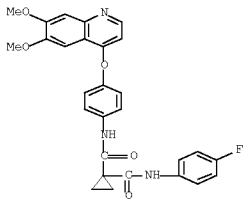
IT 849217-68-1

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(discovery and SAR study of c-Met kinase inhibitors bearing an 3-amino-benzo[d]isoxazole or 3-aminoindazole scaffold)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 170 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:2072471 CAPLUS Full-text

DOCUMENT NUMBER: 163:156450

TITLE: Adaptive Responses to Dasatinib-Treated Lung Squamous Cell Cancer Cells Harboring DDR2 Mutations

AUTHOR(S): Bai, Yun; Kim, Jae-Young; Watters, January M.; Fang, Bin; Kinose, Fumi; Song, Lanxi; Koomen, John M.; Teer, Jamie K.; Fisher, Kate; Chen, Yian Ann; Rix, Uwe; Haura, Eric B.

CORPORATE SOURCE: Department of Thoracic Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

SOURCE: Cancer Research (2014), 74(24), 7217-7228
CODEN: CNREA8; ISSN: 0008-5472

DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-14-0505

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study of cancer cell signaling perturbed by the tyrosine kinase inhibitor dasatinib suggests rational combinations to improve the efficacy of this drug in the subset of lung cancers where it is used. DDR2 mutations occur in approx. 4% of lung squamous cell cancer (SCC) where the tyrosine kinase inhibitor dasatinib has emerged as a new therapeutic option. We found that ERK and AKT phosphorylation was weakly inhibited by dasatinib in DDR2-mutant lung SCC cells, suggesting that dasatinib inhibits survival signals distinct from other oncogenic receptor tyrosine kinases (RTK) and/or compensatory signals exist that dampen dasatinib activity. To gain better insight into dasatinib's action in these cells, we assessed altered global tyrosine phosphorylation (pY) after dasatinib exposure using a mass spectrometry-based quant. phosphoproteomics approach. Overlaying protein-protein interaction relationships upon this dasatinib-regulated pY network revealed decreased phosphorylation of Src family kinases and their targets. Conversely, dasatinib enhanced tyrosine phosphorylation in a panel of RTK and their signaling adaptor complexes, including EGFR, MET/GAB1, and IGF1R/IRS2, implicating a RTK-driven adaptive response associated with dasatinib. To address the significance of this observation, these results were further integrated with results from a small-mol. chemical library screen. We found that dasatinib combined with MET and insulin-like growth factor receptor (IGF1R) inhibitors had a synergistic effect, and ligand stimulation of EGFR and MET rescued DDR2-mutant lung SCC cells from dasatinib-induced loss of cell viability. Importantly, we observed high levels of tyrosine-phosphorylated EGFR and MET in a panel of human lung SCC tissues harboring DDR2 mutations. Our results highlight potential RTK-driven adaptive-resistant mechanisms upon DDR2 targeting, and they suggest new, rationale cotargeting strategies for DDR2-mutant lung SCC. Cancer Res; 74(24); 7217-28. cpr2014 AACR.

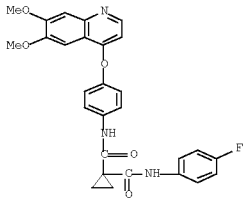
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adaptive responses to dasatinib-treated lung squamous cell cancer cells harboring DDR2 mutations)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 171 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:2068289 CAPLUS Full-text

DOCUMENT NUMBER: 162:228992

TITLE: Anti-angiogenic agents in metastatic NSCLC

AUTHOR(S): Das, Millie; Wakelee, Heather

CORPORATE SOURCE: VA Palo Alto Heath Care System, Palo Alto, CA, USA

SOURCE: Lung Cancer (4th Edition) (2014), 527-540. Editor(s): Roth, Jack A.; Hong, Waun Ki; Komaki, Ritsuko U. Wiley-Blackwell: Hoboken, N. J.
CODEN: 69THV4; ISBN: 978-1-118-46874-6

DIGITAL OBJECT ID: 10.1002/9781118468791.ch34

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB This review highlights the role of anti-angiogenic agents in metastatic non-small cell lung cancer (NSCLC). Anti-angiogenic agents being studied in NSCLC include monoclonal antibodies against VEGF, tyrosine kinase inhibitors directed at VEGF receptors, as well as vascular disrupting agents which do not involve inhibition of VEGF.

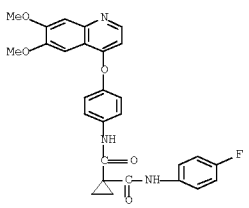
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(discussion on role of anti-angiogenic agents in metastatic non-small cell lung cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 172 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:2037552 CAPLUS Full-text

DOCUMENT NUMBER: 163:187272

TITLE: RET-Rearranged Lung Adenocarcinomas with Lymphangitic Spread, Psammoma Bodies, and Clinical Responses to Cabozantinib

AUTHOR(S): Mukhopadhyay, Sanjay; Pennell, Nathan A.; Ali, Siraj M.; Ross, Jeffrey S.; Ma, Patrick C.; Velcheti, Vamsidhar

CORPORATE SOURCE: Solid Tumor Oncology, and Translational Hematology and Oncology Research, Cleveland Clinic, Cleveland, OH, 9500, USA

SOURCE: Journal of Thoracic Oncology (2014), 9(11), 1714-1719
CODEN: JTOOB7; ISSN: 1556-0864

DIGITAL OBJECT ID: 10.1097/JTO.0000000000000323

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Oncogenic rearrangements of the RET gene have recently been described in 1% to 2% of lung adenocarcinomas. We report five cases of RET-rearranged lung adenocarcinoma with an unusual constellation of clin. and histol. features that has not previously been described in tumors with this genomic alteration. The age at diagnosis of the five patients (4F, 1M) ranged from 44 to 77 years. All were never-smokers. Radiol., four tumors showed lymphangitic spread within the lungs at presentation; three of these had multiple bilateral lung nodules. Histol. showed psammoma bodies within the tumor in four of five cases. Mol. testing for activating EGFR mutations by standard genotyping and ALK expression by immunohistochem. was neg. in all cases. Addnl. mol. anal. was prompted by the clin. profile in that all five patients were never-smokers with metastatic, relapsed, and/or refractory disease; and also by unusual histol. findings in two cases. Comprehensive genomic profiling performed by means of a clin. grade cancer gene panel next-generation sequencing assay demonstrated a KIF5B-RET fusion in three; and fluorescence in-situ hybridization documented a RET rearrangement in two. Three of the patients were treated with the RET inhibitor cabozantinib. By Response Evaluation Criteria In Solid Tumors (RECIST) criteria, two had a confirmed partial response (at 6 wk and 4 wk) and one had stable disease. Our findings suggest that the combination of lymphangitic spread and psammoma bodies may be characteristic of a subset of advanced stage RET-rearranged lung adenocarcinomas. These findings should prompt addnl. mol. testing for RET translocations, particularly in never-smokers with EGFR- and ALK-neg. lung adenocarcinoma.

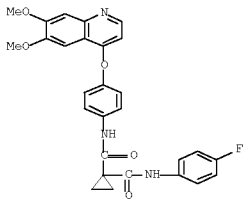
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(study on RET-rearranged lung adenocarcinomas with lymphangitic spread, psammoma bodies, and clin. responses to cabozantinib)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



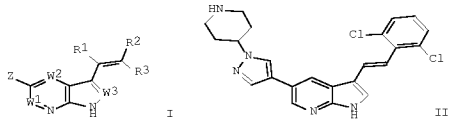
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 173 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:2015786 CAPLUS Full-text
DOCUMENT NUMBER: 162:37339
TITLE: Preparation of alkenyl-pyrrolo[2,3-b]pyridine compounds as protein tyrosine kinase modulators useful for treatment of proliferative disorders
INVENTOR(S): Xi, Ning; Li, Xiaobo
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 117pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014193647	A2	20141204	WO 2014-US37856	20140513
WO 2014193647	A3	20150129		

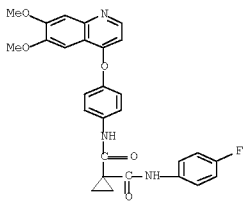
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61827599 P 20130526
OTHER SOURCE(S): CASREACT 162:37339; MARPAT 162:37339
GI

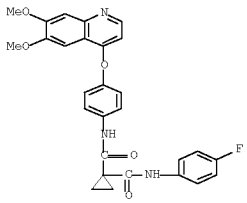


I II

AB The invention provides substituted alkenyl pyrrolo[2,3-b]pyridine compds. of formula I, pharmaceutical acceptable salts and formulations thereof as protein tyrosine kinase modulators capable of modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion and, thus useful for the treatment of proliferative disorders. I [wherein W1, W2, and W3 are independently N or (un)substituted C; R1, R2, and R3 are independently H, CN, (hetero)aryl, etc.; Z is (un)substituted 5- to 6-membered heteroaryl] or a stereoisomer, geometric isomer, tautomer, N-oxide, hydrate, solvate, metabolite, prodrug, or pharmaceutically acceptable salt thereof is claimed. (E)-II was prepared in a multistep process (preparation given). I were evaluated for kinase inhibitor activity using radiochem. anal. and [γ33P-ATP]. From this assay it was determined that (E)-II demonstrated IC50 values of 44 nM and 8 nM for ALK kinase and c-Met kinase, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of alkenyl-pyrrolo[2,3-b]pyridine compds. as protein
tyrosine kinase modulators useful for treatment of proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 174 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1955485 CAPLUS Full-text
DOCUMENT NUMBER: 164:33863
TITLE: Novel therapies for thyroid cancer
AUTHOR(S): Krajewska, Jolanta; Jarzab, Barbara
CORPORATE SOURCE: Nuclear Medicine and Endocrine Oncology Department, Gliwice Branch, M.Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Pol.
SOURCE: Expert Opinion on Pharmacotherapy (2014), 15(18), 2641-2652
CODEN: EOPHF7; ISSN: 1465-6566
DIGITAL OBJECT ID: 10.1517/14656566.2014.969240
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Introduction: New therapeutic options for both differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC) have opened up during the past few years, as the key role of tyrosine kinases in the pathogenesis of thyroid carcinoma has been proved. Recently, two tyrosine kinase inhibitors (TKIs) targeting VEGFR vandetanib (Caprelsa) and cabozantinib (Cometriq) have been approved for advanced MTC, whereas, sorafenib (Nexavar) has been accepted to treat late-stage of DTC. Their efficacy was demonstrated in Phase III studies, compared to placebo; each of them significantly prolonged the progression-free survival. Areas covered: Common adverse reactions related to VEGFR blockade are hypertension, proteinuria, impaired wound healing, hemorrhage and thrombosis, and congestive heart failure. Fatigue, different gastrointestinal disturbances with diarrhea, appetite decrease and weight loss are observed in the majority of patients. Another frequent TKI side effect is TSH increase secondary to inhibition of MCT8-dependent T3 and T4 uptake in pituitary. Expert opinion: So far, no direct comparison of both treatment outcomes and toxicity between particular drugs has been carried out. The evidence-based medicine guidelines are necessary to precisely indicate what drug to use: more effective or less toxic and when to start the treatment.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(discussion on novel therapies for thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 175 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1943046 CAPLUS Full-text
DOCUMENT NUMBER: 161:714155
TITLE: Method for the prognosis and treatment of renal cell carcinoma metastasis
INVENTOR(S): Gomis, Roger; Lacey, David L.
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014184679	A2	20141120	WO 2014-IB1715	20140313
WO 2014184679	A3	20150319		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20160032399	A1	20160204	US 2015-14776390	20150914

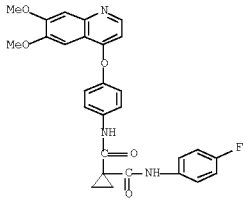
PRIORITY APPLN. INFO.: US 2013-61801642 P 20130315
WO 2014-IB1715 W 20140313

AB The present invention relates to a method for the prognosis of bone metastasis in renal cell carcinoma which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering renal cell carcinoma. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of renal cell carcinoma metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering renal cell carcinoma and for classifying a subject from renal cell carcinoma into a cohort.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MAF gene as marker for prognosis and treatment of renal cell carcinoma metastasis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 176 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1940485 CAPLUS Full-text

DOCUMENT NUMBER: 161:765704

TITLE: Short-chain phosphatidylcholine lipids and their use in therapy

INVENTOR(S): Van Hell, Albert; Verheij, Marcel; Marrink, Siewert Jan; Koning, Gerben

PATENT ASSIGNEE(S): Stichting Het Nederlands Kanker Instituut - Antoni Van Leeuwenhoek Ziekenhuis, Neth.; Erasmus University Medical Centre; Rijksuniversiteit Groningen

SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014184726	A2	20141120	WO 2014-IB61379	20140512
WO 2014184726	A3	20150219		

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2013-8753 A 20130515

OTHER SOURCE(S): MARPAT 161:765704

AB The invention pertains generally to the field of therapy and medical treatment, and more specifically to certain compds. of the following formula (for convenience, collectively referred to herein as "short-chain phosphatidylcholine lipids" and "SCPC lipids"), which, inter alia, are useful in methods of improving drug delivery, bioavailability, and efficacy. The invention also pertains to pharmaceutical formulations, and more specifically to co-formulations of known drugs (e.g., amphiphilic drugs) (e.g., anthracyclines) (e.g., doxorubicin) with these SCPC lipids, and their use in therapy, such as cancer treatment.

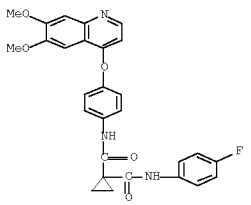
IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(short-chain phosphatidylcholine lipids co-formulations and use for treatment of diseases such as cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

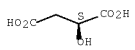
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L8 ANSWER 177 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1921290 CAPLUS Full-text

DOCUMENT NUMBER: 163:87631

TITLE: Axitinib and crizotinib combination therapy inhibits bone loss in a mouse model of castration resistant prostate cancer

AUTHOR(S): Eswaraka, Jeetendra; Giddabasappa, Anand; Han, Guangzhou; Lalwani, Kush; Eisele, Koleen; Feng, Zheng; Affolter, Timothy; Christensen, James; Li, Gang

CORPORATE SOURCE: Global Science and Technology (WCM), Pfizer Global Research and Development, San Diego, CA, 92121, USA

SOURCE: BMC Cancer (2014), 14, 742/1-742/10
CODEN: BCMACL; ISSN: 1471-2407

DIGITAL OBJECT ID: 10.1186/1471-2407-14-742

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)

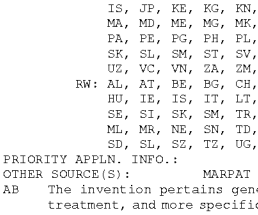
LANGUAGE: English

AB Background: Castration resistant prostate cancer (CRPC) is a leading cause of cancer-related deaths in men. The primary cause of mortality and morbidity in patients is bone metastases and remodeling resulting in osteoblastic and osteolytic lesions. Recently, cabozantinib, a multi-kinase inhibitor (VEGFR2 and c-MET inhibitor), was shown to have efficacy on bone lesions in patients. In this study we tested multi-kinase inhibitors: axitinib (VEGFR inhibitor) and crizotinib (c-MET inhibitor) in a combination trial in mice models. Methods: VCaP-Luc cells were grown as s.c. implants in intact and castrated NOD-SCID-gamma (NSG) mice to confirm the androgen dependency. For bone metastasis model two cohorts of NSG mice (castrated and intact) received orthotopic injection of VCaP-Luc cells into the bone marrow cavity of left tibia. Mice were monitored weekly for tumor growth using bioluminescence imaging. Animals were randomized into 4 groups based on the tumor bioluminescence signal: vehicle, crizotinib alone, axitinib alone, crizotinib and axitinib in combination. Animals were imaged weekly by in vivo 2-D X-ray imaging to monitor bone remodeling. At the end of the study animals were euthanized and both tibias were extracted for ex vivo high-resolution 3-D micro-computed tomog. (μCT) imaging. Results: S.c. model showed that androgen stimulation may be helpful but not essential for the growth of VCaP-Luc cells. VCaP-Luc cells grown intra-tibially in intact animals caused extensive remodeling of bone with mixed osteoblastic (bone formation) and osteolytic (bone matrix dissoln.) lesions. The osteoblastic lesions were predominant and at times extended beyond the tibial shaft into the surrounding tissue. In contrast, only osteolytic lesions were prominent throughout the study in castrated animals. Treatment with crizotinib alone reduced the osteolytic lesions in castrated animals. Axitinib alone reduced the osteoblastic lesions in the intact animals. Combination therapy with axitinib and crizotinib remarkably inhibited the tibial remodeling by VCaP-Luc cells which resulted in a significant reduction of both osteoblastic and osteolytic lesions. Conclusion: Our data show that combined inhibition of c-MET and VEGFR can be beneficial for treatment of metastatic bone disease in CRPC and that the drugs act on two different stages of the disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(axitinib and crizotinib combination therapy inhibits bone loss in mouse model of castration resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 178 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

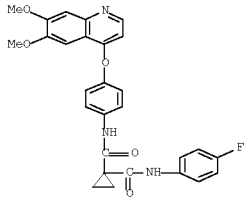
ACCESSION NUMBER: 2014:1853168 CAPLUS Full-text

DOCUMENT NUMBER: 162:33543
TITLE: Significances of RET fusion gene in non-small cell lung cancer
AUTHOR(S): Liu, Jingjing; Bi, Minghong
CORPORATE SOURCE: Department of Medical Oncology, First Affiliated Hospital of Bengbu Medical College, Bengbu, 233004, Peop. Rep. China
SOURCE: Zhongguo Feiai Zazhi (2013), 16(11), 615-620
CODEN: ZFZHAG; ISSN: 1009-3419
DIGITAL OBJECT ID: 10.3779/j.issn.1009-3419.2013.11.11
PUBLISHER: Zhongguo Feiai Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review with 33 refs. Lung cancer is the leading cause of cancer-related death worldwide, mol. target therapy has become a hot research direction of non-small cell lung cancer(NSCLC) treatment. RET fusion gene with an identifiable clin. pathol. features, is present in some subsets of lung cancer, and its treatment is effective by RET inhibitor, suggesting that RET fusion gene may be a new target for individualized treatment to the subgroup of NSCLC. This article reviews the structural characteristics of RET fusion gene and expression model in clin. samples, and treatment of NSCLC.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(significances of RET fusion gene in non-small cell lung cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 179 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1827672 CAPLUS Full-text
DOCUMENT NUMBER: 161:690410
TITLE: Pharmaceutical combinations of a protein kinase C (PKC) inhibitor and a c-MET receptor tyrosine kinase inhibitor for treatment of proliferative diseases
INVENTOR(S): Porter, Dale; Emery, Caroline; Tan, Lujian
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014174478	A1	20141030	WO 2014-IB60976	20140424

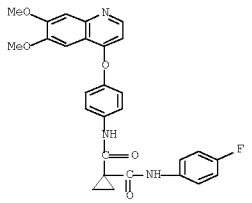
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61816266 P 20130426

AB A pharmaceutical combination comprising (a) a protein kinase C (PKC) inhibitor, or a pharmaceutically acceptable salt thereof, and (b) at least one c-MET receptor tyrosine kinase inhibitor, or a pharmaceutically acceptable salt, and optionally a pharmaceutically acceptable carrier, for simultaneous, sep. or sequential administration; the uses of such combination in the treatment of proliferative diseases; and methods of treating a subject suffering from a proliferative disease comprising administering a therapeutically effective amount of such combination.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combinations of a protein kinase C (PKC) inhibitor and a c-MET receptor tyrosine kinase inhibitor for treatment of proliferative diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 180 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1821658 CAPLUS Full-text
DOCUMENT NUMBER: 161:715766
TITLE: Preparation of quinazolineamine derivatives for treating proliferative diseases
INVENTOR(S): Zhang, Yingjun; Liu, Bing; Liu, Jinlei; Zhang, Jiancun; Zheng, Changchun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 147pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

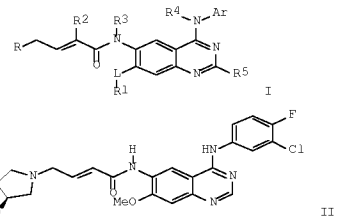
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104119350	A	20141029	CN 2014-10175636	20140428
WO 2014177038	A1	20141106	WO 2014-CN76377	20140428

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20160039838	A1	20160211	US 2015-14774702	20150911

PRIORITY APPLN. INFO.:
CN 2013-10156470 A 20130428
CN 2014-10108773 A 20140323
WO 2014-CN76377 W 20140428

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 161:715766
GI



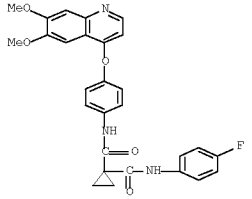
I

II

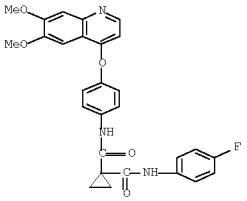
AB The present invention provides quinazolineamine derivs. I [wherein R = bicyclic heterocyclyl; R1 = H, D, F, Cl, Br, I, etc.; R2 = H, F, Cl, Br, I, NH2, etc.; R3 and R4 = independently H, D, or alkyl; R5 = H, D, F, Cl, Br, I, alkyl, etc.; Ar = (un)substituted Ph or indazole-5-yl] stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts, or prodrugs thereof for prevention, treatment, or relieving proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 3.2, 14, and 8.3 nM against EGFR, HER-2, and EGFR T790M kinases, resp. Pharmaceutical compns. comprising the title compound were also described.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of quinazolineamine derivs. for treating proliferative diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 181 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1792793 CAPLUS Full-text
DOCUMENT NUMBER: 162:498601
TITLE: Enrichment of c-Met+ tumorigenic stromal cells of giant cell tumor of bone and targeting by cabozantinib
AUTHOR(S): Liu, L.; Aleksandrowicz, E.; Fan, P.; Schoensiegel, F.; Zhang, Y.; Saehr, H.; Gladkich, J.; Mattern, J.; Depeweg, D.; Lehner, B.; Fellenberg, J.; Herr, I.
CORPORATE SOURCE: Department of Molecular OncoSurgery, General, Visceral and Transplantation Surgery, University of Heidelberg and German Cancer Research Center (DKFZ), Heidelberg, Germany
SOURCE: Cell Death & Disease (2014), 5(10), e1471
CODEN: CDDEA4; ISSN: 2041-4889
DIGITAL OBJECT ID: 10.1038/cddis.2014.440
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Giant cell tumor of bone (GCTB) is a very rare tumor entity, which is little examined owing to the lack of established cell lines and mouse models and the restriction of available primary cell lines. The stromal cells of GCTB have been made responsible for the aggressive growth and metastasis, emphasizing the presence of a cancer stem cell population. To identify and target such tumor-initiating cells, stromal cells were isolated from eight freshly resected GCTB tissues. Tumorigenic properties were examined by colony and spheroid formation, differentiation, migration, MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay, immunohistochem., antibody protein array, Alu in situ hybridization, FACS anal. and xenotransplantation into fertilized chicken eggs and mice. A sub-population of the neoplastic stromal cells formed spheroids and colonies, differentiated to osteoblasts, migrated to wounded regions and expressed the metastasis marker CXC-chemokine receptor type 4, indicating self-renewal, invasion and differentiation potential. Compared with adherent-growing cells, markers for pluripotency, stemness and cancer progression, including the CSC surface marker c-Met, were enhanced in spheroidal cells. This c-Met-enriched sub-population formed xenograft tumors in fertilized chicken eggs and mice. Cabozantinib, an inhibitor of c-Met in phase II trials, eliminated CSC features with a higher therapeutic effect than standard chemotherapy. This study identifies a c-Met+ tumorigenic sub-population within stromal GCTB cells and suggests the c-Met inhibitor cabozantinib as a new therapeutic option for targeted elimination of unresectable or recurrent GCTB.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-Met-enriched tumorigenic human stromal cells of giant cell tumor of bone formed xenograft tumors in fertilized chicken eggs and mouse where cabozantinib strongly inhibited self-renewal potential and in vivo growth of stromal cell)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



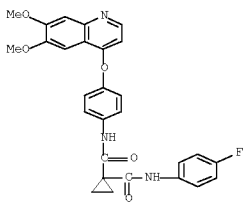
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 182 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1791911 CAPLUS Full-text
DOCUMENT NUMBER: 161:680644
TITLE: Cancer-associated chimeric genes arising from translocations and their use in diagnosis, prognosis, and therapy of cancer
INVENTOR(S): Rhodes, Daniel; Sadis, Seth; Wyngaard, Peter; Khazanov, Nikolay; Bandla, Santhoshi; Tomilo, Mark; Eddy, Sean; Bowden, Emma
PATENT ASSIGNEE(S): Life Technologies Corporation, USA
SOURCE: PCT Int. Appl., 272pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014172046	A2	20141023	WO 2014-US29592	20140314
WO 2014172046	A3	20150618		
WO 2014172046	A9	20160225		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
AU 2014254394	A1	20151203	AU 2014-254394	20140314
AU 2014254394	A9	20160317		
EP 2986736	A2	20160224	EP 2014-721666	20140314
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 105378110	A	20160302	CN 2014-80034585	20140314

PRIORITY APPLN. INFO.:
US 2013-61813182 P 20130417
US 2013-61813465 P 20130418
US 2013-61824253 P 20130516
US 2013-61860115 P 20130730
US 2013-61907939 P 20131122
US 2013-61915392 P 20131212
US 2014-61935650 P 20140204
US 2014-61940226 P 20140214
WO 2014-US29592 W 20140314

AB Chimeric genes arising from chromosomal translocations that play a role in the etiol. of cancer are identified for use in diagnosis, prognosis, and selection and monitoring of therapies. These chimeric genes were identified by a large-scale survey of 19 cancers in 4,225 patients.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selection for cancer therapy; cancer-associated chimeric genes arising from translocations and their use in diagnosis, prognosis, and therapy of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 183 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1790149 CAPLUS Full-text
DOCUMENT NUMBER: 161:686526
TITLE: Cabozantinib malate and its preparation method
INVENTOR(S): Meng, Qingyi; Zhang, Aiming; Xu, Wenwei; Zhang, Xiquan
PATENT ASSIGNEE(S): Lianyungang Runzhong Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 7pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

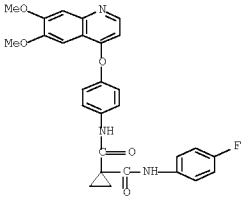
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104109128	A	20141022	CN 2013-10164410	20130419

PRIORITY APPLN. INFO.:
CN 2013-10164410 20130419

AB The present invention relates to cabozantinib malate and its prepn. method, and specifically, the present invention relates to cabozantinib·n malate, its preparation method, and a pharmaceutical composition comprising the same. The inventive cabozantinib·n malate has excellent stability, and can be used for preparing medicines for the treatment of tumors, especially in preparation of medicine for the treatment of medullary thyroid cancer. The preparation method of cabozantinib·n malate includes: (a) adding cabozantinib to an organic solvent, (b) adding malic acid n times molar amount of cabozantinib to mixture of step (a), and (c) precipitating to obtain cabozantinib·n malate, wherein, n is selected from 0.4-0.6, preferably 0.5.
IT 1140909-48-3P 1385530-43-3P 1634853-27-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cabozantinib malate and preparation method)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

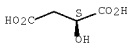
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

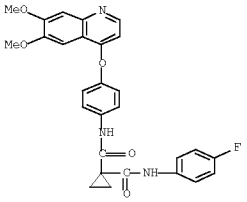
Absolute stereochemistry. Rotation (-).



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

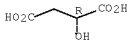
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

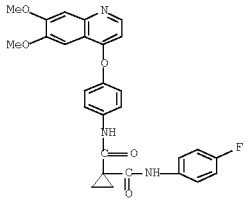
Absolute stereochemistry. Rotation (+).



RN 1634653-27-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

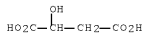
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

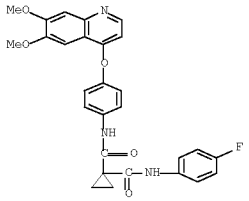


CM 2

CRN 6915-15-7
CMF C4 H6 O5



IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(cabozantinib malate and preparation method)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



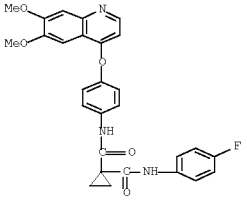
L8 ANSWER 184 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1782124 CAPLUS Full-text
DOCUMENT NUMBER: 161:705479
TITLE: Crystal of cabozantinib· 0.5 malate
INVENTOR(S): Meng, Qingyi; Zhang, Aiming; Xu, Wenwei; Zhang, Xiquan
PATENT ASSIGNEE(S): Chia Tai Tianqing Pharmaceutical Group Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104109124	A	20141022	CN 2013-10138216	20130419
PRIORITY APPLN. INFO.:			CN 2013-10138216	20130419

AB The invention relates to crystal of cabozantinib·0.5malate, a crystal composition and a pharmaceutical composition of the crystal, preparing method thereof, and application thereof in manufacture of drugs treating tumor-related diseases. In the x-ray powder diffraction spectrum of the crystal using Cu-Kα radiation, there are diffraction peaks at 2θ of 5.48°, 10.88°, 15.24°, 21.97° and 24.56°.
IT 1635373-15-7
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(0.5 malate; crystal of cabozantinib·0.5malate)
RN 1635373-15-7 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:2) (CA INDEX NAME)

CM 1

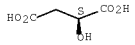
CRN 849217-68-1
CMF C28 H24 F N3 O5



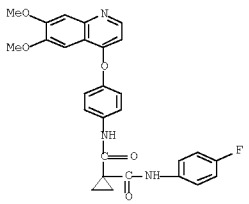
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal of cabozantinib·0.5malate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 185 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1754957 CAPLUS Full-text
DOCUMENT NUMBER: 161:635758
TITLE: Platform for targeted delivery to stem cells and tumor cells and methods thereof
INVENTOR(S): Carvalho Da Fonseca, Nuno Andre; Gomes Da Silva, Ligia Catarina; Dantas Nunes Caldeira De Moura, Vera Lucia; De Magalhaes Simoes, Sergio Paulo; Sereno De Almeida Moreira, Joao Nuno
PATENT ASSIGNEE(S): Universidade de Coimbra, Port.
SOURCE: PCT Int. Appl., 59pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

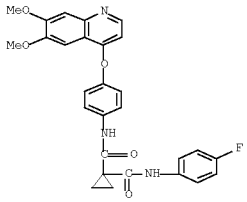
WO 2014167126	A2	20141016	WO 2014-EP57446	20140411
WO 2014167126	A3	20150108		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014253040	A1	20151105	AU 2014-253040	20140411
EP 2983720	A2	20160217	EP 2014-721226	20140411
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160058886	A1	20160303	US 2015-14784247	20151013

PRIORITY APPLN. INFO.: WO 2014-EP57446 W 20140411
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention involves therapy and diagnostics using nanoparticles that provide targeted delivery of agents to cancer cells and stem cells, including cancer stem cells, the nanoparticles being pH sensitive and incorporating cytotoxic ceramides.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(platform for targeted delivery to stem cells and tumor cells and methods thereof)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



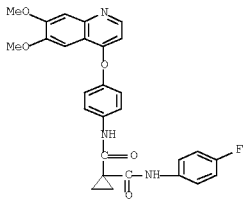
L8 ANSWER 186 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1754784 CAPLUS Full-text
DOCUMENT NUMBER: 163:225877
TITLE: Sequencing of lung cancer genomes and its translation to the therapy
AUTHOR(S): Iwakawa-Kawabata, Reika; Kohno, Takashi
CORPORATE SOURCE: Div. of Genome Biology, National Cancer Center, Japan
SOURCE: Jikken Igaku (2014), 32(12), 1865-1870
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review discussing the sequencing of lung cancer genomes and its translation to the therapy.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequencing of lung cancer genomes and its translation to the therapy)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

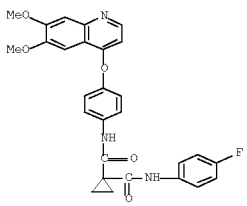


L8 ANSWER 187 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1742452 CAPLUS Full-text
DOCUMENT NUMBER: 163:438125
TITLE: A Phase I Study of Cabozantinib (XL184) in Patients with Differentiated Thyroid Cancer
AUTHOR(S): Cabanillas, Maria E.; Brose, Marcia S.; Holland, Jaymes; Ferguson, Kimberly C.; Sherman, Steven I.
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Thyroid (2014), 24(10), 1508-1514
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2014.0125
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background: Cabozantinib targets tyrosine kinases including MET, vascular endothelial growth factor (VEGF) receptor 2, and rearranged during transfection (RET). Differentiated thyroid cancer (DTC) is a tumor type that may be sensitive to cabozantinib. Therefore, we evaluated cabozantinib in a cohort of heavily pretreated patients with metastatic DTC. .Methods: This single-arm open-label phase I trial assessed the safety, tolerability, and antitumor activity of cabozantinib in DTC patients taking part in a drug-drug interaction study. Adult patients with histol. confirmed metastatic or surgically unresectable DTC (including papillary, follicular, or Huerthle cell) were enrolled. Patients received daily oral dosing of 140 mg cabozantinib. Safety was assessed by evaluation of adverse events (AEs), vital signs, electrocardiograms, laboratory tests, and concomitant medications. Tumor response by magnetic resonance imaging or computed tomog. scan was investigator assessed using Response Evaluation Criteria In Solid Tumors (RECIST) v1.0. Results: The study enrolled 15 patients who had failed standard radioactive iodine therapy. Patients had received a median of two prior systemic agents, and 11 patients (73%) had previously received at least one VEGF pathway inhibiting therapy. Common AEs included diarrhea, nausea, fatigue, and decreased appetite. Partial response was reported in eight patients (53%). Median progression-free survival and median overall survival were not reached. Conclusions: Cabozantinib demonstrates a safety profile similar to other multitargeted VEGFR inhibitors in advanced DTC patients. The antitumor activity observed in this study warrants further investigation of cabozantinib in patients with advanced DTC.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase I Study of Cabozantinib (XL184) in Patients with Differentiated Thyroid Cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

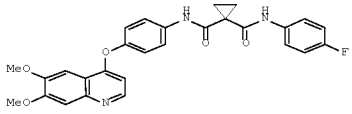


OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 188 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1716754 CAPLUS Full-text
DOCUMENT NUMBER: 161:582215
TITLE: Preparation of cabozantinib and dosage forms for treatment of cancer
INVENTOR(S): Decillis, Arthur
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165786	A1	20141009	WO 2014-US33016	20140404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2981263	A1	20160210	EP 2014-724909	20140404
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160022662	A1	20160128	US 2015-14782537	20151005

PRIORITY APPLN. INFO.: US 2013-61808511 P 20130404
WO 2014-US33016 W 20140404
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:582215
GI

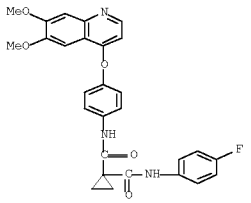


I

AB This invention relates to a dosage form of cabozantinib (I) and a method of employing the dosage form to treat cancer. I was prepared starting with 6,7-dimethoxy-4-quinolinol through a number of steps. I S-maleate was also prepared and tablets containing I were prepared

IT 849217-68-1P, Cabozantinib 1140909-48-3P, Cabozantinib S-malate 1365530-43-3P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

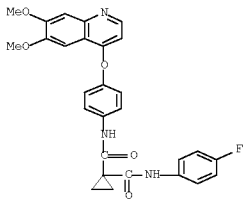
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cabozantinib and dosage forms for treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

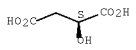
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

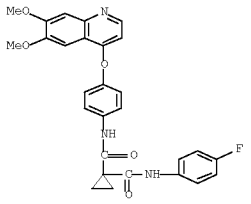
Absolute stereochemistry. Rotation (-).



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

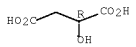
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

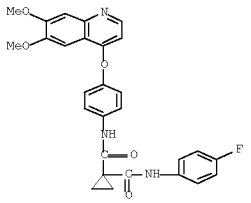


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 189 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1715795 CAPLUS Full-text
DOCUMENT NUMBER: 161:577833
TITLE: Methods and compositions for treating cancers having acquired resistance to chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): Tactical Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 23pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165412	A2	20141009	WO 2014-US32253	20140328
WO 2014165412	A3	20150129		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20140294806	A1	20141002	US 2013-13986103	20130401
US 9089570	B2	20150728		
CA 2902144	A1	20141009	CA 2014-2902144	20140328
AU 2014248377	A1	20150903	AU 2014-248377	20140328
IL 241827	A	20151130	IL 2014-241827	20140328
CN 105120663	A	20151202	CN 2014-80019712	20140328
EP 2981169	A2	20160210	EP 2014-779684	20140328
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KR 2016026824	A	20160309	KR 2015-7022953	20140328
IN 2015DN07750	A	20160122	IN 2015-DN7750	20150828
PRIORITY APPLN. INFO.:			US 2013-13986103 A	20130401
			WO 2014-US32253 W	20140328

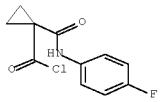
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



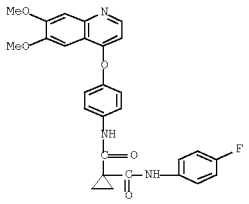
L8 ANSWER 190 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1710486 CAPLUS Full-text
DOCUMENT NUMBER: 161:577829
TITLE: Drug combinations to treat cancer
INVENTOR(S): Sweeney, Christopher J.; Kantoff, Philip W.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 78pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165779	A1	20141009	WO 2014-US33008	20140404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2908815	A1	20141009	CA 2014-2908815	20140404
AU 2014248001	A1	20151119	AU 2014-248001	20140404
IL 241868	A	20151130	IL 2014-241868	20140404
KR 2015138268	A	20151209	KR 2015-7030445	20140404

EP 2983639 A1 20160217 EP 2014-724594 20140404
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
US 20160082019 A1 20160324 US 2015-14782493 20151005
IN 2015KN03651 A 20160318 IN 2015-KN3651 20151103
PRIORITY APPLN. INFO.: US 2013-61808516 P 20130404
WO 2014-US33008 W 20140404
OTHER SOURCE(S): CASREACT 161:577829; MARPAT 161:577829
GI



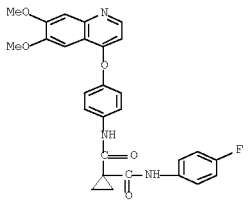
AB This invention relates to the combination of cabozantinib and abiraterone to treat cancer, particularly castration resistant prostate cancer.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug combinations to treat cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug combinations to treat cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

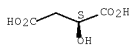
CRN 849217-68-1
CMF C28 H24 F N3 O5



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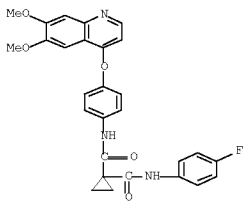
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



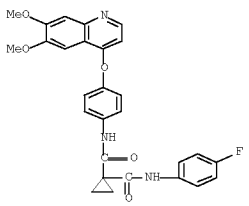
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 191 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1689164 CAPLUS Full-text
DOCUMENT NUMBER: 162:58578
TITLE: Cabozantinib inhibits growth of androgen-sensitive and castration-resistant prostate cancer and affects bone remodeling [Erratum to document cited in CA160:363229]
AUTHOR(S): Nguyen, Holly M.; Ruppender, Nazanin; Zhang, Xiaotun; Brown, Lisha G.; Gross, Ted S.; Morrissey, Colm; Gulati, Roman; Vessella, Robert L.; Schimmoller, Frauke; Aftab, Dana T.; Corey, Eva
CORPORATE SOURCE: Department of Urology, University of Washington, Seattle, WA, USA
SOURCE: PLoS One (2014), 9(8), e106797/1, 1 pp.
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0106797
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB On page 1, the funding information was incomplete; the cor. funding statement is given.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET, VEGFR2, RET expressions were found higher while cabozantinib by inhibiting these targets it safely, effectively inhibited tumor growth, improved bone remodeling in androgen-sensitive, metastatic CRPC tumor xenografted mouse (Erratum))
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



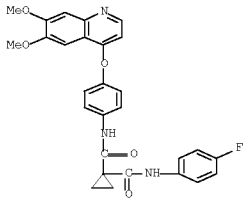
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 192 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1684883 CAPLUS Full-text
DOCUMENT NUMBER: 161:588524
TITLE: Emerging molecular targets in oncology: clinical potential of MET/hepatocyte growth-factor inhibitors
AUTHOR(S): Smyth, Elizabeth C.; Sclafani, Francesco; Cunningham, David
CORPORATE SOURCE: Department of Gastrointestinal Oncology, Royal Marsden Hospital, Sutton, UK
SOURCE: OncoTargets and Therapy (2014), 7, 1001-1014, 14 pp.
CODEN: OTNHAZ; ISSN: 1178-6930
DIGITAL OBJECT ID: 10.2147/OTT.S44941
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The MET/hepatocyte growth-factor (HGF) signaling pathway plays a key role in the processes of embryogenesis, wound healing, and organ regeneration. Aberrant activation of MET/HGF occurs through multiple mechanisms including gene amplification, mutation, protein overexpression, and abnormal gene splicing interrupting autocrine and paracrine regulatory feedback mechanisms. In many cancers including non-small-cell lung cancer, colorectal, gastric, renal, and hepatocellular cancer, dysregulation of MET may lead to a more aggressive cancer phenotype and may be a neg. prognostic indicator. Successful therapeutic targeting of the MET/HGF pathway has been achieved using monoclonal antibodies against the MET receptor and its ligand HGF in addition to MET-specific and multitargeted small-mol. tyrosine-kinase inhibitors with several drugs in late-phase clin. trials including onartuzumab, rilotumumab, tivantinib, and cabozantinib. MET frequently interacts with other key oncogenic tyrosine kinases including epidermal growth-factor receptor (EGFR) and HER-3 and these interactions may be responsible for resistance to anti-EGFR therapies. Similarly, resistance to MET inhibition may be mediated through EGFR activation, or alternatively by increasing levels of MET amplification or acquisition of novel "gatekeeper" mutations. In order to optimize development of effective inhibitors of the MET/HGF pathway clin. trials must be enriched for patients with demonstrable MET-pathway dysregulation for which robustly standardized and validated assays are required.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. targets in oncol. and clin. potential of MeT/hepatocyte growth-factor inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 140 THERE ARE 140 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 193 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1684761 CAPLUS Full-text
DOCUMENT NUMBER: 161:588517
TITLE: Cabozantinib for progressive metastatic medullary thyroid cancer: a review
AUTHOR(S): Colombo, Joshua R.; Wein, Richard O.
CORPORATE SOURCE: Department of Otolaryngology, Head and Neck Surgery, Tufts Medical Center, Boston, MA, USA
SOURCE: Therapeutics and Clinical Risk Management (2014), 10, 395-404, 10 pp.
CODEN: TCRMA6; ISSN: 1178-203X
DIGITAL OBJECT ID: 10.2147/TCRM.S46041
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Medullary thyroid cancer is uncommon and patients typically present with advanced disease. Treatment options for patients with progressive, metastatic medullary thyroid cancer had been limited until recently. Tyrosine kinase inhibitors have garnered increasing interest in this subset of patients. The US Food and Drug Administration recently approved cabozantinib, a tyrosine kinase inhibitor, after promising results were shown in a large Phase III clin. trial. This review summarizes the clin. pharmacol., clin. trials, and safety data for cabozantinib and concludes with a discussion of possible future directions for the treatment of medullary thyroid cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for progressive metastatic medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

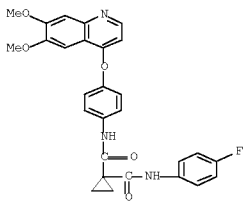


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 194 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1660666 CAPLUS Full-text
DOCUMENT NUMBER: 161:546938
TITLE: Methods and compositions for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): Tactical Therapeutics Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140294806	A1	20141002	US 2013-13986103	20130401
US 9089570	B2	20150728		
CA 2902144	A1	20141009	CA 2014-2902144	20140328
WO 2014165412	A2	20141009	WO 2014-US32253	20140328
WO 2014165412	A3	20150129		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014248377	A1	20150903	AU 2014-248377	20140328
IL 241827	A	20151130	IL 2014-241827	20140328
CN 105120663	A	20151202	CN 2014-80019712	20140328
EP 2981169	A2	20160210	EP 2014-779684	20140328
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KR 2016026824	A	20160309	KR 2015-7022953	20140328
IN 2015DN07750	A	20160122	IN 2015-DN7750	20150828

PRIORITY APPLN. INFO.: US 2013-13986103 A 20130401
WO 2014-US32253 W 20140328
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



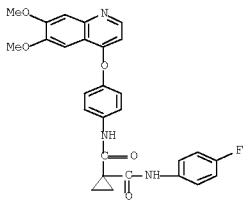
L8 ANSWER 195 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1657302 CAPLUS Full-text
DOCUMENT NUMBER: 161:559304
TITLE: Methods of treating proliferative diseases such as cancer using natural compounds and/or ketogenic diet
INVENTOR(S): Reynolds, Brent; Deleyrolle, Loic
PATENT ASSIGNEE(S): University of Florida Research Foundation, Incorporated, USA
SOURCE: PCT Int. Appl., 115pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014159500	A1	20141002	WO 2014-US23934	20140312
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2912518	A1	20141002	CA 2014-2912518	20140312
AU 2014240467	A1	20151105	AU 2014-240467	20140312
EP 2968260	A1	20160120	EP 2014-775944	20140312
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CN 105377252	A	20160302	CN 2014-80028215	20140312
US 20160038456	A1	20160211	US 2015-14775751	20150914
IN 2015DN09621	A	20160226	IN 2015-DN9621	20151014

PRIORITY APPLN. INFO.: US 2013-61784386 P 20130314
WO 2014-US23934 W 20140312
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The current invention is directed to a treatment of a proliferative disease comprising administering to a subject in need of such treatment, a composition comprising epigallocatechin-3-gallate (EGCG), curcumin, glucosinolates and, optionally Daikon radish sprout, alone or in combination with providing a ketogenic diet or a modified ketogenic diet to the subject. The invention also provides a composition comprising medium chain triglycerides, epigallocatechin-3-gallate, curcumin, compns. comprising glucosinolates and/or derivs. thereof, such as glucoraphanin and its breakdown product sulforaphane (SFN) (which are found at high levels in broccoli sprouts or sprouts of other cruciferous vegetables), and, optionally Daikon radish sprout.
IT 1140909-48-3, Cometriq
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cometriq; methods of treating proliferative diseases such as cancer using natural compds. and/or ketogenic diet)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

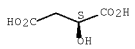
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

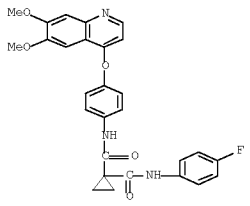


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

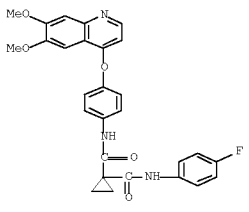
L8 ANSWER 196 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1653556 CAPLUS Full-text
DOCUMENT NUMBER: 161:542164
TITLE: Articles and methods for preventing and treating dermatologic adverse events
INVENTOR(S): Lacouture, Mario E.; Abou-Alfa, Ghassan Khaled
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 22pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014160628	A2	20141002	WO 2014-US31545	20140324
WO 2014160628	A3	20141204		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2978412	A2	20160203	EP 2014-775469	20140324
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US 20160101114	A1	20160414	US 2015-14888392	20151030
PRIORITY APPLN. INFO.:			US 2013-61804907 P	20130325
			WO 2014-US31545 W	20140324

AB The present invention provides articles and methods for preventing or treating dermatol. adverse events.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(articles and methods for preventing and treating dermatol. adverse events)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 197 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1651697 CAPLUS Full-text
DOCUMENT NUMBER: 161:710328
TITLE: Hepatocellular carcinoma: novel molecular targets in carcinogenesis for future therapies
AUTHOR(S): Bertino, Gaetano; Demma, Shirin; Ardiri, Annalisa; Proiti, Maria; Gruttadauria, Salvatore; Toro, Adriana; Malaguarnera, Giulia; Bertino, Nicoletta; Malaguarnera, Michele; Malaguarnera, Mariano; Di Carlo, Isidoro
CORPORATE SOURCE: Hepatology Unit, Department of Medical and Pediatric Sciences, University of Catania, Policlinic, Catania, 95123, Italy
SOURCE: BioMed Research International (2014) 203693/1-203693/15, 16 pp.
CODEN: BRIIDT; ISSN: 2314-6141
DIGITAL OBJECT ID: 10.1155/2014/203693
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background. Hepatocellular carcinoma is one of the most common and lethal malignant tumors worldwide. Over the past 15 years, the incidence of HCC has more than doubled. Due to late diagnosis and/or advanced underlying liver cirrhosis, only limited treatment options with marginal clin. benefit are available in up to 70% of patients. During the last decades, no effective conventional cytotoxic systemic therapy was available contributing to the dismal prognosis in patients with HCC. A better knowledge of mol. hepatocarcinogenesis provides today the opportunity for targeted therapy. Materials and Methods. A search of the literature was made using cancer literature, the PubMed, Scopus, and Web of Science (WOS) database for the following keywords: "hepatocellular carcinoma," "mol. hepatocarcinogenesis," "targeted therapy," and "immunotherapy." Discussion and Conclusion. Treatment decisions are complex and dependent upon tumor staging, presence of portal hypertension, and the underlying degree of liver dysfunction. The knowledge of mol. hepatocarcinogenesis broadened the horizon for patients with advanced HCC. During the last years, several mol. targeted agents have been evaluated in clin. trials in advanced HCC. In the future, new therapeutic options will be represented by a blend of immunotherapy-like vaccines and T-cell modulators, supplemented by molecularly targeted inhibitors of tumor signaling pathways.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatocellular carcinoma as novel mol. targets in carcinogenesis for future therapies)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

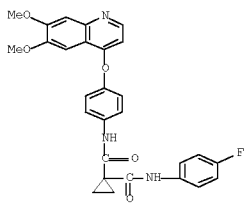


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 198 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1600971 CAPLUS Full-text
DOCUMENT NUMBER: 161:533327
TITLE: c-met cancer biomarkers for patient prognosis and selection for the therapy with c-met antagonist, particularly anti-c-met antibody
INVENTOR(S): Yauch, Robert; Koeppen, Hartmut
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 99pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014150819	A2	20140925	WO 2014-US24316	20140312
WO 2014150819	A3	20150108		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2013-61801276 P	20130315

AB The invention concerns c-met biomarkers for patient selection and prognosis in cancer, as well as methods of therapeutic treatment and diagnostic kits using anti-c-met antibodies.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-met antagonist; c-met cancer biomarkers for patient prognosis and selection for therapy with c-met antagonist, particularly anti-c-met antibody)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 199 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1599013 CAPLUS Full-text
DOCUMENT NUMBER: 161:533781
TITLE: Antibodies for treating angiogenesis-related disorders
INVENTOR(S): Gurewich, Victor
PATENT ASSIGNEE(S): FFE Therapeutics LLC, USA
SOURCE: PCT Int. Appl., 76pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

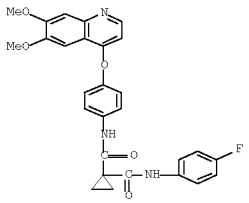
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014151917	A1	20140925	WO 2014-US26675	20140313
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2968550	A1	20160120	EP 2014-769535	20140313
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160024194	A1	20160128	US 2015-14775261	20150911
PRIORITY APPLN. INFO.:			US 2013-61785345 P	20130314
			WO 2014-US26675 W	20140313

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The author discloses anti-angiogenic monoclonal antibodies and antigen-binding antibody fragments that selectively and specifically bind to an epitope in both fibronectin and either fibrinogen or fibrin fragment E. In one example, administration of the monoclonal antibodies is shown to inhibit tumor growth and vascularization in a colon adenocarcinoma xenograft model.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination therapy with cross-reactive monoclonal antibodies to fibronectin and fibrinogen)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 200 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1596401 CAPLUS Full-text
DOCUMENT NUMBER: 161:528901
TITLE: Stapling eIF4E-eIF4G interacting peptides and their therapeutic use in cancer treatment
INVENTOR(S): Brown, Christopher John; Lane, David Philip; Quah, Soo Tng; Lama, Dilraj; Verma, Chandra Shekhar
PATENT ASSIGNEE(S): Agency for Science, Technology and Research, Singapore
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014149001	A1	20140925	WO 2014-SG94	20140228
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
SG 201400336	A1	20150828	SG 2014-336	20140115
CN 105263950	A	20160120	CN 2014-80029531	20140228
EP 2976354	A1	20160127	EP 2014-768664	20140228
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160046672	A1	20160218	US 2015-14778761	20150921

PRIORITY APPLN. INFO.:

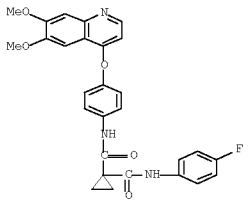
SG 2013-2065	A	20130321
SG 2014-336	A	20140115
WO 2014-SG94	W	20140228

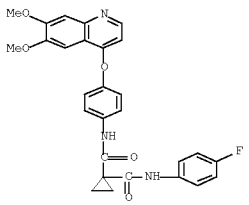
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 161:528901

AB The present invention relates to crosslinked peptides that are assocd. with human eIF4G and bind to eIF4E, uses thereof and pharmaceutical compns. comprising the peptides. Described below are crosslinked peptides related to a portion of human eIF4E. These crosslinked peptides contain at least two modified amino acids that together form an internal crosslink (also referred to as a staple) that can help to stabilize the alpha-helical secondary structure of a portion of eIF4G1 that is thought to be important for binding of eIF4E to eIF4G. Accordingly, a crosslinked peptide described herein can have improved biol. activity relative to a corresponding peptide that is not crosslinked. The crosslinked eIF4G1 peptides are thought to interfere with binding of eIF4G1 to eIF4G thereby inhibiting the increased translation of mRNAs with highly structured 5'UTRs. The crosslinked eIF4G1 peptide described herein can be used therapeutically, e.g., to treat or prevent a variety of cancers in a subject.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stapling eIF4E-eIF4G interacting peptides and their therapeutic use in cancer treatment)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

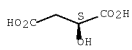
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



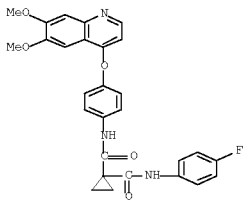
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 201 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1594844 CAPLUS Full-text
DOCUMENT NUMBER: 162:544299
TITLE: Congestive heart failure risk in cancer patients treated with vascular endothelial growth factor tyrosine kinase inhibitors: a systematic review and meta-analysis of 36 clinical trials
AUTHOR(S): Qi, Wei-Xiang; Shen, Zan; Tang, Li-Na; Yao, Yang
CORPORATE SOURCE: Department of Oncology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE: British Journal of Clinical Pharmacology (2014), 78(4), 748-762
CODEN: BCPHBM; ISSN: 1365-2125
DIGITAL OBJECT ID: 10.1111/bcp.12387
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Aims : Congestive heart failure (CHF) assocd. with vascular endothelial growth factor tyrosine-kinase inhibitors (VEGFR-TKIs) has emerged as a relevant problem in clin. and scientific communities. We performed an up-to-date, comprehensive meta-anal. to determine the overall incidence and risk of CHF in cancer patients receiving VEGFR-TKIs. Methods : The databases

of PubMed, Web of Science and abstrs. presented at the American Society of Clin. Oncol. up to August 31 2013 were searched for relevant articles. Statistical analyses were conducted to calculate the summary incidence, odds ratio (OR) and 95% confidence intervals (CIs) by using either random effects or fixed effect models according to the heterogeneity of included studies. Results : A total of 10 553 patients from 36 clin. trials were included. The overall incidence of all grade and high grade CHF associated with VEGFR-TKIs was 3.2% (95% CI 1.8%, 5.8%) and 1.4% (95% CI 0.9%, 2.3%), resp. The use of VEGFR-TKIs significantly increased the risk of developing all grade (OR 2.37, 95% CI 1.76, 3.20, P < 0.001) and high grade (OR 3.51, 95% CI 1.74, 7.05, P < 0.001) CHF. In subgroup analyses, the risk of CHF did not significantly vary with tumor types (P = 0.071 for all grade; P = 0.72 for high grade) and VEGFR-TKIs (P = 0.55 for all grade; P = 0.99 for high grade). Meta-regression indicated that CHF might possibly occur early in the treatment of VEGFR-TKIs. No evidence of publication bias was observed Conclusion : The use of VEGFR-TKIs is associated with a significantly increased risk of developing congestive heart failure in cancer patients. Clinicians should be aware of this risk and provide close monitoring in patients receiving these therapies.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(congestive heart failure risk in cancer patients treated with vascular endothelial growth factor tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

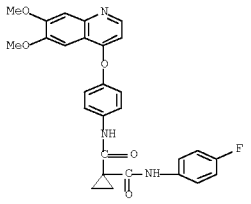
L8 ANSWER 202 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1563739 CAPLUS Full-text
DOCUMENT NUMBER: 161:496846
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Privada Institut de Recerca Biomedica, Spain; Fundacio Privada Institucio Catalana de Recerca i Estudis Avancats
SOURCE: PCT Int. Appl., 97pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014140933	A2	20140918	WO 2014-IB1253	20140314
WO 2014140933	A3	20141231		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2906394	A1	20140918	CA 2014-2906394	20140314
AU 2014229505	A1	20150903	AU 2014-229505	20140314
KR 2015122731	A	20151102	KR 2015-7026432	20140314
EP 2971113	A2	20160120	EP 2014-747411	20140314
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CN 105324491	A	20160210	CN 2014-80015564	20140314
US 20160032400	A1	20160204	US 2015-14776412	20150914

PRIORITY APPLN. INFO.: US 2013-61801718 P 20130315
WO 2014-IB1253 W 20140314

AB The invention relates to a method for the prognosis of bone metastasis in cancer which comprises using a probe to determine if a gene of interest is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise using a probe to determine the expression level of a gene of interest, or the amplification or translocation of a gene of interest. The invention also relates to a method for predicting early bone metastasis in a subject suffering cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering cancer and for classifying a subject from cancer into a cohort.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for prognosis and treatment of cancer metastasis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

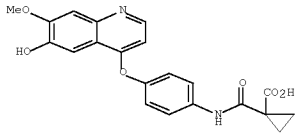


L8 ANSWER 203 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1554223 CAPLUS Full-text
DOCUMENT NUMBER: 161:496839
TITLE: Metabolites of n-[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]-n'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven; Nguyen, Linh
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014145693	A1	20140918	WO 2014-US30498	20140317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

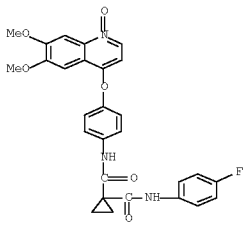
PRIORITY APPLN. INFO.: US 2013-61792562 P 20130315

OTHER SOURCE(S): CASREACT 161:496839; MARPAT 161:496839
GI

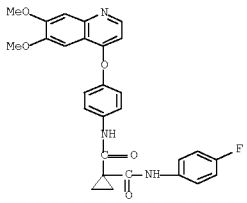


AB The invention relates to metabolites of foretinib as well as uses thereof.

IT 1621681-63-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metabolites of foretinib)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



IT 849217-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(metabolites of foretinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

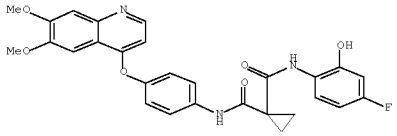


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

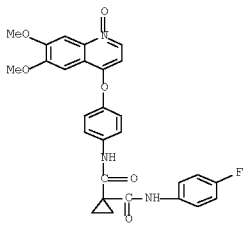
L8 ANSWER 204 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1554191 CAPLUS Full-text
DOCUMENT NUMBER: 161:496838
TITLE: Metabolites of N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl) cyclopropane-1,1-dicarboxamide
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven; Nguyen, Linh
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 65pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014145715	A1	20140918	WO 2014-US30524	20140317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2907334	A1	20140918	CA 2014-2907334	20140317
AU 2014232714	A1	20151008	AU 2014-232714	20140317
KR 2015130376	A	20151123	KR 2015-7027712	20140317
IL 241577	A	20151130	IL 2014-241577	20140317
CN 105121412	A	20151202	CN 2014-80021215	20140317
EP 2970126	A1	20160120	EP 2014-721149	20140317
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160031818	A1	20160204	US 2015-14776337	20150914
IN 2015KN03380	A	20160318	IN 2015-KN3380	20151013

PRIORITY APPLN. INFO.: US 2013-61792413 P 20130315
WO 2014-US30524 W 20140317
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:496838; MARPAT 161:496838
GI

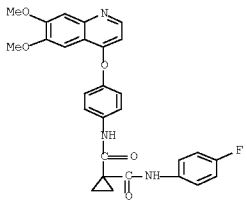


AB The invention relates to metabolites of cabozantinib as well as uses thereof.
IT 1621681-63-7P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metabolites of cabozantinib)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



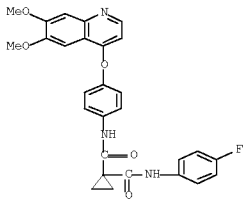
IT 1628542-34-6

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolites of cabozantinib)
RN 1628542-34-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, monohydroxy deriv. (CA INDEX NAME)



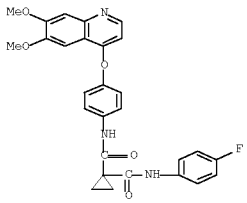
D1—OH

IT 849217-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(metabolites of cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 205 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1509904 CAPLUS Full-text
DOCUMENT NUMBER: 162:419468
TITLE: Antitumor Agent Cabozantinib Decreases RANKL Expression in Osteoblastic Cells and Inhibits Osteoclastogenesis and PTHrP-Stimulated Bone Resorption
AUTHOR(S): Stern, Paula H.; Alvares, Keith
CORPORATE SOURCE: Department of Pharmacology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
SOURCE: Journal of Cellular Biochemistry (2014), 115(11), 2033-2038
CODEN: JCEBD5; ISSN: 0730-2312
DIGITAL OBJECT ID: 10.1002/jcb.24879
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cabozantinib, an inhibitor of vascular endothelial growth factor and hepatocyte growth factor signaling, decreases bone lesions in patients with prostate cancer. To determine direct effects of cabozantinib on bone, resorption in neonatal mouse bone organ culture and on gene expression, proliferation, and phenotypic markers in osteoblast and osteoclast cell lines were examined Cabozantinib, 0.3 and 3 μM, prevented PTHrP-stimulated calcium release from neonatal mouse calvaria. Since the effect on resorption could reflect effects on osteoblasts to prevent osteoclast activation, or direct inhibition of osteoclasts, responses in osteoblastic and osteoclast precursor cell lines were examined Twenty-four-hour treatment of osteoblastic MC3T3-E1 cells with 3 μM cabozantinib decreased expression of receptor activator of NFkB ligand (RANKL) and alkaline phosphatase. Forty-eight-hour treatment of MC3T3-E1 cells with 3 μM cabozantinib inhibited cell proliferation and decreased MTT activity. Effects on alkaline phosphatase activity were biphasic, with small stimulatory effects at concns. below 3 μM. When RAW 264.7 osteoclast precursor cells differentiated with 20 ng/mL RANKL were co-treated for 24 h with 3 μM cabozantinib, expression of RANK, TRAP, cathepsin K, alpha v or beta 3 integrin, or NFATc1 were unaffected. Five-day treatment of RANKL-treated RAW 264.7 cells with 3 μM cabozantinib decreased TRAP and MTT activity. The results suggest that the osteoblast could be the initial target, with subsequent direct and indirect effects on osteoclastogenesis leading to decreased resorption. The multiple effects of cabozantinib on the cell microenvironment of bone are consistent with its effectiveness in reducing lesions from prostate cancer metastases. J. Cell. Biochem. 115: 2033-2038, 2014. © 2014 Wiley Periodicals, Inc.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agent cabozantinib decreases RANKL expression in osteoblastic cells and inhibits osteoclastogenesis and PTHrP-stimulated bone resorption)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

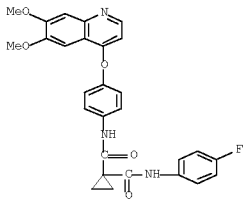
L8 ANSWER 206 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1476801 CAPLUS Full-text
DOCUMENT NUMBER: 161:446646
TITLE: Preparation of pyridine compounds as protein tyrosine kinase inhibitors for treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wang, Ruyong; Wang, Liang
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 118pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CN 104016979	A	20140903	CN 2013-10597520		20131122
PRIORITY APPLN. INFO.:			CN 2012-10480698	A	20121123
			CN 2013-10116667	A	20130403

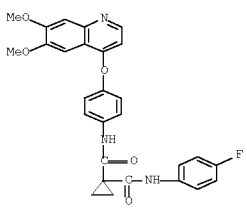
OTHER SOURCE(S): MARPAT 161:446646
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridinyl compds. of general formula I, pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. For I, each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; X is C6-C10 aryl or 5-10 membered heteroaryl that are optionally substituted; and Y is an (un)substituted bicyclic heterocyclyl. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 6-step reaction that culminated in coupling of intermediates III and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-ol. Example compds. of the invention were also tested in ALK and c-Met kinase inhibition assays. Pharmacokinetic profiles were also examined in rats, as was compound stability in human and rat liver microsomes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyridine compds. as protein tyrosine kinase inhibitors for treatment of proliferative diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 207 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1460877 CAPLUS Full-text
DOCUMENT NUMBER: 162:17927
TITLE: Comparison of the cancer gene targeting and biochemical selectivities of all targeted kinase inhibitors approved for clinical use
AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; de Man, Jos; Tanizawa, Yoshinori; Kawase, Yusuke; Yoshino, Kohichiro; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE: Netherlands Translational Research Center B.V., Oss, Neth.
SOURCE: PLoS One (2014), 9(3), e92146/1-e92146/13, 13 pp.
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0092146
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The anti-proliferative activities of all twenty-five targeted kinase inhibitor drugs that are in clin. use were measured in two large assay panels: (1) a panel of proliferation assays of forty-four human cancer cell lines from diverse tumor tissue origins; and (2) a panel of more than 300 kinase enzyme activity assays. This study provides a head-on comparison of all kinase inhibitor drugs in use, and for six of these drugs, the first kinome profiling data in the public domain. Correlation of drug activities with cancer gene mutations revealed novel drug sensitivity markers, suggesting that cancers dependent on mutant CTNNB1 will respond to trametinib and other MEK inhibitors, and cancers dependent on SMAD4 to small mol. EGFR inhibitor drugs. Comparison of cellular targeting efficacies reveals the most targeted inhibitors for EGFR-, ABL1- and BRAF(V600E)-driven cell growth, and demonstrates that the best targeted agents combine high biochem. potency with good selectivity. For ABL1 inhibitors, we computationally deduce optimized kinase profiles for use in a next generation of drugs. Our study shows the power of combining biochem. and cellular profiling data in the evaluation of kinase inhibitor drug action.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of cancer gene targeting and biochem. selectivities of all targeted kinase inhibitors approved for clin. use in human)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

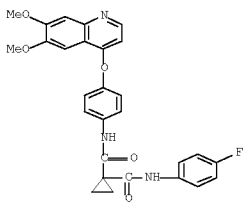


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 208 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1425621 CAPLUS Full-text
DOCUMENT NUMBER: 161:400645
TITLE: Treatment of cancer using an oncolytic virus and a receptor tyrosine kinase inhibitor
INVENTOR(S): Conner, Joe
PATENT ASSIGNEE(S): Virttu Biologics Limited, UK
SOURCE: PCT Int. Appl., 310pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2014128487	A1	20140828	WO 2014-GB50522		20140221
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
GB 2516521	A	20150128	GB 2014-3083		20140221
US 20150374767	A1	20151231	US 2015-14768549		20150818
PRIORITY APPLN. INFO.:			GB 2013-3184	A	20130222
			WO 2014-GB50522	W	20140221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method of treating cancer is disclosed, the method comprising simultaneous or sequential administration of an oncolytic virus and a receptor tyrosine kinase (RTK) inhibitor.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of cancer using an oncolytic virus and a receptor tyrosine kinase inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

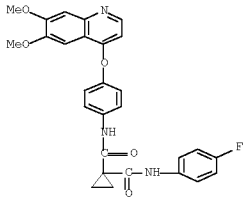


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 209 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1416968 CAPLUS Full-text
DOCUMENT NUMBER: 162:442908
TITLE: High-Grade Undifferentiated Sarcomas of the Uterus: Diagnosis, Outcomes, and New Treatment Approaches
AUTHOR(S): Philip, Charles-Andre; Pautier, Patricia; Duffaud, Florence; Ray-Coquard, Isabelle
CORPORATE SOURCE: Department of Adult Medical Oncology, Centre Leon Berard, Lyon, 69008, Fr.
SOURCE: Current Oncology Reports (2014), 16(10), 1-8
CODEN: CORUAT; ISSN: 1534-6269
DIGITAL OBJECT ID: 10.1007/s11912-014-0405-1
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. High-grade undifferentiated sarcomas (HGUS) are rare malignancies accounting for 6 % of all uterine sarcomas and have a very poor outcome. Histol. classification of HGUS is currently debated as a subgroup with uniform nucleoli, and frequently YWHAE-FAM22 transcript has been described, constituting a potential target for new therapies. In localized HGUS, surgery involving total hysterectomy and bilateral oophorectomy is recommended. Adjuvant radiotherapy has recently been suggested in a retrospective study to decrease local recurrence and improve survival vs. observation in localized HGUS. In metastatic or recurrent disease, chemotherapy with doxorubicin with or without ifosfamide constitutes the standard of care. Gemcitabine plus docetaxel also seems to be an interesting alternative. Targeted therapies such as pazopanib are now available for soft tissue sarcomas and so could be proposed for uterine sarcoma patients after first- or second-line chemotherapy in the metastatic phase. Further investigations are needed to determine their indications and targets. A European Organization for Research and Treatment of Cancer (EORTC) randomized trial testing maintenance therapy with cabozantinib after first-line chemotherapy in HGUS is ongoing.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-Grade Undifferentiated Sarcomas of the Uterus: Diagnosis, Outcomes, and New Treatment Approaches)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

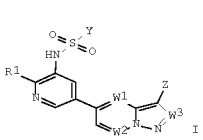


REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

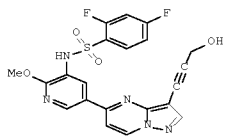
L8 ANSWER 210 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1390694 CAPLUS Full-text
DOCUMENT NUMBER: 161:375913
TITLE: Preparation of pyrazolopyridine compounds as protein kinase modulators useful for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 41pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140234254	A1	20140821	US 2014-14181670	20140215
CA 2898294	A1	20140828	CA 2014-2898294	20140215
WO 2014130375	A1	20140828	WO 2014-US16643	20140215
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014219256	A1	20150730	AU 2014-219256	20140215
KR 2015118102	A	20151021	KR 2015-7019069	20140215
EP 2958564	A1	20151230	EP 2014-754663	20140215
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2016509056	T	20160324	JP 2015-558892	20140215

PRIORITY APPLN. INFO.: US 2013-61767721 P 20130221
WO 2014-US16643 W 20140215
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:375913; MARPAT 161:375913
GI



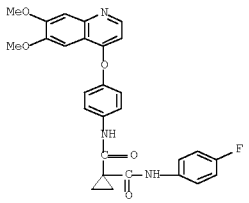
I



II

AB The invention provides heteroarom. derivs. and pharmaceutically acceptable salts and formulations thereof useful in modulating the protein kinase activity, especially phosphatidylinositol 3-kinases (PI3K) and mammalian target of rapamycin (mTOR), and in modulating inter- and/or intra-cellular signaling activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Compds. of formula I [wherein W1, W2, and W3 are independently N or CRc; Z is D, CN, N3, etc.; Y is C1-6 alkyl, C3-6 cycloalkyl, C3-C6 heterocyclyl, etc.; R1 is H, Cl, C3-6 cycloalkyl, etc.; each Rc is independently H, D, F, etc.] or stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, prodrugs, or pharmaceutically acceptable salts thereof are claimed and exemplified. Example compound II was prepared in seven steps (procedure given). Candidate compds. of I were assayed for their stability in liver microsomes, their oral and i.v. bioavailability, and inhibitory activity against PI3K and mTOR kinase (data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyrazolopyridine compds. as protein kinase modulators useful for treatment of hyperproliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 211 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1389525 CAPLUS Full-text
DOCUMENT NUMBER: 161:379820
TITLE: Efflux inhibitor compositions containing effect transporter protein inhibitors
INVENTOR(S): Bunt, Antonius Martinus Gustave; Tellingen, Olaf Van
PATENT ASSIGNEE(S): Izumi Biosciences LLC, USA; The Netherlands Cancer Institute
SOURCE: U.S. Pat. Appl. Publ., 33pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140235631	A1	20140821	US 2013-13952476	20130726

PRIORITY APPLN. INFO.: US 2013-61767689 P 20130221
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to efflux inhibitor compns. and methods of using these agents for treating conditions where the activity of efflux transporter proteins (e.g., Breast Cancer Resistance Protein (BCRP) and P-Glycoprotein (P-GP)) inhibit effective delivery of a therapeutic agent to a target tissue (e.g., brain, spinal cord, nerves, cerebrospinal fluid, testis, eyeballs, retina, inner ear, placenta, mammary gland, liver, biliary tract, kidney, intestines, lung, adrenal cortex, endometrium, hematopoietic cells, and/or stem cells). E.g., elacridar nanoparticles were prepared

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kinase inhibitor; efflux inhibitor pharmaceuticals containing effect transporter protein inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

components thereof, which can be represented as the patient's analyte index (e.g., EGFR/cMET index) and can be used to determine whether the patient is likely to respond to a particular therapy such as EGFR inhibitor therapy alone, cMET inhibitor therapy alone, or a combination thereof. The EGFR inhibitor is selected from the group consisting of cetuximab, panitumumab, matuzumab, nimotuzumab, Erbl vaccine, erlotinib, gefitinib, CL-387785 and a combination thereof, wherein the c-MET inhibitor is selected from the group consisting of ARQ197, XL184, GSK1363089/XL880, MP470, MGCD265, SGX523, PF04217903, JNJ38877605, INCB28060, AMG-458, E7050, MK-2461, BMS-777607 and a combination thereof. The invention also provides methods for determining drug resistance in non-small cell lung cancer (NSCLC) patients receiving above mentioned therapy.

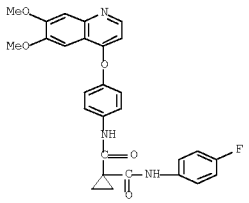
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for non-small cell lung cancer therapy)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

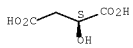
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 213 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1339983 CAPLUS Full-text
DOCUMENT NUMBER: 161:329247
TITLE: Improved treatment for adenoid cystic carcinoma comprising growth factor receptor kinase and MET kinase inhibitors
INVENTOR(S): Stenman, Goeran; Andersson, Mattias
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 116pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014123476	A1	20140814	WO 2014-SE50140	20140204
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

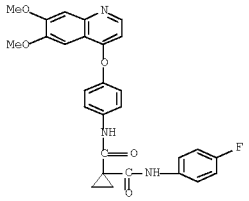
PRIORITY APPLN. INFO.: US 2013-61849920 P 20130205

AB The present application relates to inhibitors of epidermal growth factor receptor (EGFR) kinase, MET kinase, insulin receptor (IR) kinase and insulin-like growth factor 1 (IGF1R) kinase for use in the treatment of neoplastic disease such as adenoid cystic carcinoma (ACC) and dermal cylindroma characterized by MYB activation. In an optional embodiment, the kinase inhibitor inhibits the MET kinase and the EGFR kinase and/or the IGF1R/IR kinase. In an optional embodiment, the kinase inhibitor is BMS-754807. In an optional embodiment, the IGF1R/IR kinase inhibitor is selected from a group consisting of linsitinib and BMS-754807. In an optional embodiment, the EGFR kinase inhibitor is selected from a group consisting of gefitinib, erlotinib, BMS-690514 and cetuximab. In an optional embodiment, the MET kinase inhibitor is selected from a group consisting of crizotinib, BMS-907351, BMS-777607 and BMS-754807.

IT 849217-68-1, BMS 907351
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BMS 907351; improved treatment for adenoid cystic carcinoma comprising growth factor receptor kinase and MET kinase inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

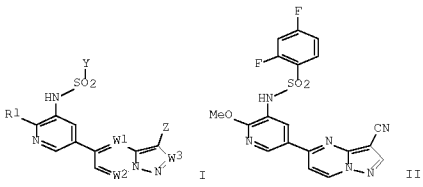


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 214 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1274352 CAPLUS Full-text
DOCUMENT NUMBER: 161:361023
TITLE: Preparation of aryl-heterocyclic compounds for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 59pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103965199	A	20140806	CN 2014-10041929	20140128
PRIORITY APPLN. INFO.:			CN 2013-10040391 A	20130202
			CN 2013-10117077 A	20130404

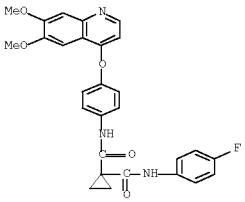
OTHER SOURCE(S): CASREACT 161:361023; MARPAT 161:361023
GI



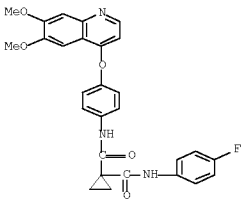
AB The present invention discloses aryl-heterocyclic compd. (with structure as shown in formula I), stereo isomers, geometrical isomers, tautomers, oxynitride, hydrates, solvates, metabolic products, pharmaceutically acceptable salts or prodrugs, pharmaceutical compns. containing thereof and application thereof in preparing agents for inhibiting or regulating the activity of protein kinases in biol. specimens. For example, compound II was prepared in a multi-step synthesis. The present invention also relates to pharmaceutical compns. containing the inventive compound, and application of the pharmaceutical compns. for treating mammal, particular human hyperproliferative disorders.

IT **849217-68-1**, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of aryl-heterocyclic compds. for treatment of hyperproliferative disorders)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 215 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1273412 CAPLUS Full-text
DOCUMENT NUMBER: 162:67014



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 216 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1270460 CAPLUS Full-text
DOCUMENT NUMBER: 161:351479
TITLE: Degradation kinetics study of cabozantinib by a novel stability-indicating LC method and identification of its major degradation products by LC/TOF-MS and LC-MS/MS
AUTHOR(S): Wu, Chunyong; Xu, Xue; Feng, Chao; Shi, Yuanyuan; Liu, Wenyuan; Zhu, Xiaoyun; Zhang, Junying
CORPORATE SOURCE: Key Laboratory of Drug Quality Control and Pharmacovigilance, Ministry of Education, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2014), 98, 356-363
CODEN: JPBADA; ISSN: 0731-7085
DIGITAL OBJECT ID: 10.1016/j.jpba.2014.06.008
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB The chem. stability of cabozantinib (CBZ) was investigated using a novel stability-indicating LC method. Forced degradation of CBZ was carried out under acidic, basic, thermal, oxidative and photolytic stress conditions. Hydrolysis and oxidation were the primary pathways for this compound and three major unknown degradation products were characterized by LC/TOF-MS and LC-MS/MS. The major oxidative degradation product was isolated by preparative LC and identified by UV, HRMS and NMR techniques to be N-(4-[(N-oxide-6,7-dimethoxyquinolin-4-yl)oxy]phenyl)-N'-(4-fluorophenyl)- cyclopropane-1,1-dicarboxamide. The developed method was validated as per ICH guidelines and then successfully applied to investigate the degradation kinetics of CBZ. Degradation of CBZ followed first-order kinetics under all exptl. conditions. A V-shaped pH-rate profile over the pH range 2-10 was observed with maximum stability at pH 6. The effect of temperature on the rate of CBZ degradation was characterized using the Arrhenius equation. The activation energy for hydrolysis was 57.31 kJ mol-1 in alkaline solution

IT **849217-68-1**, Cabozantinib **1140909-48-3**, Cabozantinib

TITLE: Development of cabozantinib for the treatment of prostate cancer
AUTHOR(S): Vaishampayan, Ulka N.
CORPORATE SOURCE: Department of Oncology, Wayne State University/Karmanos Cancer Institute, Detroit, MI, USA
SOURCE: Core Evidence (2014), 9, 61-67, 7 pp.
CODEN: CEOVAF; ISSN: 1555-1741
DIGITAL OBJECT ID: 10.2147/CE.S67095
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

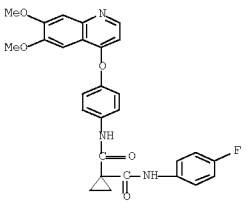
AB A review. Cabozantinib (XL184) is a multitargeted receptor tyrosine kinase with predominantly MET and vascular endothelial growth factor inhibition properties. It is currently approved by the US Food and Drug Administration for the treatment of progressive metastatic medullary thyroid cancer. The agent has a convenient once-daily oral dosing schedule and has demonstrated encouraging activity in metastatic castrate-resistant prostate cancer (CRPC). A Phase I/II trial demonstrated responses in soft tissue, visceral disease, and bone metastases in CRPC. An objective response rate of 5%, a stable disease rate of 75%, and a median progression-free survival of 6 mo was observed As compared with the 140 mg daily dose used in thyroid cancer, a lower dose of 60 mg daily is currently being utilized in prostate cancer studies due to the fact that toxicity could be reduced without compromising efficacy. Randomized trials are ongoing in comparison with prednisone or with mitoxantrone and prednisone in pretreated metastatic CRPC. Cabozantinib has demonstrated a unique mechanism of action and preliminary efficacy in the crowded therapeutic field of prostate cancer. Since multiple therapies have recently demonstrated overall survival benefit in metastatic CRPC, cabozantinib will likely face some challenges in clin. application. At present, in this rapidly evolving field, it is unclear what proportion of patients with prostate cancer will be eligible to receive this therapy. The cost of cabozantinib is likely to be another deterrent, especially if it remains more expensive than other oral therapies, such as abiraterone and enzalutamide. Defining the role of MET overexpression and RET mutations as biomarkers in prostate cancer may help to guide patient selection, and enrich and enhance the future applications of this targeted novel agent.

IT **849217-68-1**, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of cabozantinib for treatment of prostate cancer in patients)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

(S)-Malate
RL: AMX (Analytical matrix); PEP (Physical, engineering or chemical process); PRP (Properties); ANST (Analytical study); PROC (Process)
(degradation kinetics study of cabozantinib by novel stability-indicating LC method and identification of major degradation products by LC/TOF-MS and LC-MS/MS)

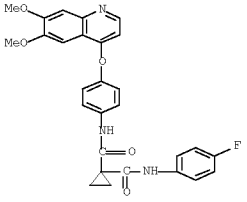
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

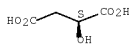
CRN 849217-68-1
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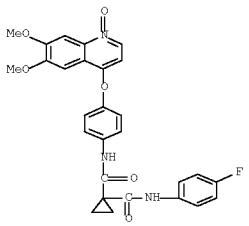
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 1621681-63-7
RL: ANT (Analyte); FMU (Formation, unclassified); PRP (Properties); ANST (Analytical study); FORM (Formation, nonpreparative)
(degradation kinetics study of cabozantinib by novel stability-indicating LC method and identification of major degradation products by LC/TOF-MS and LC-MS/MS)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)

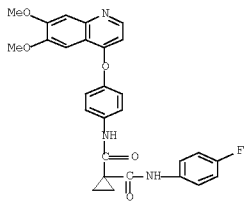


OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 217 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1237165 CAPLUS Full-text
DOCUMENT NUMBER: 162:55826
TITLE: Recent orphan drugs that are first-in-class
AUTHOR(S): Phillips, M. Ian; Lee, Jongserk R.
CORPORATE SOURCE: Keck Graduate Institute, Center for Rare Disease Therapies, 535 Watson Drive, Claremont, CA, 91711, USA
SOURCE: Expert Opinion on Orphan Drugs (2014), 2(8), 759-763
CODEN: EOODAJ; ISSN: 2167-8707
DIGITAL OBJECT ID: 10.1517/21678707.2014.931806
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Although the pipeline for new drugs seemed to be drying up, the number of new 'first-in-class' drugs appeared to be increasing. First-in-class drugs are those which use a new and unique mechanism for treating a disease or medical condition. They are a subset of new mol. entities (NMEs). The FDA reports that in 2012, 39 NMEs were approved. Twenty of these NMEs (.apprx. 50%) were identified by the FDA as first-in-class drugs. Of the 39 NMEs, 13 were designated orphan drugs and 9 of those orphan drugs were first-in-class. In 2013, there were 27 NMEs of which 9 were first-in-class. In 2013, nos. of NMEs are lower than the 2011 or 2012 but are based on fewer applications than in those years. There were 33% of NMEs that were first-in-class and 33% of the NMEs were orphan drugs. The FDA data indicate that creative new products are being developed for rare diseases.
IT 1140909-48-3, Cometriq
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(movement toward first-in-class drugs, indicating more innovation in drug discovery and utilizing orphan drugs)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

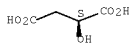
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

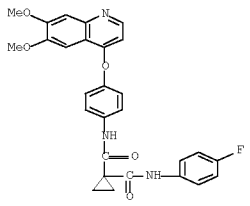
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 218 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1222486 CAPLUS Full-text
DOCUMENT NUMBER: 161:744871
TITLE: Cabozantinib-Induced Thyroid Dysfunction: A Review of Two Ongoing Trials for Metastatic Bladder Cancer and Sarcoma
AUTHOR(S): Yavuz, Sahzene; Apolo, Andrea B.; Kummar, Shivaani; del Rivero, Jaydira; Madan, Ravi A.; Shawker, Thomas; Reynolds, James; Celi, Francesco S.
CORPORATE SOURCE: National Institute of Diabetes and Digestive and Kidney Diseases, Diabetes, Endocrine, and Obesity Branch, National Institutes of Health, Bethesda, MD, USA
SOURCE: Thyroid (2014), 24(8), 1223-1231
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2013.0621
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Background: Thyroid dysfunction is a common adverse event associated with tyrosine kinase inhibitors (TKI), but its underlying pathophysiol. is unclear. Cabozantinib is a novel TKI currently Food and Drug Administration approved for advanced medullary thyroid cancer and tested in clin. trials on solid tumors including prostate, liver, bladder, breast, and ovarian cancer. Methods: We analyzed the thyroid function of patients enrolled in two phase 2 clin. trials using cabozantinib at the National Institutes of Health Clin. Center. Two cases of thyroiditis associated with cabozantinib therapy are presented in detail, and a systematic review of the literature on TKI-associated thyroid dysfunction is also discussed. Results: Between Sept. 2012 and Sept. 2013, 33 patients were treated with cabozantinib, and follow-up thyroid function tests were available for 31 (20 males, 11 females; age 59±1 years). Thyroid dysfunction was recorded in the majority of patients (93.1%), with a predominance of subclin. hypothyroidism. Two cases showed a biphasic pattern of thyroid dysfunction characterized by a transient thyrotoxicosis followed by hypothyroidism. Color Doppler demonstrated an increase in vascularization during the thyrotoxic phase, but no uptake was visualized on nuclear medicine imaging. A systematic review of the literature resulted in the identification of 40 original manuscripts, of which 13 were case series and 6 were case reports describing TKI-associated thyroid dysfunction. Conclusion: TKI therapy often results in clin. significant thyroid dysfunction. Cabozantinib treatment commonly results in thyroid dysfunction varying from subclin. hypothyroidism to symptomatic thyrotoxicosis. Early detection and characterization of cabozantinib-associated thyroid dysfunction and close follow-up are essential to provide adequate management of this common adverse event.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(review of two ongoing trials for metastatic bladder cancer and sarcoma and cabozantinib-induced thyroid dysfunction)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 219 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1212244 CAPLUS Full-text
DOCUMENT NUMBER: 161:731791
TITLE: Cabozantinib: A Review of Its Use in Patients with Medullary Thyroid Cancer
AUTHOR(S): Hoy, Sheridan M.
CORPORATE SOURCE: Springer, Auckland, N. Z.
SOURCE: Drugs (2014), 74(12), 1435-1444
CODEN: DRUGAY; ISSN: 0012-6667
DIGITAL OBJECT ID: 10.1007/s40265-014-0265-x
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (Cometriq) is an orally administered small mol. inhibitor of multiple tyrosine kinase receptors, including those involved in the pathogenesis of medullary thyroid cancer (MTC) [i.e. rearranged during transfection (RET), MET and vascular endothelial growth factor receptor (VEGFR)-2]. Cabozantinib is indicated for the treatment of adults with progressive, unresectable locally advanced (in the EU) or metastatic (in the EU and USA) MTC. Compared with placebo, cabozantinib significantly prolonged progression-free survival, reflecting a 72 % reduction in the risk of disease progression or death, in patients with unresectable, locally advanced or metastatic MTC participating in a multinational, phase III study. A significantly higher proportion of patients receiving cabozantinib than those receiving placebo achieved an objective response or disease

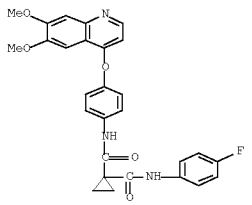
stabilization (i.e. a complete or partial response, or stable disease). The overall survival benefit with cabozantinib is as yet unclear, with no significant benefit observed in two interim analyses (one prespecified, and one unplanned and conducted at the request of the US FDA). The tolerability profile of oral cabozantinib is typical for a small mol. targeting the VEGFR and other tyrosine kinase-mediated pathways, with adverse events associated with the inhibition of the VEGF pathway (e.g. gastrointestinal perforation, hemorrhage, hypertension and venous thrombosis) reported in the phase III study. Treatment-emergent adverse events were generally managed with supportive therapy, dose redns. and/or dose interruptions. Although final overall survival data are awaited, current evidence suggests cabozantinib to be a valuable treatment option for adults with progressive, unresectable locally advanced or metastatic MTC.

IT 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cabozantinib in patients with medullary thyroid cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

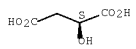
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 221 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1202788 CAPLUS Full-text
DOCUMENT NUMBER: 161:269285
TITLE: Oligooxopiperazines for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer
INVENTOR(S): Arora, Paramjit S.; Pan, Quintin; Mapp, Anna
PATENT ASSIGNEE(S): New York University, USA; The Ohio State University Research Foundation; The Regents of the University of Michigan
SOURCE: PCT Int. Appl., 95pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014113794	A2	20140724	WO 2014-US12337	20140121
WO 2014113794	A3	20140912		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2898329	A1	20140724	CA 2014-2898329	20140121
US 20140205655	A1	20140724	US 2014-14160037	20140121
AU 2014207311	A1	20150820	AU 2014-207311	20140121
EP 2945631	A2	20151125	EP 2014-741084	20140121
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 105246481	A	20160113	CN 2014-80010794	20140121
JP 2016510327	T	20160407	JP 2015-553892	20140121

PRIORITY APPLN. INFO.: US 2013-61754575 P 20130119
WO 2014-US12337 W 20140121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:269285; MARPAT 161:269285

AB The present invention relates to oligooxopiperazines for reactivating p53. Methods of using the oligooxopiperazines are also disclosed. A first aspect of the present invention relates to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, the method comprising administering to the subject an oligooxopiperazine that substantially mimics helix αB of the C-terminal transactivation domain of Hypoxia-Inducible Factor Iα under conditions effective to treat or prevent the disorder. A second aspect of the present invention relates to a method of inducing apoptosis or decreasing survival and/or proliferation of a cell, the method comprising contacting the cell with an oligooxopiperazine. In this study, the authors took a novel approach and functionally reactivated p53 in Human papillomaviruses (HPV)-pos. head and neck squamous cell carcinoma (HNSCC) by blocking the interaction between E6 and p300. Ectopic expression of the CH1 domain of p300 squelched E6 to disrupt E6-p300 association resulting in an increase in p53 acetylation, accumulation, and activity. CH1 domain inhibitors reactivated p53 and dramatically potentiated the efficacy of cisplatinum in HPV-pos. HNSCC. Taken together, the authors work revealed a novel druggable approach to reactivate p53 in HPV-pos. HNSCC that is expected to translate to other

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 220 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:1205266 CAPLUS Full-text
DOCUMENT NUMBER: 161:269288
TITLE: Hydrogen-bond surrogate peptides and peptidomimetics for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer
INVENTOR(S): Arora, Paramjit S.; Pan, Quintin; Mapp, Anna
PATENT ASSIGNEE(S): New York University, USA; The Ohio State University Research Foundation; University of Michigan
SOURCE: PCT Int. Appl., 98pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014113792	A1	20140724	WO 2014-US12331	20140121
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20140205681	A1	20140724	US 2014-14160018	20140121
US 20140220159	A1	20140807	US 2014-14160001	20140121
EP 2964245	A1	20160113	EP 2014-740418	20140121
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

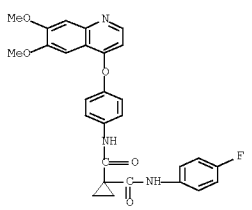
PRIORITY APPLN. INFO.: US 2013-61754574 P 20130119
US 2013-61874190 P 20130905
WO 2014-US12331 W 20140121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 161:269288

AB The present invention relates to peptidomimetics for reactivating p53. Methods of using the peptidomimetics are also disclosed. One aspect of the present invention relates to a peptidomimetic, where the peptidomimetic mimics a helix having the formula X1-X2-X2-X3-X2-X2-X1-X4, wherein each X1 is any neg. charged residue, each X2 is any hydrophobic residue, X3 is any pos.-charged residue, and X4 is any polar residue. Addnl., the peptidomimetic may contain one or more bridges linking the side chains of its component amino

acids. Another aspect of the present invention relates to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, the method comprising administering to the subject a peptidomimetic of the present invention under conditions effective to treat or prevent the disorder. Another aspect of the present invention relates to a method of inducing apoptosis and decreasing survival and/or proliferation of a cell, the method comprising contacting the cell with a peptidomimetic. In this study, the authors took a novel approach and functionally reactivated p53 in Human papillomaviruses (HPV)-pos. head and neck squamous cell carcinoma (HNSCC) by blocking the interaction between E6 and p300. Ectopic expression of the CH1 domain of p300 squelched E6 to disrupt E6-p300 association resulting in an increase in p53 acetylation, accumulation, and activity. CH1 domain inhibitors reactivated p53 and dramatically potentiated the efficacy of cisplatinum in HPV-pos. HNSCC. Taken together, the authors work revealed a novel druggable approach to reactivate p53 in HPV-pos. HNSCC that is expected to translate to other HPV-pos. carcinomas.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidomimetics for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer and combination with other agents)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

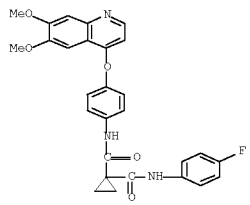


HPV-pos. carcinomas. HMD: helix αB of C-terminal transactivation domain, of HIF-1α, mimics.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligooxopiperazines for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer and combination with other agents)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 222 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1160177 CAPLUS Full-text

DOCUMENT NUMBER: 161:239766

TITLE: Androgen receptor modulator for treatment of prostate cancer and other conditions

INVENTOR(S): Chen, Isan; Hager, Jeffrey H.; Maneval, Edna Chow; Herbert, Mark R.; Smith, Nicholas D.

PATENT ASSIGNEE(S): Aragon Pharmaceuticals, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 46pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140199236	A1	20140717	US 2014-14151106	20140109
CA 2898025	A1	20140724	CA 2014-2898025	20140109
WO 2014113260	A1	20140724	WO 2014-US10777	20140109

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AU 2014207839	A1	20150723	AU 2014-207839	20140109
IL 239741	A	20150831	IL 2014-239741	20140109
KR 2015105464	A	20150916	KR 2015-7021865	20140109
CN 105007920	A	20151028	CN 2014-80015802	20140109
EP 2945628	A1	20151125	EP 2014-701865	20140109

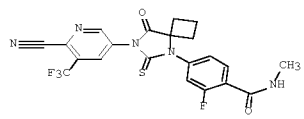
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JP 2016508991	T	20160324	JP 2015-552756	20140109
AR 94654	A1	20150819	AR 2014-100116	20140113
CR 20150357	A	20150824	CR 2015-357	20150708
MX 2015009090	A	20151005	MX 2015-9090	20150714

PRIORITY APPLN. INFO.: US 2013-61752842 P 20130115
WO 2014-US10777 W 20140109

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

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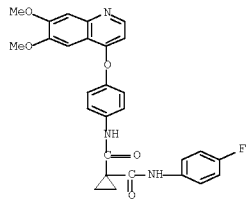
I

AB The invention discloses the androgen receptor modulator I for the treatment of prostate cancer in combination with other therapeutic options and for the treatment of diseases or conditions that are amenable to treatment with the androgen receptor modulator, as well as pharmaceutical compns. and medicaments that include I.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androgen receptor modulator for treatment of prostate cancer and other conditions)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 223 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1154296 CAPLUS Full-text

DOCUMENT NUMBER: 161:209516

TITLE: Predictive biomarker and method for combination therapy of EGFR and c-MET inhibitors in non-small cell lung cancer with wild type EGFR

INVENTOR(S): Lee, Mun Ja; Kim, Hyeon Jeong; Kang, Han Na

PATENT ASSIGNEE(S): JEUK Co., Ltd., S. Korea

SOURCE: Repub. Korea, 20pp.
CODEN: KRXXFC

DOCUMENT TYPE: Patent

LANGUAGE: Korean

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 1418970	B1	20140711	KR 2013-29977	20130320

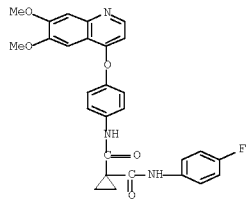
PRIORITY APPLN. INFO.: KR 2013-29977 20130320

AB The title method comprises the steps of: detg. the p53 genotypes of patients, separating out the patients having cooperation tumor effect probability of combination therapy according to EGFR and c-MET inhibitors. Therefore, the condition of p53 can be used as predicative factor for combination therapy of EGFR and c-MET inhibitors.

IT 849217-68-1, Cabozantinib, co-use with EGFR inhibitors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MET inhibitor; predictive biomarker and method for combination therapy of EGFR and c-MET inhibitors in non-small cell lung cancer with wild type EGFR)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 224 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1134083 CAPLUS Full-text

DOCUMENT NUMBER: 162:254986

TITLE: A Melanoma Cell State Distinction Influences Sensitivity to MAPK Pathway Inhibitors

AUTHOR(S): Konieczkowski, David J.; Johannessen, Cory M.; Abudayyeh, Omar; Kim, Jong Wook; Cooper, Zachary A.; Piris, Adriano; Frederick, Dennie T.; Barzily-Rokni, Michal; Straussman, Ravid; Haq, Rizwan; Fisher, David E.; Mesirov, Jill P.; Hahn, William C.; Flaherty, Keith T.; Wargo, Jennifer A.; Tamayo, Pablo; Garraway, Levi A.

CORPORATE SOURCE: Broad Institute of Harvard and MIT, Cambridge, MA, USA

SOURCE: Cancer Discovery (2014), 4(7), 816-827
CODEN: CDAIB2; ISSN: 2159-8274

DIGITAL OBJECT ID: 10.1158/2159-8290.CD-13-0424

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Most melanomas harbor oncogenic BRAFv600 mutations, which constitutively activate the MAPK pathway. Although MAPK pathway inhibitors show clin. benefit in BRAFV600-mutant melanoma, it remains incompletely understood why 10% to 20% of patients fail to respond. Here, we show that RAF inhibitor-sensitive and inhibitor-resistant BRAFv600-mutant melanomas display distinct transcriptional profiles. Whereas most drug-sensitive cell lines and patient biopsies showed high expression and activity of the melanocytic lineage transcription factor MITF, intrinsically resistant cell lines and biopsies displayed low MITF expression but higher levels of NF-κ signaling and the receptor tyrosine kinase AXL. In vitro, these MITF-low/NF-κβ-high melanomas were resistant to inhibition of RAF and MEK singly or in combination, and ERK. Moreover, in cell lines, NF- activation antagonized MITF expression and induced both resistance marker genes and drug resistance. Thus, distinct cell states characterized by MITF or NF-κβ activity may influence intrinsic resistance to MAPK pathway inhibitors in BRAFv600-mutant melanoma.

IT 1160908-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

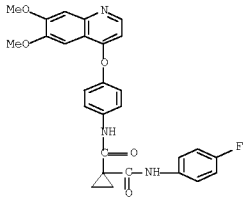
(RAF inhibitor resistant human melanoma cells carrying mutant BRAF showed low MITF and high NFκB levels which influence intrinsic resistance to MAPK pathway inhibitors)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

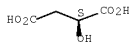
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 225 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1064742 CAPLUS Full-text

DOCUMENT NUMBER: 161:455975

TITLE: A targeted next-generation sequencing assay detects a high frequency of therapeutically targetable alterations in primary and metastatic breast cancers: implications for clinical practice

AUTHOR(S): Vasan, Neil; Yelensky, Roman; Wang, Kai; Moulder, Stacy; Dzimitrowicz, Hannah; Avritscher, Rony; Wang, Bauang; Wu, Yun; Cronin, Maureen T.; Palmer, Gary; Symmans, W. Fraser; Miller, Vincent A.; Stephens, Phiup; Pusztai, Lajos

CORPORATE SOURCE: Yale University School of Medicine, Connecticut, New Haven, USA

SOURCE: Oncologist (2014), 19(5), 453-458
CODEN: OCOLF6; ISSN: 1083-7159

DIGITAL OBJECT ID: 10.1634/theoncologist.2013-0377

PUBLISHER: AlphaMed Press

DOCUMENT TYPE: Journal

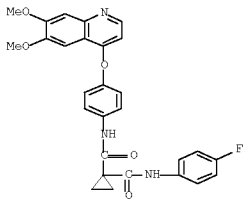
LANGUAGE: English

AB Background. The aim of this study was to assess the frequency of potentially actionable genomic alterations in breast cancer that could be targeted with approved agents or investigational drugs in clin. trials using a next-generation sequencing-based genomic profiling assay performed in a Clin. Laboratory Improvement Amendments-certified and College of American Pathologists-accredited com. laboratory Methods. Fifty-one breast cancers were analyzed, including primary tumor biopsies of 33 stage I-II and 18 stage IV cancers (13 soft tissue, 3 liver, and 2 bone metastases). We assessed 3,230 exons in 182 cancer-related genes and 37 introns in 14 genes often rearranged in cancer for base substitutions, indels, copy number alterations, and gene fusions. The average median sequencing depth was 1,154×. Results. We observed 158 genomic alterations in 55 genes in 48 of 51 (94%) tumors (mean 3.1, range 0-9). The average number of potentially therapeutically relevant alterations was similar in primary (1.6, range 0-4) and in heavily pretreated metastatic cancers (2.0, range 0-4) (p = .24). The most common actionable alterations were in PIK3CA (n = 9, phosphatidylinositol 3-kinase [PI3K]/mammalian target of rapamycin [mTOR] inhibitors), NF1 (n = 7, PI3K/mTOR/mitogen-activated protein kinase inhibitors), v-akt murine thymoma viral oncogene homolog 1-3 (n = 7, PI3K/mTOR/AKT inhibitors), BRCA1/2 (n = 6, poly[ADP-ribose] polymerase inhibitors), and CCND1,2 and CCNE (n = 8)/cycline dependent kinase (CDK)6 (n = 1) (CDK4/6 inhibitors), KIT (n = 1, imatinib/sunitinib), ALK (n = 1, crizotinib), FGFR1,2 (n = 5, fibroblast growth factor receptor inhibitors), and EGFR (n = 2, epidermal growth factor receptor inhibitors). Our sequencing assay also correctly identified all six cases with HER2 (ERBB2) amplification by fluorescence in situ hybridization when tumor content was adequate. In addition, two known activating HER2 mutations were identified, both in unamplified cases. Conclusion. Overall, 84% of cancers harbored at least one genomic alteration linked to potential treatment options. Systematic evaluation of the predictive value of these genomic alterations is critically important for further progress in this field.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeted next-generation sequencing assay detects a high frequency of therapeutically targetable alterations in primary and metastatic breast cancers and its implications for clin. practice)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 226 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1049484 CAPLUS Full-text

DOCUMENT NUMBER: 161:246290

TITLE: Design, synthesis and evaluation of highly selective pyridone-based class II MET inhibitors

AUTHOR(S): She, Nengfang; Zhuo, Linsheng; Jiang, Wen; Zhu, Xiaolei; Wang, Jia; Ming, Zhihui; Zhao, Xinge; Cong, Xin; Huang, Wei

CORPORATE SOURCE: Key Laboratory of Pesticide and Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Wuhan, 430079, Peop. Rep. China

SOURCE: Bioorganic & Medicinal Chemistry Letters (2014), 24(15), 3351-3355
CODEN: BMCLE8; ISSN: 0960-894X

DIGITAL OBJECT ID: 10.1016/j.bmcl.2014.05.097

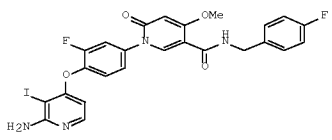
PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

OTHER SOURCE(S): CASREACT 161:246290

GI



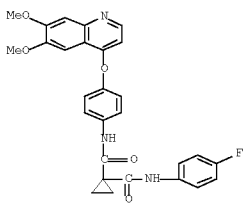
I

AB The high incidence of MET oncogene activation in human malignancies has prompted researchers to develop MET inhibitors. As part of our efforts to developing effective and safe therapeutic agents against MET-dependent tumors, a pyridone-based class II MET inhibitor, namely, 1-(4-((2-amino-3-iodopyridin-4-yl)-oxy)-3-fluorophenyl)-N-(4-fluorobenzyl)- 4-methoxy-6-oxo-1,6-dihydropyridine-3-carboxamide (3s, I), was identified. Knowledge of the binding mode of class II MET inhibitors led to the design of new inhibitors that utilize 2-pyridone to conformationally restrain key pharmacophoric groups within the mol. Integrated mol. docking and SAR studies resulted in the discovery of a novel class of pyridone MET inhibitors with high potency (IC50 of 0.005 μM) and efficient selectivity (>5000 fold) to VEGFR-2, c-Kit and RET kinases.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(docking and kinase selectivity study; design, synthesis and evaluation of highly selective pyridone-based class II MET inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 227 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:1006107 CAPLUS Full-text

DOCUMENT NUMBER: 161:238658

TITLE: Advanced thyroid cancers: new era of treatment

AUTHOR(S): Mohammed, Amrallah A.; El-Shentenawy, Ayman

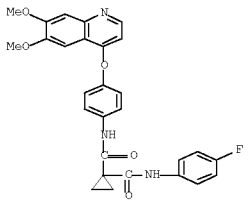
CORPORATE SOURCE: Oncology Center, King Abdullah Medical City-Holy Capital, Makkah, 21995, Saudi Arabia

SOURCE: Medical Oncology (New York, NY, United States) (2014), 31(7), 1-8
CODEN: MONCEZ; ISSN: 1357-0560

DIGITAL OBJECT ID: 10.1007/s12032-014-0049-x

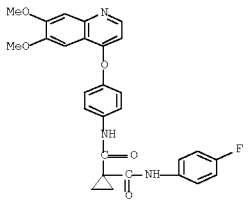
PUBLISHER: Springer

DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Since chemotherapy has been shown to be unsuccessful in case of advanced thyroid carcinomas, the research for new therapies is fundamental. Clin. trials of many tyrosine kinase inhibitors as well as anti-angiogenic inhibitors suggest that patients with thyroid cancer could have an advantage with new target therapy. Recently, Food and Drug Administration approved two targeted therapies, vandetanib and cabozantinib for the treatment of metastatic thyroid carcinomas with acceptable outcome. We summarized the results and the toxic effects associated with these treatments reported in clin. trials. Future trials should aim at combinations of targeted agents with or without other treatment modalities to obtain a more effective result in thyroid carcinoma treatment.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new era of treatment for advanced thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 228 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:969861 CAPLUS Full-text
DOCUMENT NUMBER: 161:455940
TITLE: Role of salvage targeted therapy in differentiated thyroid cancer patients who failed first-line sorafenib
AUTHOR(S): Dadu, Ramona; Devine, Catherine; Hernandez, Mike; Waguespack, Steven G.; Busaidy, Naifa L.; Hu, Mimi I.; Jimenez, Camilo; Habra, Mouhammad A.; Sellin, Rena V.; Ying, Anita K.; Cote, Gilbert J.; Sherman, Steven I.; Cabanillas, Maria E.
CORPORATE SOURCE: Departments of Endocrine Neoplasia and Hormonal Disorders, Baylor College of Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2014), 99(6), 2086-2094
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2013-3588
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Context: Sorafenib, a tyrosine kinase inhibitor, is a common first-line therapy for advanced differentiated thyroid cancer (DTC). However, responses are not durable and drug toxicity remains a problem. Objective: The objective of the study was to determine the efficacy of salvage therapy after first-line sorafenib failure. Design: This was a retrospective review at M. D. Anderson Cancer Center from Jan. 2005 to May 2013. Patients: The study included patients with metastatic DTC who received salvage therapy after their initial sorafenib failure (group 2). Patients who received first-line sorafenib only (group 1) were evaluated for comparison of overall survival (OS). Outcome Measures: Progression-free survival, best response, and median OS were measured. Results: Sixty-four patients with metastatic, radioactive iodine refractory DTC were included; 35 were in group 1 and 25 were in group 2, and the groups were well balanced. Median OS of all 64 patients receiving first line sorafenib was 37 mo; median OS was significantly longer with salvage therapy compared with sorafenib alone (58 vs 28 mo, P = .013). In group 2, 17 patients were evaluable for best response, although two patients had toxicity with sorafenib, which was discontinued before restaging. Best responses with first-line sorafenib were partial response in 2 of 15 (13%), stable disease in 10 of 15 (67%), and progressive disease in 3 of 15 (20%) patients. With salvage therapy, partial responses were seen in 7 of 17 (41%) and stable disease in 10 of 17 (59%) patients. Median progression-free survival was 7.4 mo with first-line sorafenib and 11.4 mo with salvage therapy. Salvage therapy included sunitinib (n = 4), pazopanib (n = 3), cabozantinib (n = 4), lenvatinib (n = 3), and vemurafenib (n = 3). Conclusions: Other targeted agents are effective salvage treatments after sorafenib failure, despite similar mechanisms of action, and should be offered to patients who are able to receive salvage therapy.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salvage targeted treatment with sunitinib, pazopanib, cabozantinib, lenvatinib and vemurafenib was effective in treatment of patient with metastatic differentiated thyroid cancer who failed first-line sorafenib therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 229 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:951549 CAPLUS Full-text
DOCUMENT NUMBER: 161:86164
TITLE: Preparation of pyridine compounds as protein tyrosine kinase inhibitors for treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wang, Ruyong; Wang, Liang
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 158pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

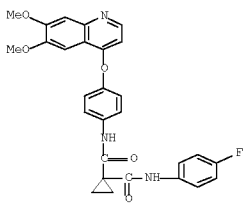
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014089324	A1	20140612	WO 2013-US73367	20131205

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61734903 P 20121207
US 2013-61880184 P 20130920
OTHER SOURCE(S): CASREACT 161:86164; MARPAT 161:86164
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridinyl compds. of general formula I, pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. For I, each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; X is C6-C10 aryl or 5-10 membered heteroaryl that are optionally substituted; and Y is an (un)substituted bicyclic heterocyclyl. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 6-step reaction that culminated in coupling of intermediates III and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-ol. Example compds. of the invention were tested in ALK and c-Met kinase inhibition assays. Pharmacokinetic profiles were also examined in rats, as was compound stability in human and rat liver microsomes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyridine compds. as protein tyrosine kinase inhibitors for treatment of proliferative diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

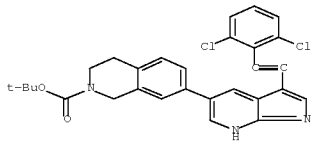
L8 ANSWER 230 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:951212 CAPLUS Full-text
DOCUMENT NUMBER: 161:94410
TITLE: Alkynyl compounds and methods of use
INVENTOR(S): Xi, Ning; Li, Xiaobo; Zhou, Shiqing

PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

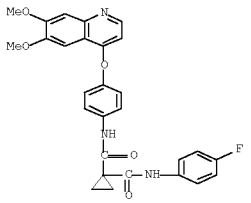
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014089280	A1	20140612	WO 2013-US73286	20131205

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61734897 P 20121207
OTHER SOURCE(S): CASREACT 161:94410; MARPAT 161:94410
GI

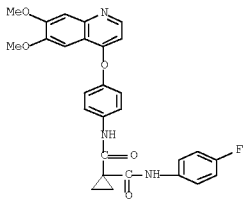


AB The present invention provides novel substituted alkynyl compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkynyl compds. and methods of use)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



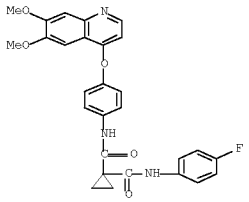
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 232 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:926742 CAPLUS Full-text
DOCUMENT NUMBER: 161:316322
TITLE: Cabozantinib Suppresses Tumor Growth and Metastasis in Hepatocellular Carcinoma by a Dual Blockade of VEGFR2 and MET
AUTHOR(S): Xiang, Qingfeng; Chen, Weiqiang; Ren, Meng; Wang, Jingnan; Zhang, Hongwu; Deng, David Y. B.; Zhang, Lei; Shang, Changzhen; Chen, Yajin
CORPORATE SOURCE: Departments of Hepatopancreatobiliary Surgery, Sun Yat-sen University, Guangzhou, Peop. Rep. China
SOURCE: Clinical Cancer Research (2014), 20(11), 2959-2970
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-2620
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB MET signaling was suggested a potential role in hepatocellular carcinoma (HCC) and associated with prometastasis during antiangiogenesis therapy. We investigated the potential association between MET expression and therapeutic response to sorafenib in patients with HCC. Antitumor effects of cabozantinib, a dual inhibitor of MET and VEGFR2, were examined in cultured HCC cells as well as in vivo models. Total MET and phosphorylated MET (p-MET) were measured in 29 resected HCC specimens, and correlated with response to sorafenib as postoperative adjuvant therapy. In the second set of expts. using cultured HCC cells, and mouse xenograft and metastatic models, effects of cabozantinib were examined High level of p-MET in resected HCC specimens was associated with resistance to adjuvant sorafenib therapy. In cultured HCC cells that expressed p-MET, cabozantinib inhibited the activity of MET and its downstream effectors, leading to G1-phase arrest. Cabozantinib inhibited tumor growth in p-MET-pos. and p-MET-neg. HCC by decreasing angiogenesis, inhibiting proliferation, and promoting apoptosis, but it exhibited more profound efficacy in p-MET-pos. HCC xenografts. Cabozantinib blocked the hepatocyte growth factor (HGF)-stimulated MET pathway and inhibited the migration and invasion of the HCC cells. Notably, cabozantinib reduced the number of metastatic lesions in the lung and liver in the exptl. metastatic mouse model. Patients with HCC with high level of p-MET are associated with resistance to adjuvant sorafenib treatment. The dual blockade of VEGFR2 and MET by cabozantinib has significant antitumor activities in HCC, and the activation of MET in HCC may be a promising efficacy-predicting biomarker. Clin Cancer Res; 20(11); 2959-70. ©2014 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib suppresses tumor growth and metastasis in hepatocellular carcinoma by dual blockade of VEGFR2 and MET)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 231 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:943695 CAPLUS Full-text
DOCUMENT NUMBER: 161:196584
TITLE: Adverse events of targeted therapies
AUTHOR(S): Klastersky, Jean A.
CORPORATE SOURCE: Institut Jules Bordet, Centre des Tumeurs de l'Universite Libre de Bruxelles, Brussels, Belg.
SOURCE: Current Opinion in Oncology (2014), 26(4), 395-402
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0000000000000096
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Purpose of review: There is currently an explosion in the no. of so-called targeted therapies. As new indications for these agents multiply, there is also an increase of new and less new side-effects. Recent findings: Given this rapidly evolving field, any literature on that topic is rapidly obsolete and needs re-evaluation. Summary: Targeted therapies are associated with a wide spectrum of adverse events, which cannot always be easily separated from the complications linked to cancer, its therapy, and comorbidities. A high awareness of these events might improve the patient's quality of life and contribute to the recognition of new syndromes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adverse events of targeted therapies)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



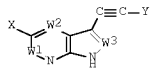
OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 233 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:923002 CAPLUS Full-text
DOCUMENT NUMBER: 161:99226
TITLE: Heterocyclic alkynyl compound, and its use and application as cell proliferation inhibitor and for regulating the activity of protein kinases
INVENTOR(S): Xi, Ning; Li, Xiaobo; Zhou, Shiqing
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 64pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

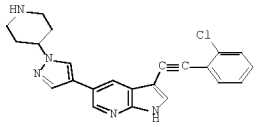
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103833753	A	20140604	CN 2013-10590780	20131121

PRIORITY APPLN. INFO.: CN 2012-10477798 A 20121122

OTHER SOURCE(S): MARPAT 161:99226
GI



I

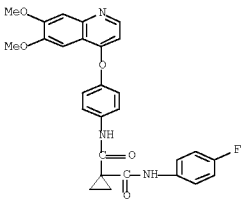


II

AB The present invention provides new substituted alkynyl compds. with the formula of I [W1-4 independently = N or CRc, wherein Rc = H, D, F, Cl, Br, etc.; X = Ph, pyridinyl, pyrrolyl, pyrazolyl, etc.; Y = (un)substituted aryl or heteroaryl], pharmaceutically acceptable salts thereof, pharmaceutical formulation thereof, and their use in regulating the activity of protein kinases and regulating the signal response in cells or between cells. Thus, e.g., II was prepared in a multi-step synthesis. Compds. of the invention were tested for their stability and Alk, c-Met kinase inhibitory activity, e.g., II showed IC50 value of 58 nM against Alkaline The present invention also relates to pharmaceutical compns. comprising a compound of the present invention, and using the pharmaceutical composition for treating a mammal, particularly to human hyperproliferative disorders.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; heterocyclic alkynyl compound, and its use and application as cell proliferation inhibitor and for regulating the activity of protein kinases)

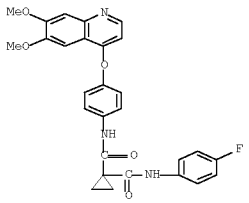
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 235 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:873778 CAPLUS Full-text
DOCUMENT NUMBER: 161:77594
TITLE: Hydrophilic linkers and their uses for conjugation of drugs to cell binding molecules
INVENTOR(S): Zhao, R. Yongxin
PATENT ASSIGNEE(S): Hangzhou Dac Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 102pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014080251	A1	20140530	WO 2012-IB56700	20121124
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2891280	A1	20140530	CA 2012-2891280	20121124
AU 2012395148	A1	20150521	AU 2012-395148	20121124
EP 2922818	A1	20150930	EP 2012-888899	20121124
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				



L8 ANSWER 234 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:913474 CAPLUS Full-text
DOCUMENT NUMBER: 161:46548
TITLE: Cabozantinib capsule composition and its production method
INVENTOR(S): Wang, Luanqiu; Wang, Xinyao
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103830203	A	20140604	CN 2014-10078549	20140305
PRIORITY APPLN. INFO.:			CN 2014-10078549	20140305

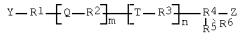
AB The invention provides a cabozantinib capsule compn. and its prodn. method. The cabozantinib capsule composition is composed of cabozantinib 10-60wt%, carrier 15-70 wt%, organic solvent 10-30wt%, surfactant 0.5-3.0wt%, micronized silica gel 1.0-3.0wt% and starch 5.0-20wt%. The carrier comprises one or more of glycerol monostearate, polyethylene glycol 6000, cetyl alc. and octyl alc. The organic solvent comprises one or more of ethanol, methanol and acetone. The surfactant comprises one or more of sodium dodecyl sulfate, Tween 80 and lecithin. The production method includes adding carrier into organic solvent, heating to 60°C, adding cabozantinib and surfactant, vacuum drying at 40°C, comminution by gas stream to obtain powder with grain size of 1-8 μm, adding micronized silica gel and starch, mixing, and packaging in. The produced cabozantinib capsule preparation has good oral absorption, high dissoln. rate, high bioavailability, and can remarkably inhibit the growth of tumor volume The invention has simple preparation process, low cost, and applicability for com. process.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for producing cabozantinib capsule composition)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

JP 2016501859	T	20160121	JP 2015-543532	20121124
US 20150250896	A1	20150910	US 2015-14432073	20150327
PRIORITY APPLN. INFO.:			WO 2012-IB56700 W	20121124

OTHER SOURCE(S): CASREACT 161:77594; MARPAT 161:77594
GI

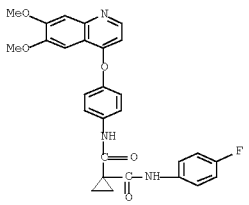


I

AB Prepn. of cell binding agent-drug conjugates comprising hydrophilic linker of formula (I), wherein:Y represents a functional group that enables reaction with a cell-binding agent; Q and T are either -P(=O)(OM)-, or -S(O)-; m and n are integer from 0 to 5, but not 0 at the same time; In addition, when m = 1, n = 0, Q is not -P(=O)(OM)-; or when n = 1, m = 0, T is not -P(=O)(OM)-; Z represents a functional group that enables linkage of a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ether, ester, carbamate, carbonate, amine (secondary, tertiary, or quartary), imine, cycloheteroalkyane, heteroarom., alkoxime or amide bond; R1, R2, R3, R4, R5 and R6, are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl, or 1-6 carbon atoms of esters, ether, amide, or polyethyleneoxy unit of formula (OCH2CH2)p, wherein p is an integer from 0 to about 1000, or combination thereof and methods of using such linkers and conjugates in pharmaceutical dosage forms for combination therapy of cancer, autoimmune and infectious diseases are provided.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(hydrophilic linkers and their uses in preparation of cell binding agent-drug conjugates useful in combination therapy of cancer, autoimmune and infectious diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

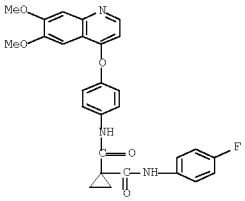


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 236 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:814874 CAPLUS Full-text
DOCUMENT NUMBER: 161:466864
TITLE: Aerodigestive Fistula Formation as a Rare Side Effect of Antiangiogenic Tyrosine Kinase Inhibitor Therapy for Thyroid Cancer
AUTHOR(S): Blevins, Dean P.; Dadu, Ramona; Hu, Mimi; Baik, Christina; Balachandran, Diwakar; Ross, William; Gunn, Brandon; Cabanillas, Maria E.
CORPORATE SOURCE: Department of Internal Medicine, University of Texas Health Science Center at Houston, Houston, TX, USA
SOURCE: Thyroid (2014), 24(5), 918-922
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2012.0598
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background: In the past decade, targeted therapy with antiangiogenic drugs has become standard of care for most types of metastatic, progressive thyroid cancer. While these drugs were thought initially to be less toxic than traditional chemotherapy, they can have rare but serious and fatal toxicities. Once such toxicity that has been reported in other tumor types is upper airway fistula formation, which can be life-threatening. Summary: Here, we describe three patients treated with antiangiogenic tyrosine kinase inhibitors at two academic institutions who developed aerodigestive fistula. All three patients had risk factors for fistula formation, which included external beam radiation and/or large tumor with invasion of the tracheal wall. Conclusions: Fistula formation is a known but rare side effect of antiangiogenic tyrosine kinase inhibitors. Knowledge of the risk factors that may predispose thyroid cancer patients to this serious adverse event is vital prior to prescribing antiangiogenics. Particular caution should be observed when using these drugs in patients undergoing radiation therapy or surgery, or in patients whose tumor is invading vital structures of the neck, as they may be at higher risk of developing this rare complication. In these patients, antiangiogenic tyrosine kinase inhibitors should be used cautiously, patients should be aware of the risk, and physicians should monitor patients for symptoms of fistula.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aerodigestive fistula formation as a rare side effect of antiangiogenic tyrosine kinase inhibitor therapy for thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

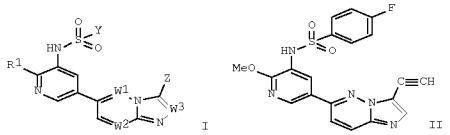


OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 237 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:794981 CAPLUS Full-text
DOCUMENT NUMBER: 160:740120
TITLE: Preparation of heteroaromatic compounds as protein kinase modulators for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 57pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140134133	A1	20140515	US 2013-14076256	20131110
CA 2889346	A1	20140522	CA 2013-2889346	20131110
WO 2014078211	A1	20140522	WO 2013-US69366	20131110
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2013345107	A1	20150430	AU 2013-345107	20131110
AU 2013345107	B2	20160225		
CN 104755085	A	20150701	CN 2013-80054625	20131110
KR 2015083833	A	20150720	KR 2015-7008264	20131110
EP 2919784	A1	20150923	EP 2013-855522	20131110
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015536994	T	20151224	JP 2015-541973	20131110
PRIORITY APPLN. INFO.:			US 2012-61726139 P	20121114
			WO 2013-US69366 W	20131110

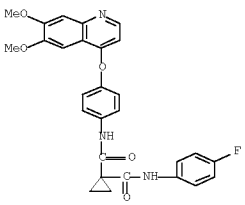
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:740120; MARPAT 160:740120
GI



I II

AB The invention provides heteroarom. derivs. and pharmaceutically acceptable salts and formulations thereof useful in modulating the protein kinase activity, especially phosphatidylinositol 3-kinases (PI3K) and mTOR kinase, and in modulating inter- and/or intra-cellular signaling activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Compds. of formula I [wherein W1, W2, and W3 are independently N or CRc; Z is D CN, N3, etc.; Y is C1-C6 alkyl, C3-C6 cycloalkyl, C3-C6 heterocyclyl, etc.; R1 is H, Cl, C3-C6 cycloalkyl, etc.; each Rc is independently H, D, F, etc.] or stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, prodrugs, or pharmaceutically acceptable salts thereof are claimed and exemplified. For example, II was prepared in five steps (procedure given). Candidate compds. of I were assayed for their stability in liver microsomes, their oral and i.v. bioavailability, and inhibitory activity against PI3K and mTOR kinase (data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of heteroarom. compds. as protein kinase modulators for treatment of hyperproliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 238 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:718961 CAPLUS Full-text
DOCUMENT NUMBER: 160:630742
TITLE: Replication-competent retroviral vectors for gene therapy using mini-promoters
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Lin, Amy H.; Logg, Christopher R.; Kasahara, Noriyuki
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: PCT Int. Appl., 89pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014066700	A1	20140501	WO 2013-US66709	20131024
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2909324	A1	20150826	EP 2013-849839	20131024
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104884627	A	20150902	CN 2013-80067486	20131024
JP 2015533510	T	20151126	JP 2015-539817	20131024
US 20150273029	A1	20151001	US 2015-14438564	20150424
PRIORITY APPLN. INFO.:			US 2012-61718610 P	20121025
			WO 2013-US66709 W	20131024

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Compact replicating retroviral vectors using a minimal promoter to express a therapeutic gene with a size of 0.9-1.9 kb are described. An internal ribosome entry sequence may be used for polycistronic expression cassettes. The vectors do not use the prior art SCP1, Ad, or CMV core promoters. Development and optimization of vectors is described.

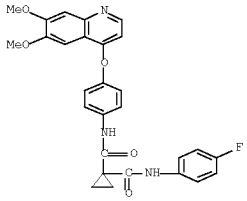
IT 1140909-48-3, XL-184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in cancer therapy with retroviral gene therapy vectors; retroviral vectors for gene therapy using mini-promoters)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

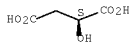
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 239 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:711027 CAPLUS Full-text

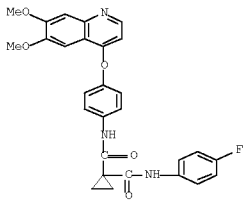
TITLE: Cabozantinib: a new molecular targeted antitumor drug
AUTHOR(S): Zhang, Xiu-ying; Liu, Yao; Bai, Qiu-jiang; Wang, Nan
CORPORATE SOURCE: Department of Pharmacy, Kailuan General Hospital, Tangshan, Hebei Province, 063000, Peop. Rep. China
SOURCE: Yiyao Daobao (2013), 32(11), 1468-1470
CODEN: YDIAAL; ISSN: 1004-0781
DIGITAL OBJECT ID: 10.3870/yydb.2013.11.021
PUBLISHER: Yiyao Daobao Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review. Cabozantinib, a new mol. targeted antitumor drug, was introduced with several subsections as follow: action mechanisms, pharmacokinetics, adverse reactions, drug interactions, clin. trials, and conclusions.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib: a new mol. targeted antitumor drug)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 241 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:653844 CAPLUS Full-text
DOCUMENT NUMBER: 161:257408
TITLE: Preclinical Evaluation of Imaging Biomarkers for Prostate Cancer Bone Metastasis and Response to Cabozantinib
AUTHOR(S): Graham, Timothy J.; Box, Gary; Tunariu, Nina; Crespo, Mateus; Spinks, Terry J.; Miranda, Susana; Attard, Gerhardt; de Bono, Johann; Eccles, Suzanne A.; Davies, Faith E.; Robinson, Simon P.
CORPORATE SOURCE: Division of Radiotherapy and Imaging, Institute of Cancer Research and Royal Marsden NHS Trust, Surrey, SM2 5NG, UK
SOURCE: Journal of the National Cancer Institute (2014), 106(4), ???
CODEN: JNCIEQ; ISSN: 0027-8874
DIGITAL OBJECT ID: 10.1093/jnci/dju033

DOCUMENT NUMBER: 160:643049
TITLE: Cabozantinib dispersible tablet and preparation method thereof
INVENTOR(S): Peng, Zongyu; Li, Ran; Zheng, Feibo
PATENT ASSIGNEE(S): Qingdao Cancer Hospital, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103751140	A	20140430	CN 2014-10017920	20140115

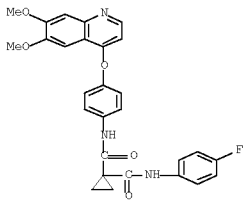
PRIORITY APPLN. INFO.: CN 2014-10017920 20140115

AB The invention discloses Cabozantinib dispersible tablet and prepn. method and application thereof. The inventive Cabozantinib dispersible tablet consists of the following component according to weight percentage: Cabozantinib 10-60%, filler 10-40%, disintegrant 10-50%, acidulant 10-50%, binder 0.1-10%, and lubricant and glidant 0.1-20%. Compared with the common tablet, the inventive dispersible tablet contains no surfactant, its solubility, dispersivity, and disintegrability are good, and it can be completely disintegrated within 1 min. The prepared Cabozantinib dispersible tablet has high dissoln. rate, high bioavailability, rapid distribution in vivo, stable quality, and good taste. The preparation method is simple, and suitable for industrial production

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib dispersible tablet)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 240 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:679549 CAPLUS Full-text
DOCUMENT NUMBER: 161:30896

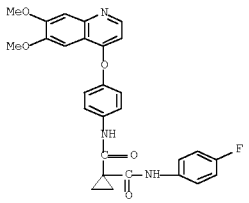
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background Prostate cancer is incurable once it has metastasized to the bone. Appropriate preclin. models are lacking. The therapeutic efficacy of the multikinase inhibitor cabozantinib was assessed in an orthotopic xenograft model of castration-resistant prostate cancer (CRPC) bone metastasis using noninvasive, multimodality functional imaging. Methods NOD/SCID mice were injected intratibially with luciferase-expressing ERG (v-ets avian erythroblastosis virus E26 oncogene homolog) rearranged VCaP human prostate carcinoma cells. The response of VCaP xenografts (n = 7 per group) to cabozantinib was investigated using bioluminescence imaging and anatomical and diffusion weighted magnetic resonance imaging. This enabled quantitation of tumor volume and apparent diffusion coefficient (ADC). Bone uptake of technetium-methylene diphosphonate (99mTc-MDP) was assessed by single-photon emission computed tomog. Ex vivo micro computed tomog. was used to quantify bone volume and correlated with appropriate histopathol. Statistical significance was determined using the two-sided Mann-Whitney test or Wilcoxon signed rank test. Results VCaP xenografts were predominantly osteosclerotic with some osteolytic activity. Fluorescent in situ hybridization anal. confirmed retention of ERG oncogene rearrangements. Cabozantinib induced a statistically significant 52% reduction in tumor luminance (P = .02) and stasis in tumor volume after 15 days of treatment. Tumor ADC statistically significantly increased with cabozantinib and was associated with extensive necrosis (after 10 days, mean tumor ADC ± SD = 556±43×10-6 mm2/s vs pretreatment ADC = 485±43×10-6 mm2/s; P = .02). Tumor-associated uptake of 99mTc-MDP was statistically significantly reduced after 3 days of treatment (P = .02), sustained over 15 days treatment, and associated with a statistically significant (P = .048) reduction in bone growth on the tibial cortex, yet a highly statistically significant (P = .001) increase in trabecular bone volume Conclusions The intratibial VCaP model faithfully emulates clin. disease. Cabozantinib exerts potent effects on both tumor and tumor-induced bone matrix remodeling, and quantitation of ADC provides a clin. translatable imaging biomarker for early, sensitive assessment of treatment response in CRPC bone metastasis.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(noninvasive, multimodality functional imaging was effective in imaging biomarkers in response to cabozantinib in xenografted mouse model of human bone metastatic castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 242 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:628215 CAPLUS Full-text
DOCUMENT NUMBER: 160:542029
TITLE: Method for the diagnosis, prognosis and treatment of prostate cancer metastasis
INVENTOR(S): Gomis, Roger; Jean-Mairet, Joel
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 140pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014057357	A2	20140417	WO 2013-IB2866	20131009
WO 2014057357	A3	20140530		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2888122	A1	20140417	CA 2013-2888122	20131009
US 20140105918	A1	20140417	US 2013-14050262	20131009
AU 2013328385	A1	20150507	AU 2013-328385	20131009
EP 2906718	A2	20150819	EP 2013-821939	20131009
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015105297	A	20150916	KR 2015-7012297	20131009
CN 104995313	A	20151021	CN 2013-80060218	20131009
JP 2016500517	T	20160114	JP 2015-536237	20131009
MX 2015004610	A	20151022	MX 2015-4610	20150410
US 20150362495	A1	20151217	US 2015-14435128	20150410

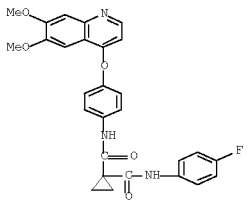
PRIORITY APPLN. INFO.: US 2012-61713318 P 20121012
WO 2013-IB2866 W 20131009

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to a method for the diagnosis or the prognosis of metastasis in prostate cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for the diagnosis or the prognosis of metastasis in prostate cancer, as well as to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which, comprise determining the c-MAF expression level. Finally, the invention relates to the use of a c-MAF inhibitor as therapeutic target for treating the prostate cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MAF gene for diagnosis, prognosis and treatment of prostate cancer metastasis)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 243 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:581585 CAPLUS Full-text
DOCUMENT NUMBER: 160:555604
TITLE: Phage display derived peptides highly specific against Mdm2/Mdm4 and methods for treating cancer
INVENTOR(S): Joseph, Thomas Leonard; Verma, Chandra Shekhar; Lane, David Phillip; Brown, Christopher John
PATENT ASSIGNEE(S): Agency for Science, Technology and Research, Singapore
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014055039	A1	20140410	WO 2013-SG428	20131001
WO 2014055039	A9	20141106		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2904000	A1	20150812	EP 2013-844064	20131001
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20150246946	A1	20150903	US 2015-14432729	20150331

PRIORITY APPLN. INFO.: SG 2012-7302 A 20121001
WO 2013-SG428 W 20131001

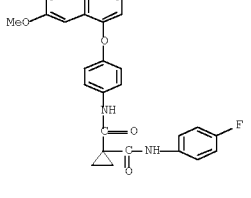
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 160:555604

AB By using a phage display derived peptide as an initial template, compds. have been developed that are highly specific against Mdm2/Mdm4. These compds. exhibit greater potency in p53 activation and protein-protein interaction assays than a compound derived from the p53 wild-type sequence. Unlike nutlin, a small mol. inhibitor of Mdm2/Mdm4, the phage derived compds. can arrest cells resistant to p53 induced apoptosis over a wide concentration range without cellular toxicity, suggesting they are highly suitable for cyclo-therapy. In one embodiment, there is disclosed the peptide comprising or consisting o f the amino acid sequence of SEQ ID NO 1 (TSFXaaiEYWXaa3LLXaai), wherein Xaa3 can be N or A and wherein in case Xaa3 is N, Xaai is not A and/or Xaa2 is not S. In one embodiment, Xaa3 can be any type of amino acid other than A and wherein in case Xaa3 is N, Xaaj is not A and/or Xaa2 is not S. Those peptides have been shown to inhibit the p53:Mdm2 interactions with a nanomolar affinity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL184; phage display derived peptides highly specific against Mdm2/Mdm4 and methods for treating cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 244 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:565947 CAPLUS Full-text
DOCUMENT NUMBER: 161:208503
TITLE: First-, second-, third-line therapy for mRCC: benchmarks for trial design from the IMDC
AUTHOR(S): Ko, J. J.; Choueiri, T. K.; Rini, B. I.; Lee, J.-L.; Kroeger, N.; Srinivas, S.; Harshman, L. C.; Knox, J. J.; Bjarnason, G. A.; MacKenzie, M. J.; Wood, L.; Vaishampayan, U. N.; Agarwal, N.; Pal, S. K.; Tan, M.-H.; Rha, S. Y.; Yuasa, T.; Donskov, F.; Bamias, A.; Heng, D. Y. C.
CORPORATE SOURCE: Tom Baker Cancer Center, University of Calgary, Calgary, AB, Can.
SOURCE: British Journal of Cancer (2014), 110(8), 1917-1922
CODEN: BJCAAI; ISSN: 0007-0920
DIGITAL OBJECT ID: 10.1038/bjc.2014.25
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

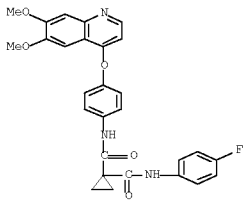
AB Background: Limited data exist on outcomes for metastatic renal cell carcinoma (mRCC) patients treated with multiple lines of therapy. Benchmarks for survival are required for patient counselling and clin. trial design. Methods: Outcomes of mRCC patients from the International mRCC Database Consortium database treated with 1, 2, or 3+ lines of targeted therapy (TT) were compared by proportional hazards regression. Overall survival (OS) and progression-free survival (PFS) were calculated using different population inclusion criteria. Results: In total, 2705 patients were treated with TT of which 57% received only first-line TT, 27% received two lines of TT, and 16% received 3+ lines of TT. Overall survival of patients who received 1, 2, or 3+ lines of TT were 14.9, 21.0, and 39.2 mo, resp., from first-line TT (P<0.0001). On multivariable anal., 2 lines and 3+ lines of therapy were each associated with better OS (HR=0.738 and 0.626, P<0.0001). Survival outcomes for the subgroups were as follows: for all patients, OS 20.9 mo and PFS 7.2 mo; for those similar to eligible patients in the first-line ADAPT trial, OS 14.7 mo and PFS 5.6 mo; for those similar to patients in first-line TIVO-1 trial, OS 24.8 mo and PFS 8.2 mo; for those similar to patients in second-line INTORSECT trial, OS 13.0 mo and PFS 3.9 mo; and for those similar

to patients in the third-line GOLD trial, OS 18.0 mo and PFS 4.4 mo. Conclusions: Patients who are able to receive more lines of TT live longer. Survival benchmarks provide context and perspective when interpreting and designing clin. trials.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(first-, second-, third-line therapy for metastatic renal cell carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 245 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:542996 CAPLUS Full-text

DOCUMENT NUMBER: 161:267984

TITLE: Bone-targeted therapies in metastatic castration-resistant prostate cancer: evolving paradigms

AUTHOR(S): El-Amm, Joelle; Freeman, Ashley; Patel, Nihar; Aragon-Ching, Jeanny B.

CORPORATE SOURCE: Division of Hematology/Oncology, Department of Medicine, George Washington University Medical Center, Washington, DC, 20037, USA

SOURCE: Prostate Cancer (2013) 210686/1-210686/11, 11 pp. CODEN: PCRACU; ISSN: 2090-312X

DIGITAL OBJECT ID: 10.1155/2013/210686

PUBLISHER: Hindawi Publishing Corp.

DOCUMENT TYPE: Journal; General Review; (online computer file)

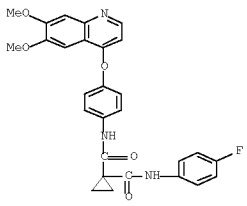
LANGUAGE: English

AB A review. Majority of patients with metastatic castrate resistant prostate cancer (mCRPC) develop bone metastases which results in significant morbidity and mortality as a result of skeletal-related events (SREs). Several bone-targeted agents are either in clin. use or in development for prevention of SREs. Bisphosphonates were the first class of drugs investigated for prevention of SREs and zoledronic acid is the only bisphosphonate that is FDA-approved for this indication. Another bone-targeted agent is denosumab which is a fully humanized monoclonal antibody that binds to the RANK-L thereby inhibiting RANK-L mediated bone resorption.While several radiopharmaceuticals were a approved for pain palliation in mCRPC including strontium and samarium, alpharadin is the first radiopharmaceutical to show significant overall survival benefit. Contemporary therapeutic options including enzalutamide and abiraterone have effects on pain palliation and SREs as well. Other novel bone-targeted agents are currently in development, including the receptor tyrosine kinase inhibitors cabozantinib and dasatinib. Emerging therapeutics in mCRPC has resulted in great strides in preventing one of the most significant sources of complications of bone metastases.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evolving paradigms of bone-targeted therapies in metastatic castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 246 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:479457 CAPLUS Full-text

DOCUMENT NUMBER: 160:515456

TITLE: Synthesis method of antitumor therapeutic drug of cabozantinib

INVENTOR(S): Cai, Jianping; Chen, Zengfei; Zhang, Lifeng; Fang, Ying

PATENT ASSIGNEE(S): Suzhou Moer Pharmaceutical Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 9pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

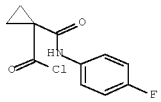
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103664778	A	20140326	CN 2013-10631287	20131127

PRIORITY APPLN. INFO.: CN 2013-10631287 20131127

OTHER SOURCE(S): CASREACT 160:515456; MARPAT 160:515456

GI

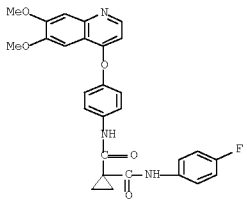


AB The invention discloses a synthesis method of antitumor therapeutic drug of cabozantinib., comprising: using 4-(6, 7- dimethoxy quinoline -4- oxy)-phenylamine to react with 1-((4- fluorophenyl) carbamoyl) cyclopropyl acyl halide, an acid-binding agent in organic solvent at -5~20 ℃ for 0.5~2h to obtain cabozantinib; the inventive method uses cheap raw materials, has mild conditions, simple and convenient operation, stable process, good repeatability, high molar yield, low cost, so invention is an applicable method for com. production of cabozantinib. Cabozantinib was prepared via chlorination of 6,7-dimethoxyquinolin-4-ol; the resulting 4-chloro-6,7-dimethoxyquinoline underwent condensation with 4-aminophenol or 4-nitrophenol to give the corresponding ethers, which underwent redn and/or acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropylcarbonyl halides to give cabozantinib. The said 1-[(4-fluorophenyl)carbamoyl]cyclopropylcarbonyl halides were prepared via condensation of 1,1-cyclopropanedicarboxylic acid with p-fluoroaniline followed by halogenation. The inventive method uses cheap raw materials, has mild conditions, simple and convenient operation, stable process, good repeatability, high molar yield, low cost, so invention is an applicable method for com. production of cabozantinib.

IT 849217-68-1P, Cabozantinib
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor drug cabozantinib starting from (dimethoxy)quinolinol and cyclopropanedicarboxylic acid by using etherification and amidation as the key steps)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 247 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:478399 CAPLUS Full-text

DOCUMENT NUMBER: 160:501685

TITLE: Process for the preparation of cabozantinib and its intermediate

INVENTOR(S): Shi, Xiangfei; Zhao, Rui; Meng, Qingyi; Zhang, Xiquan

PATENT ASSIGNEE(S): Chia Tai Tianqing Pharmaceutical Group Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 18pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

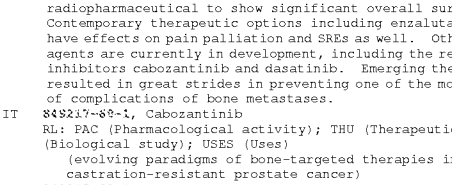
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103664776	A	20140326	CN 2012-10374723	20120926

PRIORITY APPLN. INFO.: CN 2012-10374723 20120926

OTHER SOURCE(S): MARPAT 160:501685

GI



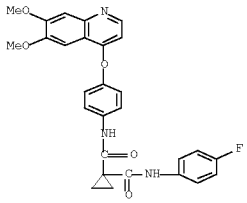
AB The invention relates to process for the prepn. of cabozantinib and its intermediate of formula I from 1,1-cyclopropane dicarboxylic acid diester of formula II [R1 = C1-10 alkyl]. For example, cabozantinib was prepared by hydrolysis of compound II [R1 = Et] to afford 1-(ethoxycarbonyl)cyclopropanecarboxylic acid, which underwent amidation

reaction with 4-aminophenol followed by arylation with 4-chloro-6,7-dimethoxyquinoline to afford compound I [R1 = Et], which underwent hydrolysis followed by amidation with 4-fluoroaniline to afford cabozantinib.

IT **849217-68-1**, Cabozantinib
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of cabozantinib and its intermediate)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 248 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:448281 CAPLUS Full-text

DOCUMENT NUMBER: 160:480988

TITLE: Inhibition of viral infection-triggered asthma with c-kit inhibitor

INVENTOR(S): Umetsu, Dale T.; Chang, Ya-Jen; De Kruyff, Rosemarie Helena; Baumgarth, Nicole

PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA

SOURCE: PCT Int. Appl., 128pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014043442	A1	20140320	WO 2013-US59609	20130913
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2895170	A1	20150722	EP 2013-836850	20130913
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20150297593	A1	20151022	US 2015-14428272	20150313
PRIORITY APPLN. INFO.:			US 2012-61701296 P	20120914
			WO 2013-US59609 W	20130913

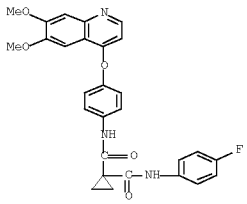
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods, compns., and kits featuring a c-Kit kinase inhibitor for use in preventing or treating virus-induced respiratory pathol.

IT **849217-68-1**, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-kit inhibitors for treatment of viral infection-triggered asthma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 249 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:443739 CAPLUS Full-text

DOCUMENT NUMBER: 160:485576

TITLE: Combination therapy for prevention or treatment of c-met or angiogenesis factor induced diseases

INVENTOR(S): Jeong, Yun Ju; Kim, Kyung Ah; Song, Yun Jeong; Lee, Ji Min; Lee, Hyo Seon; Choi, Jae Hyun; Lee, Saet Byoul

PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea

SOURCE: Eur. Pat. Appl., 168pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2708556	A1	20140319	EP 2013-184072	20130912
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2014035266	A	20140321	KR 2013-108913	20130911
US 20140086926	A1	20140327	US 2013-14025403	20130912
PRIORITY APPLN. INFO.:			KR 2012-101177 A	20120912
			KR 2013-108913 A	20130911

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The authors disclose combination therapy for prevention or treatment of c-Met-induced or angiogenesis factor-induced diseases. The therapy comprises the co-administration of an angiogenesis inhibitor and an anti-c-Met antibody. In one example, the metastatic potential (migration) of HUVEC cells is shown to be inhibited by the combined effects of an anti-c-Met antibody and an anti-VEGF antibody.

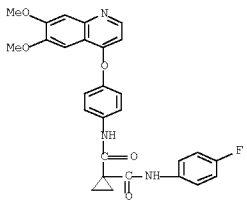
IT **1140909-48-3**, XL 184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination therapy with anti-MET receptor antibodies)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

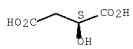
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 250 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:431636 CAPLUS Full-text

DOCUMENT NUMBER: 163:325757

TITLE: Effects of Cabozantinib on Pain and Narcotic Use in Patients with Castration-resistant Prostate Cancer: Results from a Phase 2 Nonrandomized Expansion Cohort

AUTHOR(S): Basch, Ethan; Autio, Karen A.; Smith, Matthew R.; Bennett, Antonia V.; Weitzman, Aaron L.; Scheffold, Christian; Sweeney, Christopher; Rathkopf, Dana E.; Smith, David C.; George, Daniel J.; Higano, Celestia S.; Harzstark, Andrea L.; Sartor, A. Oliver; Gordon, Michael S.; Vogelzang, Nicholas J.; de Bono, Johann S.; Haas, Naomi B.; Corn, Paul G.; Schimmoller, Frauke; Scher, Howard I.

CORPORATE SOURCE: Cancer Outcomes Research Program, Lineberger Cancer Center, University of North Carolina, Chapel Hill, NC, USA

SOURCE: European Urology (2015), 67(2), 310-318
CODEN: EUURAV; ISSN: 0302-2838

DIGITAL OBJECT ID: 10.1016/j.eururo.2014.02.013

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)

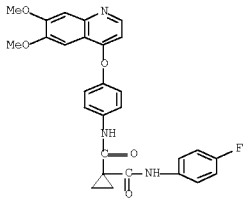
LANGUAGE: English

AB Pain neg. affects quality of life for cancer patients. Preliminary data in metastatic castration-resistant prostate cancer (mCRPC) suggested a benefit of the oral tyrosine kinase inhibitor cabozantinib to pain palliation. Prospective evaluation of cabozantinib's benefits on pain and narcotic use in mCRPC.This was a nonrandomized expansion (NRE) cohort (n = 144) of a phase 2 randomized discontinuation trial in docetaxel-refractory mCRPC patients. Pain and interference of symptoms with sleep and general activity were electronically self-reported daily for 7-d intervals at baseline and regularly scheduled throughout the study. Mean per-patient scores were calculated for each interval. Narcotic use was recorded daily during the same intervals.Open-label cabozantinib (100 mg or 40 mg). The following stringent response definition was used: clin. meaningful pain reduction (≥30% improvement in mean scores from baseline) confirmed at a later interval without concomitant increases in narcotics. Only patients with moderate or severe baseline pain were analyzed.Sixty-five patients with moderate or severe baseline pain were evaluable. Of these, 27 (42%) experienced pain palliation according to the stringent response definition. Thirty-seven patients (57%) had clin. meaningful pain relief at two consecutive intervals, reported ≥6 wk apart in the majority. Forty-four patients (68%) had palliation at one or more intervals; 36 (55%) decreased narcotics use during one or more intervals. Clin. meaningful pain reduction was associated with significant ($p \leq 0.001$) improvements in sleep quality and general activity. A limitation of this study was its open-label design. Cabozantinib demonstrated clin. meaningful pain palliation, reduced or eliminated patients' narcotic use,

and improved patient functioning, thus meriting prospective validation in phase 3 studies.We evaluated the potential of cabozantinib to improve symptoms in patients with metastatic prostate cancer that no longer responds to standard therapies. We saw a promising reduction in pain and reduced need for narcotic painkillers. Larger, well-controlled trials are necessary to confirm these findings.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase 2 nonrandomized expansion cohort study on effects of cabozantinib on pain and narcotic use in patients with castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 251 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:410366 CAPLUS Full-text
DOCUMENT NUMBER: 160:451706
TITLE: Inhibitors of Met, VEGFR and Ret for use in the treatment of lung adenocarcinoma
INVENTOR(S): Aftab, Dana T.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014039971	A1	20140313	WO 2013-US58768	20130909

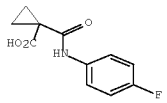
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140121239	A1	20140501	US 2013-14021614	20130909
CN 104703600	A	20150610	CN 2013-80052164	20130909
EP 2892532	A1	20150715	EP 2013-765886	20130909

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2015530389	T	20151015	JP 2015-531283	20130909
US 20150238477	A1	20150827	US 2015-14426580	20150306

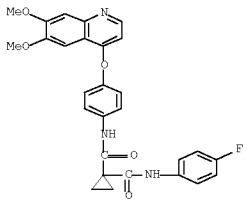
PRIORITY APPLN. INFO.: US 2012-61698143 P 20120907
WO 2013-US58768 W 20130909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:451706; MARPAT 160:451706
GI



AB This invention is directed to the treatment of cancer in a patient, particularly a patient with lung adenocarcinoma, and more particularly a patient with KIF5B-RET fusion-pos. non-small cell lung cancer, with an inhibitor of MET, VEGF, and RET.

IT 849217-68-1
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

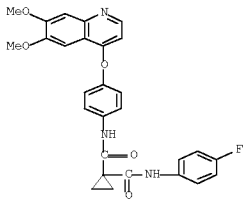


IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

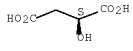
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

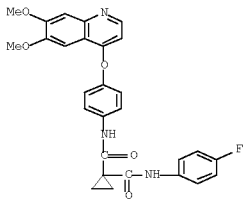


IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)

RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

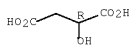
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD

(3 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 252 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:327215 CAPLUS Full-text
DOCUMENT NUMBER: 160:370140
TITLE: Preparation of substituted azaindole prodrugs, salts, pharmaceutical compositions thereof and methods of use in treating cancer and other proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Tingjin; Tang, Yin; Sun, Mingming; Wang, Qian
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 53pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140056849	A1	20140227	US 2013-13975371	20130826
CA 2882157	A1	20140306	CA 2013-2882157	20130826
WO 2014035846	A2	20140306	WO 2013-US56548	20130826
WO 2014035846	A3	20150625		

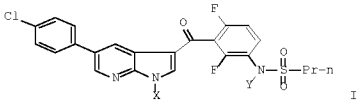
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

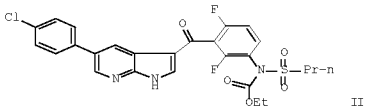
AU 2013309143	A1	20150212	AU 2013-309143	20130826
EP 2888260	A2	20150701	EP 2013-832403	20130826

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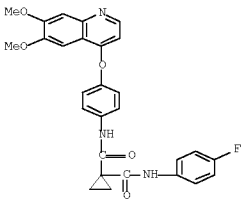
PRIORITY APPLN. INFO.:	US 2012-61693335	P	20120827
	WO 2013-US56548	W	20130826

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:370140; MARPAT 160:370140
GI

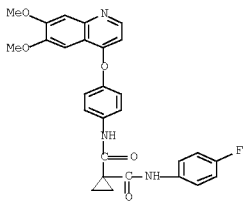

I


II

AB The present invention provides substituted azaindole prodrugs of vemurafenib, methods of making said prodrugs, pharmaceutical compns. of said prodrugs and methods of using said prodrugs and pharmaceutical compns. thereof to treat or prevent diseases or disorders such as cancer. The prodrugs have general formula I, wherein each of X and Y is independently H, -C(:O)R3, -C(:O)OR4, -C(R1R2)OC(:O)R3, -C(R1R2)OC(:O)OR4 or -C(R1R2)OP(:O)(OR4)(OR4a), with the proviso that when Y is H, X is not -C(:O)CH3 or H; each R1 and R2 is independently H, D, C1-6alkyl, etc.; each R3 is independently H, D, C1-10alkyl, etc.; and each R4 and R4a is independently H, C1-10alkyl, C3-8cycloalkyl, etc. Example compound II was prepared by reacting vemurafenib with Et chloroformate. Various prodrugs of the invention were studied for their stability in liver microsomes, their oral and i.v. bioavailability, and their antitumor properties.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted azaindole prodrugs., salts, pharmaceutical compns. thereof and methods of use in treating cancer and other proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



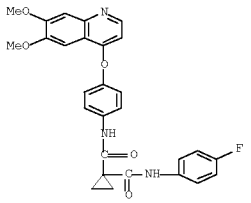
L8 ANSWER 253 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:211024 CAPLUS Full-text
DOCUMENT NUMBER: 161:316285
TITLE: Cabozantinib Inhibits Prostate Cancer Growth and Prevents Tumor-Induced Bone Lesions
AUTHOR(S): Dai, Jinlu; Zhang, Honglai; Karatsinides, Andreas; Keller, Jill M.; Kozloff, Kenneth M.; Aftab, Dana T.; Schimmoller, Frauke; Keller, Evan T.
CORPORATE SOURCE: Departments of Urology and Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA
SOURCE: Clinical Cancer Research (2014), 20(3), 617-630
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-0839
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Cabozantinib, an orally available multityrosine kinase inhibitor with activity against mesenchymal epithelial transition factor (MET) and VEGF receptor 2 (VEGFR2), induces resolution of bone scan lesions in men with castration-resistant prostate cancer bone metastases. The purpose of this study was to determine whether cabozantinib elicited a direct antitumor effect, an indirect effect through modulating bone, or both. Exptl. Design: Using human prostate cancer xenograft studies in mice, we determined the impact of cabozantinib on tumor growth in soft tissue and bone. In vitro studies with cabozantinib were performed using (i) prostate cancer cell lines to evaluate its impact on cell growth, invasive ability, and MET and (ii) osteoblast cell lines to evaluate its impact on viability and differentiation and VEGFR2. Results: Cabozantinib inhibited progression of multiple prostate cancer cell lines (Ace-1, C4-2B, and LuCaP 35) in bone metastatic and soft tissue murine models of prostate cancer, except for PC-3 prostate cancer cells in which it inhibited only s.c. growth. Cabozantinib directly inhibited prostate cancer cell viability and induced apoptosis in vitro and in vivo and inhibited cell invasion in vitro. Cabozantinib had a dose-dependent biphasic effect on osteoblast activity and inhibitory effect on osteoclast production in vitro that was reflected in vivo. It blocked MET and VEGFR2 phosphorylation in prostate cancer cells and osteoblast-like cells, resp. Conclusion: These data indicate that cabozantinib has direct antitumor activity, and that its ability to modulate osteoblast activity may contribute to its antitumor efficacy. Clin Cancer Res; 20(3); 617-30. ©2013 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib inhibits prostate cancer growth and prevents tumor-induced bone lesions)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 254 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:211001 CAPLUS Full-text
DOCUMENT NUMBER: 161:316087
TITLE: Cabozantinib and Prostate Cancer: Inhibiting Seed and Disrupting Soil?
AUTHOR(S): Lee, Richard J.; Smith, Matthew R.
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA
SOURCE: Clinical Cancer Research (2014), 20(3), 525-527
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-2636
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Treatment with cabozantinib, an inhibitor of MET and VEGFR2 signaling, has demonstrated clin. benefit in early trials in men with metastatic prostate cancer. Preclin. evidence suggests that cabozantinib can kill cancer cell seeds while disrupting angiogenesis and stromal cells in the metastatic soil.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cabozantinib in treatment of prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

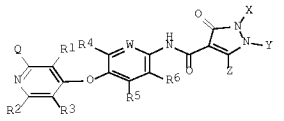


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

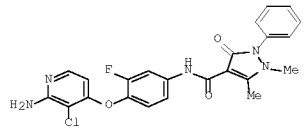
L8 ANSWER 255 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:175942 CAPLUS Full-text
DOCUMENT NUMBER: 160:310859
TITLE: Preparation of substituted pyrazolone compounds as protein tyrosine kinase modulators useful in treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022117	A1	20140206	WO 2013-US51175	20130719
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150050239	A1	20150219	US 2013-13945925	20130719
US 8969388	B2	20150303		
EP 2879676	A1	20150610	EP 2013-825325	20130719
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015523390	T	20150813	JP 2015-524334	20130719

PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
WO 2013-US51175 W 20130719
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:310859; MARPAT 160:310859
GI



I

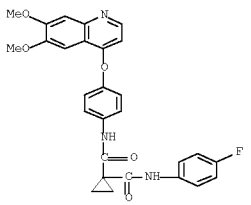


II

AB The invention provides substituted pyrazolone compds.of formula I, stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, and pharmaceutical preparation for regulating the activity of protein kinases and adjusting the signal response in the cell or between cells. The invention also relates to pharmaceutical compns. comprising the compds. and a method for treating hyperproliferative disorder of mammal, particularly human using the compns. Compds. of formula I [wherein Q is H, NH2 and derivative, OH and derivs., -NHCOR, etc.; W is (un)substituted CH or N; X, Y, and Z are independently H, D, C1-6 alkyl, C3-8 cycloalkyl-C1-4 alkylene, etc.; R1-R6 are independently H, D, F, Cl, Br, CN, etc.; R is H, C1-6 alkyl, C3-8 cycloalkyl-C1-4 alkylene, C3-7 heterocycloalkyl, etc.] and their stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, are claimed and exemplified. For example, II was prepared in a multistep process (procedure given). I were evaluated for stability in liver microsomes and pharmacokinetic properties in mice, rats, dogs, and monkeys (data given). Binding of I to receptor tyrosine kinases was determined using KINOMEscan where II exhibited binding constant (Kd) values of 23 nM for KDR tyrosine kinase and 4.4 nM for c-Met tyrosine kinase.

IT 849217-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolone compds. useful as protein tyrosine kinase modulators for treatment of proliferative disorders)

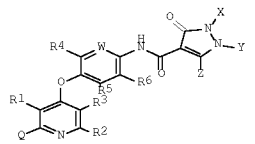
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



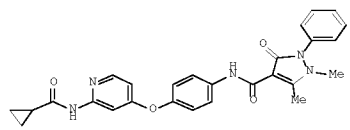
L8 ANSWER 256 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:175941 CAPLUS Full-text
DOCUMENT NUMBER: 160:310858
TITLE: Preparation of substituted pyrazolone compounds as protein tyrosine kinase modulators for treatment of proliferative disease
INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 110pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022116	A2	20140206	WO 2013-US51174	20130719
WO 2014022116	A3	20150716		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2876246	A1	20140206	CA 2013-2876246	20130719
AU 2013296897	A1	20141218	AU 2013-296897	20130719
AU 2013296897	B2	20150917		
US 20150050239	A1	20150219	US 2013-13945925	20130719
US 8969388	B2	20150303		
EP 2879677	A2	20150610	EP 2013-826459	20130719
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015530975	T	20151029	JP 2015-524333	20130719

PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
WO 2013-US51174 W 20130719
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:310858; MARPAT 160:310858
GI



I



II

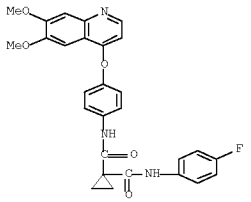
AB The invention provides substituted pyrazolone compds.of formula I, stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, and pharmaceutical preparation for regulating the activity of protein kinases and adjusting the signal response in the cell or between cells. The invention also relates to pharmaceutical compns. comprising the

compds. and a method for treating hyperproliferative disorder of mammal, particularly human using the comps. Compds. of formula I [wherein Q is D, NH2 and derivs., -NHCOR, etc.; W is (un)substituted CH or N; each X, Y, and Z is independently H, D, C1-6 alkyl, C3-8 cycloalkyl, etc.; each R1-R6 is independently H, D, F, Cl, Br, CN, etc.; R is D, C3-8 cycloalkyl, -C1-4 alkylene -C6-10 aryl, etc.] and their stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, are claimed and exemplified. For example, II was prepared in a multistep process (procedure given). Candidate compds. of I were evaluated for stability in liver microsomes and pharmacokinetic properties in mice, rats, dogs, and monkeys (data given). Binding of I to receptor tyrosine kinases was determined using KINOMEscan where II exhibited binding constant (Kd) values of 2.9 nM for KDR tyrosine kinase and 0.21 nM for c-Met tyrosine kinase.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolone compds. useful as protein tyrosine kinase modulators for treatment of proliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 257 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:173876 CAPLUS Full-text

DOCUMENT NUMBER: 160:294980

TITLE: Preparation of N-[3-(quinolin-6-yl)pyridin-5-yl] benzenesulfonamides as PI3 kinase modulators

INVENTOR(S): Xi, Ning; Li, Zhuo; Wang, Tingjin; Wu, Zuping; Wen, Qiuling

PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.

SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022128	A1	20140206	WO 2013-US51405	20130719

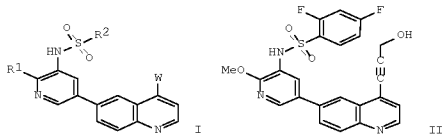
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61676966 P 20120729

OTHER SOURCE(S): CASREACT 160:294980; MARPAT 160:294980

GI



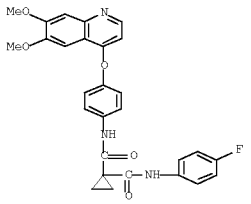
I II

AB This invention relates to the field of lipid kinases and modulators thereof. In particular, the invention relates to compds. I [W = D, CN, N3, (un)substituted C5-12 spirobicyclyl or C≡CX; X = H, D, alkyl, cycloalkyl, etc.; R1 = H, D, Cl, alkyl, etc.; R2 = alkyl, cycloalkyl, aryl, etc.] as modulators of phosphatidylinositol 3-kinases (PI3 kinases or PBKs) signaling pathways, and methods of their use. Twenty-nine compds. I were prepared and disclosed. E.g., a multi-step synthesis of II, starting from 5-bromo-2-chloro-3-nitropyridine, was described. Exemplified compds. I exhibited potent activities in the PI3Kα(h) and mTOR(h) assays (data given for representative compds. I). The invention also provides pharmaceutically acceptable compns. comprising compds. I and methods of using the compns. in modulating of PI3K signaling pathways and their related disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-[3-(quinolin-6-yl)pyridin-5-yl] benzenesulfonamides as PI3
kinase modulators)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L8 ANSWER 258 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2014:151402 CAPLUS Full-text

DOCUMENT NUMBER: 160:242457

TITLE: In-frame fusion of genes CEP55 and RET associated with diffuse-type gastric cancer and their use in drug discovery and cancer therapy

INVENTOR(S): Shibata, Tatsuhiro; Hosoda, Fumie

PATENT ASSIGNEE(S): National Cancer Center, Japan

SOURCE: PCT Int. Appl., 53pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014017491	A1	20140130	WO 2013-JP69929	20130723

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CN 104619841	A	20150513	CN 2013-80039589	20130723
EP 2878672	A1	20150603	EP 2013-822713	20130723

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US 20150177246	A1	20150625	US 2015-14417052	20150123

PRIORITY APPLN. INFO.: JP 2012-165694 A 20120726
WO 2013-JP69929 W 20130723

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Through transcriptome an in-frame fusion of 2 genes (CEP55 and RET) of human chromosome 10 was found in patients with diffuse-type gastric cancer. The fused genes can be used for evaluation of the effectiveness of an antitumor agent such as RET tyrosine kinase inhibitors. Antibody to CEP55 or RET protein is also claimed.

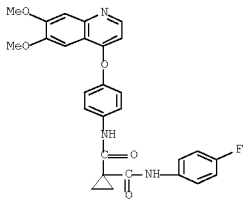
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RET tyrosine kinase inhibitors; in-frame fusion of genes CEP55 and RET associated with diffuse-type gastric cancer and their use in drug discovery and cancer therapy)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

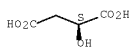
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

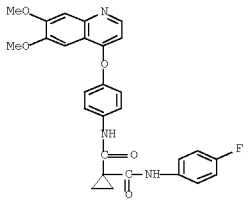


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 259 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:146206 CAPLUS full-text
DOCUMENT NUMBER: 160:225648
TITLE: Efflux inhibitor compositions and methods of treatment using the same
INVENTOR(S): Bunt, Antonius Martinus Gustave; Van Tellingen, Olaf
PATENT ASSIGNEE(S): Neth.
SOURCE: PCT Int. Appl., 74pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

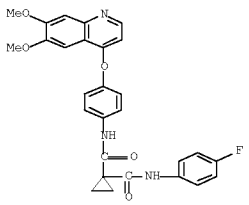
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014018932	A2	20140130	WO 2013-US52402	20130726
WO 2014018932	A3	20140320		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2880236	A1	20140130	CA 2013-2880236	20130726
AU 2013295549	A1	20150319	AU 2013-295549	20130726
EP 2877159	A2	20150603	EP 2013-745549	20130726
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104736144	A	20150624	CN 2013-80050643	20130726
JP 2015523400	T	20150813	JP 2015-524485	20130726
MX 2015001194	A	20151123	MX 2015-1194	20150126
IN 2015MN00408	A	20150904	IN 2015-MN408	20150225
PRIORITY APPLN. INFO.:			US 2012-61676689 P	20120727
			WO 2013-US52402 W	20130726

AB The present invention relates to efflux inhibitor compns. and methods of using these agents for treating conditions where the activity of efflux transporter proteins (e.g., Breast Cancer Resistance Protein (BCRP) and P-Glycoprotein (P-GP)) inhibit effective delivery of a therapeutic agent to a target tissue (e.g., brain, spinal cord, nerves, cerebrospinal fluid, testis, eyeballs, retina, inner ear, placenta, mammary gland, liver, biliary tract, kidney, intestines, lung, adrenal cortex, endometrium, hematopoietic cells, and/or stem cells).
IT 849217-68-1, Cabozantinib
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efflux inhibitor compns. and methods of treatment using same)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



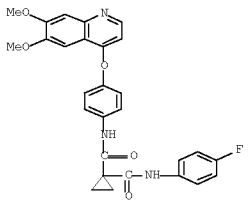
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 260 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:127915 CAPLUS full-text
DOCUMENT NUMBER: 160:362955
TITLE: Novel tyrosine kinase inhibitors for renal cell carcinoma
AUTHOR(S): Dorff, Tanya B.; Pal, Sumanta K.; Quinn, David I.
CORPORATE SOURCE: Department of Medicine, USC Norris Comprehensive Cancer Center, USC Keck School of Medicine, Los Angeles, CA, 90033, USA
SOURCE: Expert Review of Clinical Pharmacology (2014), 7(1), 67-73
CODEN: ERCPAG; ISSN: 1751-2433
DIGITAL OBJECT ID: 10.1586/17512433.2014.862496
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Although targeted therapy against VEGF and mTOR have revolutionized the treatment of advanced renal cell carcinoma (RCC), addnl. agents are required due to toxicity and resistance to currently available drugs. Some next-generation tyrosine kinase inhibitors have focused on VEGF, narrowing the spectrum of receptors which are inhibited and enhancing binding affinity. However, targeting novel receptors with tyrosine kinase inhibition of addnl. receptor targets has also emerged as an important future therapeutic strategy for RCC, both clear cell and variant histol. New pathways being targeted include FGF, angiopoietin and MET. In this review, we highlight five novel tyrosine kinase inhibitors in development for RCC: tivozanib; dovitinib; regorafenib; cabozantinib; and tivantinib.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel tyrosine kinase inhibitors for renal cell carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

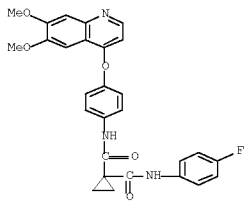
L8 ANSWER 261 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2014:93138 CAPLUS full-text
DOCUMENT NUMBER: 160:289739
TITLE: c-MET kinase inhibitors: a patent review (2011 - 2013)
AUTHOR(S): Zhu, Kongkai; Kong, Xiangqian; Zhao, Dan; Liang, Zhongjie; Luo, Cheng
CORPORATE SOURCE: Center for Systems Biology, Soochow University, Jiangsu, 215006, Peop. Rep. China
SOURCE: Expert Opinion on Therapeutic Patents (2014), 24(2), 217-230
CODEN: EOTPEG; ISSN: 1354-3776
DIGITAL OBJECT ID: 10.1517/13543776.2014.864279
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Introduction: The receptor tyrosine kinase c-MET displays aberrant activation in the malignant phenotype of various tumors, and thus, has drawn considerable attention as drug target for cancer therapy. Many c-MET inhibitors are now under clin. investment, and one of them - Cabozantinib - has been approved by US FDA in 2012 for the treatment of medullary thyroid cancer, which further proved the feasibility of c-MET inhibition method in cancer therapy. Areas covered: This article briefly outlines the role of c-MET in oncogenesis and provides a broad overview of the assays used to characterize new inhibitors. Then, a series of representative small-mol. inhibitors of c-MET, especially from the published patent literature from 2011 to 2013, are recorded. Herein, the challenges in the kinase inhibitor design, such as the inhibitor selectivity and resistance mutations, are also discussed. Expert opinion: Up to now, at least 17 inhibitors of c-MET are under clin. evaluation, and several agents exhibit encouraging results. Thus, inhibiting c-MET signaling has major therapeutic value in cancer therapy. Focus on the selectivity of both types of inhibitors, with potent selectivity or multi-targets, have demonstrated antitumor efficacy. The network pharmacol. and clin. trials integrated would provide powerful tools to further evaluate the superiority of both inhibitors in continued efficacy and toxicity.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(application of c-MET kinase inhibitors for the treatment of medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



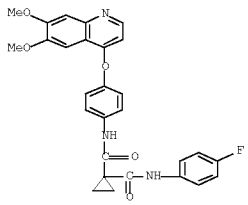
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 262 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:2007812 CAPLUS full-text
DOCUMENT NUMBER: 160:380536
TITLE: Newly approved antitumor drugs by FDA in 2012
AUTHOR(S): Yang, Minglun
CORPORATE SOURCE: Department of Pharmacy, Linqu County People's Hospital, Linqu, Shandong Province, 262600, Peop. Rep. China
SOURCE: Yaoxue Fuwu Yu Yanjiu (2013), 13(4), 304-306
CODEN: YFYYAH; ISSN: 1671-2838
DIGITAL OBJECT ID: 10.5428/pcar20130420
PUBLISHER: Yaoxue Fuwu Yu Yanjiu Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Newly approved antitumor drugs by FDA in 2012 were introduced.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(newly approved antitumor drugs by FDA in 2012)
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

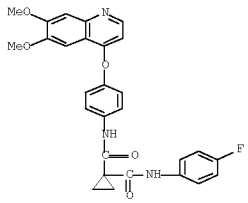


L8 ANSWER 263 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:2006727 CAPLUS Full-text
DOCUMENT NUMBER: 160:380516
TITLE: Pharmacological and clinical studies of cabozantinib
AUTHOR(S): Zheng, Xi-yuan; Jiang, Han-jie; Pu, Xiao-ping
CORPORATE SOURCE: Department of Molecular and Cellular Pharmacology, School of Pharmaceutical Sciences, Peking University, Beijing, 100191, Peop. Rep. China
SOURCE: Zhongguo Xinyao Zazhi (2013), 22(17), 1990-1993
CODEN: ZXZHA6; ISSN: 1003-3734
PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Cabozantinib, a new drug for medullary thyroid cancer treatment, is a potent inhibitor of MET, RET, and vascular endothelial factor receptor 2 (VEGFR2) as well as other tyrosine kinases that have been implicated in tumor development and progression. The mechanism, pharmacokinetics, drug interaction, clin. evaluation, and safety of cabozantinib were reviewed.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. and clin. studies of cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

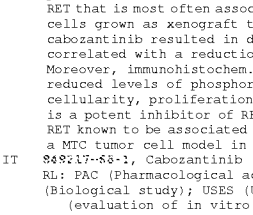


OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

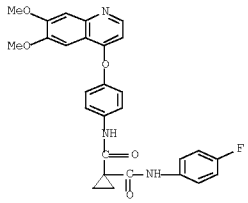
L8 ANSWER 265 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1898455 CAPLUS Full-text
DOCUMENT NUMBER: 160:555100
TITLE: In Vitro and In Vivo Activity of Cabozantinib (XL184), an Inhibitor of RET, MET, and VEGFR2, in a Model of Medullary Thyroid Cancer
AUTHOR(S): Bentzien, Frauke; Zuzow, Marcus; Heald, Nathan; Gibson, Anna; Shi, Yongchang; Goon, Leanne; Yu, Peiwen; Engst, Stefan; Zhang, Wentao; Huang, Donghui; Zhao, Lora; Vysotskaia, Valentina; Chu, Felix; Bautista, Rajana; Cancilla, Belinda; Lamb, Peter; Joly, Alison H.; Yakes, F. Michael
CORPORATE SOURCE: ., Exelixis, Inc., South San Francisco, CA, USA
SOURCE: Thyroid (2013), 23(12), 1569-1577
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2013.0137
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: A limited no. of approved therapeutic options are available to metastatic medullary thyroid cancer (MTC) patients, and the response to conventional chemotherapy and/or radiotherapy strategies is inadequate. Sporadic and inherited mutations in the tyrosine kinase RET result in oncogenic activation that is associated with the pathogenesis of MTC.



L8 ANSWER 264 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1965166 CAPLUS Full-text
DOCUMENT NUMBER: 160:155703
TITLE: Metastatic castration-resistant prostate cancer reveals intrapatient similarity and interpatient heterogeneity of therapeutic kinase targets
AUTHOR(S): Drake, Justin M.; Graham, Nicholas A.; Lee, John K.; Stoyanova, Tanya; Faltermeier, Claire M.; Sud, Sudha; Titz, Bjorn; Huang, Jiaoti; Pienta, Kenneth J.; Graeber, Thomas G.; Witte, Owen N.
CORPORATE SOURCE: Department of Microbiology, Immunology, and Molecular Genetics, David Geffen School of Medicine, University of California, Los Angeles, CA, 90095, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2013), 110(49), E4762-E4769,SE4762/1-SE4762/23
CODEN: PNASA6; ISSN: 0027-8424
DIGITAL OBJECT ID: 10.1073/pnas.1319948110
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In prostate cancer, multiple metastases from the same patient share similar copy number, mutational status, erythroblast transformation specific (ETS) rearrangements, and methylation patterns supporting their clonal origins. Whether actionable targets such as tyrosine kinases are also similarly expressed and activated in anatomically distinct metastatic lesions of the same patient is not known. We evaluated active kinases using phosphotyrosine peptide enrichment and quant. mass spectrometry to identify druggable targets in metastatic castration-resistant prostate cancer obtained at rapid autopsy. We identified distinct phosphopeptide patterns in metastatic tissues compared with treatment-naive primary prostate tissue and prostate cancer cell line-derived xenografts. Evaluation of metastatic castration-resistant prostate cancer samples for tyrosine phosphorylation and upstream kinase targets revealed SRC, epidermal growth factor receptor (EGFR), rearranged during transfection (RET), anaplastic lymphoma kinase (ALK), and MAPK1/3 and other activities while exhibiting intrapatient similarity and interpatient heterogeneity. Phosphoproteomic analyses and identification of kinase activation states in metastatic castration-resistant prostate cancer patients have allowed for the prioritization of kinases for further clin. evaluation.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphokinase profiling for drug targets of metastatic castration-resistant prostate cancer reveals intrapatient similarity and interpatient heterogeneity)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 266 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1873443 CAPLUS Full-text
DOCUMENT NUMBER: 160:155702
TITLE: Cabozantinib Inhibits Tumorigenicity and Metastasis in a Preclinical Model of Medullary Thyroid Cancer
AUTHOR(S): Yakes, F. Michael; Chen, Jinhua; Tan, Jian; Yamaguchi, Kenji; Shi, Yongchang; Yu, Peiwen; Qian, Fengrong; Chu, Felix; Bentzien, Frauke; Cancilla, Belinda; Orf, Jennifer; You, Angela; Laird, Alan D.; Engst, Stefan; Lee, Lawrence; Lombardo, John; Wong, Lyra; Elujoba, Adeyinka A.; Luo, Yan; Lee, Jeffrey; Xia, Jing; Svensson, Carl; Bender, Steven; Vojkovich, Dan; Wilhelm, Scott; Kharbanda, Surendra; Merajver, Sofia D.
CORPORATE SOURCE: ., Exelixis, Inc., South San Francisco, CA, USA
SOURCE: Molecular Cancer Therapeutics (2011), 10(12), 2298-2308
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-11-0264
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is a potent inhibitor of MET, RET, and vascular endothelial factor receptor 2 (VEGFR2), as well as other tyrosine kinases that have been implicated in tumor development and progression. The object of this study was to determine the in vitro biochem. and cellular inhibitory profile of cabozantinib against RET, and in vivo antitumor efficacy using a xenograft model of MTC.Methods: Cabozantinib was evaluated in biochem. and cell-based assays that determined the potency of the compound against wild type and activating mutant forms of RET. Addnl., the pharmacodynamic modulation of RET and MET and in vivo antitumor activity of cabozantinib was examined in a MTC tumor model following subchronic oral administration.Results: In biochem. assays, cabozantinib inhibited multiple forms of oncogenic RET kinase activity, including M918T and Y791F mutants. Addnl., it inhibited proliferation of TT tumor cells that harbor a C634W activating mutation of RET that is most often associated with MEN2A and familial MTC. In these same cells grown as xenograft tumors in nude mice, oral administration of cabozantinib resulted in dose-dependent tumor growth inhibition that correlated with a reduction in circulating plasma calcitonin levels. Moreover, immunohistochem. analyses of tumors revealed that cabozantinib reduced levels of phosphorylated MET and RET, and decreased tumor cellularity, proliferation, and vascularization.Conclusions: Cabozantinib is a potent inhibitor of RET and prevalent mutationally activated forms of RET known to be associated with MTC, and effectively inhibits the growth of a MTC tumor cell model in vitro and in vivo.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of in vitro and in vivo antitumor efficacy of cabozantinib in preclin. model of medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



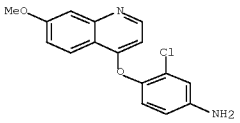
OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 160:50465
TITLE: Substituted quinoline compounds and use as Antitumor agents
INVENTOR(S): Xi, Ning; Wang, Tingjin; Zeng, Shan; Sun, Mingming; Wang, Kunrui
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013180949	A1	20131205	WO 2013-US41036	20130515

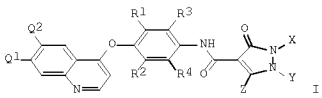
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61652210 P 20120527
OTHER SOURCE(S): CASREACT 160:50465; MARPAT 160:50465
GI

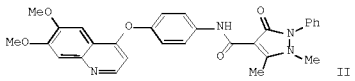


AB The present invention provides novel substituted quinoline compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted quinoline compds. and methods of use)



I

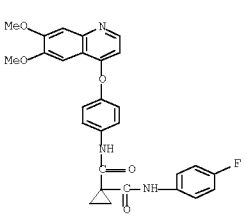


II

AB The invention relates to substituted quinoline compds. of formula I as protein kinase regulator useful in treatment of proliferative diseases and their preparation Compound I, wherein R1, R2, R3, and R4 are independently H, D, F, Cl, or Br; Q1 and Q2 are independently H, D, C1-6 alkyl, etc.; X and Z are independently H, D, C1-6 alkyl, etc.; Y is H, D, C2-6 alkynyl, etc.; their stereoisomers, N-oxides, solvates, pharmaceutically acceptable salts, are claimed. Compound II was prepared by multi-step procedure (procedure given). The present invention also relates to the pharmaceutical compns. containing the inventive compds., and method of application of the pharmaceutical composition for treatment of a mammal, especially hyperproliferative disease.

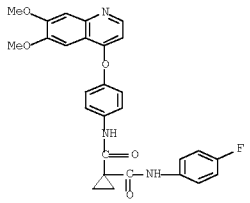
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted quinoline compound useful in treatment of hyperproliferative diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 268 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 267 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1866363 CAPLUS Full-text
DOCUMENT NUMBER: 160:33885
TITLE: Substituted quinoline compound useful in treatment of hyperproliferative diseases and its preparation
INVENTOR(S): Xi, Ning; Wang, Tingjin; Zeng, Shan; Sun, Mingming; Wang, Kunrui
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 57pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103420986	A	20131204	CN 2013-10179608	20130515
PRIORITY APPLN. INFO.:			CN 2012-10154478 A	20120518
			CN 2013-10118880 A	20130403

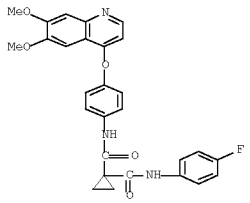
OTHER SOURCE(S): CASREACT 160:33885; MARPAT 160:33885
GI

ACCESSION NUMBER: 2013:1864045 CAPLUS Full-text
DOCUMENT NUMBER: 161:30833
TITLE: An update on clinical trials of targeted therapies in thyroid cancer
AUTHOR(S): Haraldsdottir, Sigurdis; Shah, Manisha H.
CORPORATE SOURCE: The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA
SOURCE: Current Opinion in Oncology (2014), 26(1), 36-44
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0000000000000029
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB Purpose of review: Several new targeted therapies with multikinase inhibitors targeting vascular endothelial growth factor (VEGF), rearranged during transfection and v-raf murine sarcoma viral oncogene homolog B1 pathways have been tested in clin. trials for radioiodine-refractory differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC) in the past 10 years. Recent findings: Results of the first phase III trial of VEGF-targeted therapy (sorafenib) in DTC were presented in June 2013, and two phase III trials with VEGF and rearranged during transfection-targeted therapies (vandetanib and cabozantinib) in MTC have led to approval by US Food and Drug Administration in the past 2 years. Whereas such therapies increase median progression-free survival compared to placebo, there is no therapy proven to improve overall survival yet. Significant potential adverse event risks associated with such therapies need to be recognized. Dissemination of knowledge about targeted therapies is critical for various medical specialists as patient care for thyroid cancers is best delivered in a multidisciplinary setting. Summary: Successful development of targeted systemic therapies in DTC and MTC in the past 5 years is incredibly exciting in the field and patients with advanced DTC/MTC now have new standard-of-care therapy options.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(update on clin. trials of targeted therapies in thyroid cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



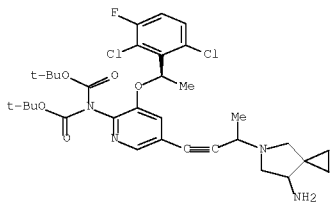
OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 269 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1837363 CAPLUS Full-text
DOCUMENT NUMBER: 160:28188
TITLE: Substituted alkynyl pyridine compounds and methods of use
INVENTOR(S): Xi, Ning; Yin, Lihua; Li, Xiaobo; Yu, Na; Wu, Yanjun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

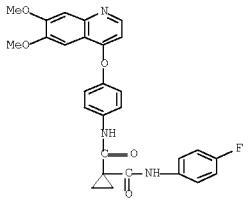
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013177092	A1	20131128	WO 2013-US41918	20130521

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61650513 P 20120523
OTHER SOURCE(S): CASREACT 160:28188; MARPAT 160:28188
GI



AB The present invention provides novel substituted alkynyl pyridine compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted alkynyl pyridine compds. and methods of use)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

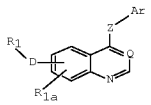


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 270 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1836624 CAPLUS Full-text
DOCUMENT NUMBER: 160:28252
TITLE: Compounds and methods of use thereof for treating neurodegenerative disorders
INVENTOR(S): Zack, Donald J.; Welsbie, Derek Stuart; Yang, Zhiyong
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

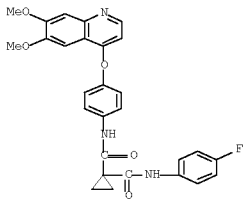
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013177367	A2	20131128	WO 2013-US42367	20130523

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
EP 2852388 A2 20150401 EP 2013-793466 20130523
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
US 20150164906 A1 20150618 US 2014-14403523 20141124
PRIORITY APPLN. INFO.: US 2012-61650613 P 20120523
US 2012-61680931 P 20120808
WO 2013-US42367 W 20130523
GI

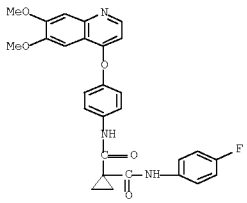


I

AB In some embodiments, the presently disclosed subject matter provides a method for treating or preventing a neurodegenerative disease, disorder, or condition in a subject in need thereof, the method comprising administering to the subject a 15 therapeutically effective amount of a compound of Formula I (wherein D is selected from the group consisting of O, S(O)0-2, and NR1b; R1a is selected from the group consisting of H, substituted or unsubstituted alkyl, halogen, OR1b, NO2, NR1bR1c; wherein: R1b and R1c are each independently selected from the group consisting of H or substituted or unsubstituted alkyl, aryl, etc.; R1 is H, substituted alkyl, aryl, etc.; Q is CR2a or N wherein R2a is H, alkyl or cyano; Z is O, NR1b and S(O)0-2; and Ar is substituted aryl or substituted heteroaryl), or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, thereby treating or preventing the neurodegenerative disease, disorder, or condition.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. and methods of use thereof for treating neurodegenerative disorders in relation to use of other agents and diagnosis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

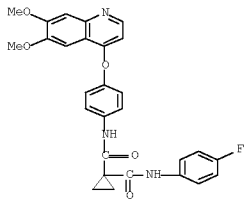


L8 ANSWER 271 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1823382 CAPLUS Full-text
DOCUMENT NUMBER: 161:178446
TITLE: Ocular adverse events of molecularly targeted agents approved in solid tumours: A systematic review
AUTHOR(S): Huillard, Olivier; Bakalian, Silvin; Levy, Christine; Desjardins, Laurence; Lumbroso-Le Rouic, Livia; Pop, Simona; Sablin, Marie-Paule; Le Tourneau, Christophe
CORPORATE SOURCE: Department of Medical Oncology, Clinical Trial Unit, Institut Curie, Paris, Fr.
SOURCE: European Journal of Cancer (2014), 50(3), 638-648
CODEN: EJCAEL; ISSN: 0959-8049
DIGITAL OBJECT ID: 10.1016/j.ejca.2013.10.016
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB When using molecularly targeted agents (MTAs), oncologists and patients face new and sometimes unexpected toxicities. Though ocular adverse events (OAEs) are not uncommon with chemotherapy, they are rarely severe or dose limiting. Ocular toxicity profile may differ with MTAs, indeed severe and dose limiting toxicities have been described with targeted therapies currently under investigation. Our study aimed to review OAEs experienced with MTAs approved in solid tumors. This review revealed that many OAEs, frequent and potentially severe, exist and concern most MTAs. The suggestion is prompt referral of patients with severe pain and/or visual impairment to the ophthalmologist since these symptoms can be associated with potentially severe OAE and need ophthalmic assessment. Oncologists must be aware of such events and their potential severity for better treatment and better diagnosis in daily practice as well as in clin. trials.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ocular adverse events of molecularly targeted agents approved in solid tumors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



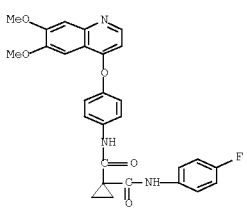
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 272 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1802363 CAPLUS Full-text
DOCUMENT NUMBER: 160:509021
TITLE: Multivoxel 1H MR spectroscopy is superior to contrast-enhanced MRI for response assessment after anti-angiogenic treatment of orthotopic human glioma xenografts and provides handles for metabolic targeting
AUTHOR(S): Hamans, Bob; Navis, Anna Catharina; Wright, Alan; Wesseling, Pieter; Heerschap, Arend; Leenders, William
CORPORATE SOURCE: Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.
SOURCE: Neuro-Oncology (Cary, NC, United States) (2013), 15(12), 1615-1624
CODEN: NEURJR; ISSN: 1522-8517
DIGITAL OBJECT ID: 10.1093/neuonc/not129
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background Anti-angiogenic treatment of glioblastoma characteristically results in therapy resistance and tumor progression via diffuse infiltration. Monitoring tumor progression in these patients is thwarted because therapy results in tumor invisibility in contrast-enhanced (CE) MRI. To address this problem, we examined whether tumor progression could be monitored by metabolic mapping using 1H MR spectroscopic imaging (MRSI). Methods We treated groups of BALB/c nu/nu mice carrying different orthotopic diffuse-infiltrative glioblastoma xenografts with bevacizumab (anti-vascular endothelial growth factor [VEGF] antibody, n = 13), cabozantinib (combined VEGF receptor 2/c-Met tyrosine kinase inhibitor, n = 11), or placebo (n = 15) and compared CE-MRI with MRS-derived metabolic maps before, during, and after treatment. Metabolic maps and CE-MRIs were subsequently correlated to histol. and immunohistochem. Results In vivo imaging of choline/n-acetyl aspartate ratios via multivoxel MRS is better able to evaluate response to therapy than CE-MRI. Lactate imaging revealed that diffuse infiltrative areas in glioblastoma xenografts did not present with excessive glycolysis. In contrast, glycolysis was observed in hypoxic areas in angiogenesis-dependent compact regions of glioma only, especially after anti-angiogenic treatment. Conclusion Our data present MRSI as a powerful and feasible approach that is superior to CE-MRI and may provide handles for optimizing treatment of glioma. Furthermore, we show that glycolysis is more prominent in hypoxic areas than in areas of diffuse infiltrative growth. The Warburg hypothesis of persisting glycolysis in tumors under normoxic conditions may thus not be valid for diffuse glioma.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolic mapping via multivoxel magnetic resonance spectroscopy imaging than contrast-enhanced MRI showed better tumor progression after antiangiogenic Avastin and Exelixis treatment in mouse xenografted with human glioma cell)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 273 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1792084 CAPLUS Full-text
DOCUMENT NUMBER: 159:737215
TITLE: Cabozantinib in progressive medullary thyroid cancer
AUTHOR(S): Elisei, Rossella; Schlumberger, Martin J.; Mueller, Stefan P.; Schoffski, Patrick; Brose, Marcia S.; Shah, Manisha H.; Licitra, Lisa; Jarzab, Barbara; Medvedev, Viktor; Kreissl, Michael C.; Niederle, Bruno; Cohen, Ezra E. W.; Wirth, Lori J.; Ali, Haythem; Hessel, Colin; Yaron, Yifah; Ball, Douglas; Nelkin, Barry; Sherman, Steven I.
CORPORATE SOURCE: University of Pisa, Pisa, Italy
SOURCE: Journal of Clinical Oncology (2013), 31(29), 3639-3646
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.48.4659
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Cabozantinib, a tyrosine kinase inhibitor (TKI) of hepatocyte growth factor receptor (MET), vascular endothelial growth factor receptor 2, and rearranged during transfection (RET), demonstrated clin. activity in patients with medullary thyroid cancer (MTC) in phase I. Patients and Methods: We conducted a double-blind, phase III trial comparing cabozantinib with placebo in 330 patients with documented radiog. progression of metastatic MTC. Patients were randomly assigned (2:1) to cabozantinib (140 mg per day) or placebo. The primary end point was progression-free survival (PFS). Addnl. outcome measures included tumor response rate, overall survival, and safety. Results: The estimated median PFS was 11.2 mo for cabozantinib vs. 4.0 mo for placebo (hazard ratio, 0.28; 95% CI, 0.19 to 0.40; P < .001). Prolonged PFS with cabozantinib was observed across all subgroups including by age, prior TKI treatment, and RET mutation status (hereditary or sporadic). Response rate was 28% for cabozantinib and 0% for placebo; responses were seen regardless of RET mutation status. Kaplan-Meier ests. of patients alive and progression-free at 1 yr are 47.3% for cabozantinib and 7.2% for placebo. Common cabozantinib-associated adverse events included diarrhea, palmar-plantar erythrodysesthesia, decreased weight and appetite, nausea, and fatigue and resulted in dose redns. in 79% and holds in 65% of patients. Adverse events led to treatment discontinuation in 16% of cabozantinib-treated patients and in 8% of placebo-treated patients. Conclusion: Cabozantinib (140 mg per day) achieved a statistically significant improvement of PFS in patients with progressive metastatic MTC and represents an important new treatment option for patients with this rare disease. This dose of cabozantinib was associated with significant but manageable toxicity.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in progressive medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 110 THERE ARE 110 CAPLUS RECORDS THAT CITE THIS RECORD (112 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 274 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1772555 CAPLUS Full-text
DOCUMENT NUMBER: 159:738209
TITLE: Methods for determining nucleotide sequence
INVENTOR(S): Iafrate, Anthony John; Le, Long Phi; Zheng, Zongli
PATENT ASSIGNEE(S): The General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

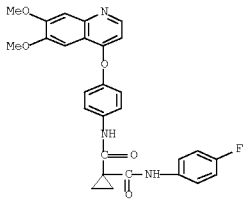
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013169939	A1	20131114	WO 2013-US30201	20130311
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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US 20130303461	A1	20131114	US 2013-13793564	20130311
EP 2847353	A1	20150318	EP 2013-787745	20130311
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CN 104603287	A	20150506	CN 2013-80037100	20130311
JP 2015517307	T	20150622	JP 2015-511444	20130311

PRIORITY APPLN. INFO.:		
US 2012-61645364	P	20120510
US 2012-61679302	P	20120803
WO 2013-US30201	W	20130311

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The technol. described herein is directed to methods of detg. oligonucleotide sequences, e.g. by enriching target sequences prior to sequencing the sequences. The invention provides the sequences of the DNA primers used for sequencing anal. The target sequence may be genomic DNA, RNA or cDNA with or without gene rearrangement.
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for determining nucleotide sequence)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

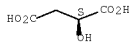
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

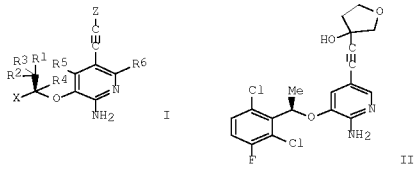


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

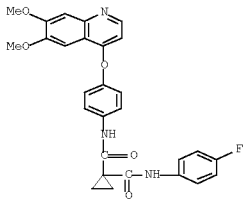
L8 ANSWER 275 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1771791 CAPLUS Full-text
DOCUMENT NUMBER: 159:742705
TITLE: Substituted alkynyl pyridine compounds as protein kinase regulator useful in treatment various diseases and their preparation
INVENTOR(S): Xi, Ning; Yin, Lihua; Li, Xiaobo; Yu, Na; Wu, Yanjun
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 65pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103387535	A	20131113	CN 2013-10173770	20130510
PRIORITY APPLN. INFO.:			CN 2012-10141993	A 20120510
			CN 2013-10116652	A 20130403

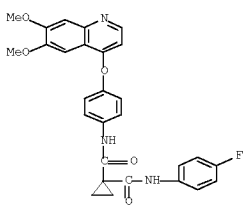
OTHER SOURCE(S): CASREACT 159:742705; MARPAT 159:742705
GI



AB The invention relates to substituted alkynyl pyridine compds. of formula I as protein kinase regulator useful in treatment of various diseases and their preparation Compds. I, wherein R1, R2, R3, R4, R5 and R6 are independently H, D or F; X is C6-10 aryl or heteroaryl containing 5-10 atoms; Z is C1-6 alkyl, C3-6 cycloalkyl, C3-6 heterocyclic radical, etc.; their stereoisomers, solvates, N-oxidants, pharmaceutically acceptable salts, are claimed. Compound II was prepared by multi-step procedure (procedure given). The invention compds. were evaluated for their ALK(h) kinase activity. From assay, it was determined that II exhibited the IC50 value of 52 nM against ALK(h).
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted alkynyl pyridine compds. as protein kinase regulator useful in treatment of various diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 276 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1746648 CAPLUS Full-text
DOCUMENT NUMBER: 160:200751
TITLE: Cabozantinib: a novel agent with a dual mechanism of action for castration-resistant prostate carcinoma
AUTHOR(S): Pinto, Alvaro
CORPORATE SOURCE: Medical Oncology Department, University Hospital La Paz-IdiPAZ, Madrid, Spain
SOURCE: Cancer Chemotherapy and Pharmacology (2014), 73(2), 219-222
CODEN: CCPHDZ; ISSN: 0344-5704
DIGITAL OBJECT ID: 10.1007/s00280-013-2343-2
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The landscape of castration-resistant prostate carcinoma has changed completely in the last few years, with the approval of four new agents with proven benefit in overall survival. Abiraterone, cabazitaxel, enzalutamide and radium-223 dichloride have been added to the armamentarium of available agents for the treatment of these patients. We still lack information about which agent works best in an individual patient and how to optimally use them in a sequential strategy. Cabozantinib, a targeted agent against MET and vascular endothelial growth factor receptor-2, has shown promising results and could become the first targeted therapy to be approved for castration-resistant prostate carcinoma. This paper reviews the clin. development of cabozantinib in prostate cancer and future research possibilities for this drug.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib, a novel agent with a dual mechanism of action for castration-resistant prostate carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

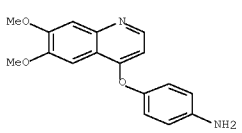


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 277 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1734775 CAPLUS Full-text
DOCUMENT NUMBER: 159:691817
TITLE: A dual MET-VEGF modulator for treating osteolytic bone metastases
INVENTOR(S): Aftab, Dana T.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013166296	A1	20131107	WO 2013-US39284	20130502
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2844254	A1	20150311	EP 2013-722238	20130502
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015515988	T	20150604	JP 2015-510456	20130502
US 20150133494	A1	20150514	US 2014-14398188	20141031
PRIORITY APPLN. INFO.:			US 2012-61641837 P	20120502
			WO 2013-US39284 W	20130502

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 159:691817; MARPAT 159:691817
GI

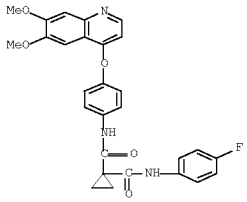


AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and osteolytic bone metastases, with a dual inhibitor of MET and VEGF.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



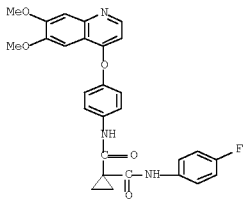
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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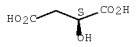
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



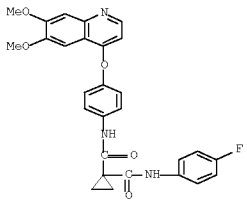
IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)

RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

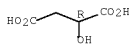
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 278 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1717033 CAPLUS Full-text

DOCUMENT NUMBER: 160:363229

TITLE: Cabozantinib inhibits growth of androgen-sensitive and castration-resistant prostate cancer and affects bone remodeling

AUTHOR(S): Nguyen, Holly M.; Ruppender, Nazanin; Zhang, Xiaotun; Brown, Lisha G.; Gross, Ted S.; Morrissey, Colm; Gulati, Roman; Vessella, Robert L.; Schimmoller, Frauke; Aftab, Dana T.; Corey, Eva

CORPORATE SOURCE: Department of Urology, University of Washington, Seattle, WA, USA

SOURCE: PLoS One (2013), 8(10), e78881
CODEN: POLNCL; ISSN: 1932-6203

DIGITAL OBJECT ID: 10.1371/journal.pone.0078881

PUBLISHER: Public Library of Science

DOCUMENT TYPE: Journal; (online computer file)

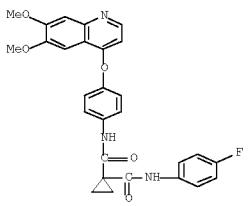
LANGUAGE: English

AB Cabozantinib is an inhibitor of multiple receptor tyrosine kinases, including MET and VEGFR2. In a phase II clin. trial in advanced prostate cancer (PCa), cabozantinib treatment improved bone scans in 68% of evaluable patients. Our studies aimed to determine the expression of cabozantinib targets during PCa progression and to evaluate its efficacy in hormone-sensitive and castration-resistant PCa in preclin. models while delineating its effects on tumor and bone. Using immunohistochem. and tissue microarrays containing normal prostate, primary PCa, and soft tissue and bone metastases, our data show that levels of MET, P-MET, and VEGFR2 are increasing during PCa progression. Our data also show that the expression of cabozantinib targets are particularly pronounced in bone metastases. To evaluate cabozantinib efficacy on PCa growth in the bone environment and in soft tissues we used androgen-sensitive LuCaP 23.1 and castration-resistant C4-2B PCa tumors. In vivo, cabozantinib inhibited the growth of PCa in bone as well as growth of s.c. tumors. Furthermore, cabozantinib treatment attenuated the bone response to the tumor and resulted in increased normal bone volume In summary, the expression pattern of cabozantinib targets in primary and castration-resistant metastatic PCa, and its efficacy in two different models of PCa suggest that this agent has a strong potential for the effective treatment of PCa at different stages of the disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET, VEGFR2, RET expressions were found higher while cabozantinib by inhibiting these targets, it safely, effectively inhibited tumor growth, improved bone remodeling in human androgen-sensitive, metastatic CRPC tumor xenografted mouse)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 279 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1698309 CAPLUS Full-text

DOCUMENT NUMBER: 159:662217

TITLE: Detection of RET fusions in cancer

INVENTOR(S): Doebele, Robert; Garcia, Marileila Varella; Le, Anh T.; Xu, Liangguo

PATENT ASSIGNEE(S): University of Colorado, USA
SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013163428	A1	20131031	WO 2013-US38215	20130425

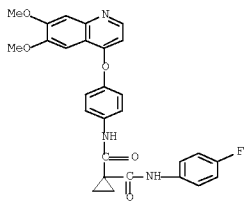
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61638452 P 20120425

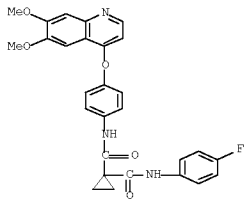
AB Disclosed are methods and assay systems for the identification of chromosomal rearrangements involving the RET kinase gene in cellular samples. Further described are methods for identifying cancer patients who are predicted to respond, or not respond to the therapeutic administration of a chemotherapeutic regimen including one or more kinase inhibitor(s), to treat cancer in the patient.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detection of RET fusions in cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 281 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1655693 CAPLUS Full-text
DOCUMENT NUMBER: 159:632725
TITLE: Menainv and cancer invasion and metastasis diagnosis and antitumor screening
INVENTOR(S): Gertler, Frank B.; Hughes-Alford, Shannon K.; Lauffenburger, Douglas A.; Neil, Jason; White, Forest; Condeelis, John S.; Oudin, Madeleine J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA; Albert Einstein College of Medicine of Yeshiva University
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013158485	A1	20131024	WO 2013-US36336	20130412

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20150044234 A1 20150212 US 2014-14390113 20141002
PRIORITY APPLN. INFO.: US 2012-61625985 P 20120418
US 2013-61778767 P 20130313
WO 2013-US36336 W 20130412

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

L8 ANSWER 280 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1679191 CAPLUS Full-text
DOCUMENT NUMBER: 160:82446
TITLE: Commentary on "Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial." Smith DC, Smith MR, Sweeney C, Elfiky AA, Logothetis C, Corn PG, Vogelzang NJ, Small EJ, Harzstark AL, Gordon MS, Vaishampayan UN, Haas NB, Spira AI, Lara PN Jr, Lin CC, Srinivas S, Sella A, SchoffskiSchoeffski P, Scheffold C, Weitzman AL, Hussain M, University of Michigan, Ann Arbor, MI
AUTHOR(S): Trump, Donald L.
CORPORATE SOURCE: Neth.
SOURCE: Urologic Oncology: Seminars and Original Investigations (2013), 31(8), 1848
CODEN: UOSOAA; ISSN: 1078-1439
DIGITAL OBJECT ID: 10.1016/j.urolonc.2013.07.012
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib (XL184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. Patients received 100 mg of cabozantinib daily. Those with stable disease per RECIST at 12 wk were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 wk and progression-free survival (PFS) after random assignment. One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 wk was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 wk (95% CI, 10.7 to 62.4 wk) with cabozantinib and 5.9 wk (95% CI, 5.4 to 6.6 wk) with placebo (hazard ratio, 0.12; P<.001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by≥50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot syndrome (8%). Cabozantinib has clin. activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and redns. in bone turnover markers, pain, and narcotic use.

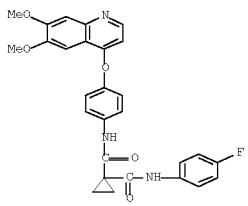
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in patients with advanced prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

AB Methods and compns. are provided for diagnosing or inhibiting invasion or metastasis of a cancer in a subject based on MenaINV. A method is provided of identifying an agent as an inhibitor of sarcoma or carcinoma cell invasion or as an inhibitor of metastasis of a carcinoma or sarcoma, comprising contacting a preparation comprising a growth factor receptor and a protein tyrosine phosphatase 1b (PTP1b) in the presence of an amount of MenaINV and an amount of Mena and quantifying the association of the growth factor receptor and PTP1b in the presence of the agent and in the absence of the agent. An agent that increases the association of growth factor receptor and PTP1b in the presence of the agent as compared to in the absence of the agent is identified as an inhibitor of sarcoma or carcinoma cell invasion or of metastasis, and an agent that does not increase, or decreases, the association of growth factor receptor and PTP1b in the presence of the agent as compared to in the absence of the agent is not identified as an inhibitor of sarcoma or carcinoma cell invasion or metastasis. A further method is provided of identifying an agent as an inhibitor of sarcoma or carcinoma cell invasion or of metastasis of a carcinoma or sarcoma, the method comprising contacting a preparation comprising an amount of MenaINV, an amount of Mena, and a protein, wherein the protein is phosphorylated, with the agent and PTP1b and quantifying phosphorylation of the protein at the site or sites. A decrease in phosphorylation in (a) the presence of the agent and PTP1b as compared to (b) in the absence of the agent and presence of PTP1b identifies the agent as an inhibitor of sarcoma or carcinoma cell invasion or metastasis, and wherein an increase in, or no change in, phosphorylation in (i) the presence of the agent and PTP1b as compared to (ii) in the absence of the agent and presence of PTP1b does not identify the agent as an inhibitor of sarcoma or carcinoma cell invasion or metastasis.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Menainv and cancer invasion and metastasis diagnosis and antitumor screening)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

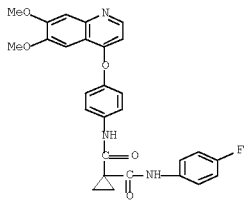
L8 ANSWER 282 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1629334 CAPLUS Full-text
DOCUMENT NUMBER: 159:602931
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Arnal, Anna; Tarragona, Maria; Pavlovic, Milica; Planet, Evarist; Gomis, Roger
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 150pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013153458	A2	20131017	WO 2013-IB1204	20130315
WO 2013153458	A3	20140227		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2650682	A1	20131016	EP 2012-382139	20120409
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CA 2891609	A1	20131017	CA 2013-2891609	20130315
AU 2013246618	A1	20141106	AU 2013-246618	20130315
KR 2015014919	A	20150209	KR 2014-7031148	20130315
EP 2836837	A2	20150218	EP 2013-731875	20130315
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104797935	A	20150722	CN 2013-80027292	20130315
JP 2015520606	T	20150723	JP 2015-505034	20130315
US 20150293100	A1	20151015	US 2014-14391085	20141007
MX 2014012233	A	20150617	MX 2014-12233	20141009

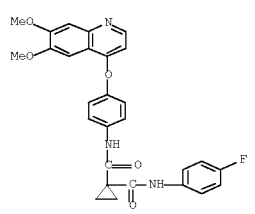
PRIORITY APPLN. INFO.:

EP 2012-382139	A	20120409
US 2012-61621949	P	20120409
US 2012-61724807	P	20121109
US 2012-61732175	P	20121130
US 2012-61732174	P	20121130
WO 2013-IB1204	W	20130315

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention relates to a method for the prognosis of bone metastasis in triple neg. (including basal-like) breast cancer or, alternatively, ER+ breast cancer (including luminal A and β) which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of triple neg. (including basal-like) breast cancer metastasis or, alternatively, ER+ breast cancer (including luminal A and B) metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for the prognosis and treatment of cancer metastasis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 283 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1622779 CAPLUS Full-text
DOCUMENT NUMBER: 160:260019
TITLE: Novel Modeling of Cancer Cell Signaling Pathways Enables Systematic Drug Repositioning for Distinct Breast Cancer Metastases
AUTHOR(S): Zhao, Hong; Jin, Guangxu; Cui, Kemi; Ren, Ding; Liu, Timothy; Chen, Peikai; Wong, Solomon; Li, Fuhai; Fan, Yubo; Rodriguez, Angel; Chang, Jenny; Wong, Stephen T. C.
CORPORATE SOURCE: Department of Systems Medicine and Bioengineering; NCI Center for Modeling Cancer Development, The Methodist Hospital Research Institute, Weill Cornell Medical College; Methodist Cancer Center, The Methodist Hospital, Dan L. Duncan Cancer Center, Baylor College of Medicine, Houston, TX, USA
SOURCE: Cancer Research (2013), 73(20), 6149-6163
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-12-4617
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new type of signaling network element, called cancer signaling bridges (CSB), has been shown to have the potential for systematic and fast-tracked drug repositioning. On the basis of CSBs, we developed a computational model to derive specific downstream signaling pathways that reveal previously unknown target-disease connections and new mechanisms for specific cancer subtypes. The model enables us to reposition drugs based on available patient gene expression data. We applied this model to repurpose known or shelved drugs for brain, lung, and bone metastases of breast cancer with the hypothesis that cancer subtypes have their own specific signaling mechanisms. To test the hypothesis, we addressed specific CSBs for each metastasis that satisfy (i) CSB proteins are activated by the maximal number of enriched signaling pathways specific to a given metastasis, and (ii) CSB proteins are involved in the most differential expressed coding genes specific to each breast cancer metastasis. The identified signaling networks for the three types of breast cancer metastases contain 31, 15, and 18 proteins and are used to reposition 15, 9, and 2 drug candidates for the brain, lung, and bone metastases. We conducted both in vitro and in vivo preclin. expts. as well as anal. on patient tumor specimens to evaluate the targets and repositioned drugs. Of special note, we found that the Food and Drug Administration-approved drugs, sunitinib and dasatinib, prohibit brain metastases derived from breast cancer, addressing one particularly challenging aspect of this disease.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel developed cancer signaling bridges-based computational model enabled systematic drug repositioning for brain, lung and bone metastasis in human breast cancer cell and in xenografted mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 284 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1619978 CAPLUS Full-text
DOCUMENT NUMBER: 159:634400
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis Cabre, Roger; Planet, Evarist; Pavlovic, M. Milica
PATENT ASSIGNEE(S): Fundacio Privada Institut de Recerca Biomedica, Spain; Fundacio Privada Institucio Catalana de Recerca i Estudis Avancats
SOURCE: Eur. Pat. Appl., 51pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2650682	A1	20131016	EP 2012-382139	20120409
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CA 2891609	A1	20131017	CA 2013-2891609	20130315
WO 2013153458	A2	20131017	WO 2013-IB1204	20130315
WO 2013153458	A3	20140227		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2013246618	A1	20141106	AU 2013-246618	20130315
KR 2015014919	A	20150209	KR 2014-7031148	20130315
EP 2836837	A2	20150218	EP 2013-731875	20130315
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104797935	A	20150722	CN 2013-80027292	20130315
JP 2015520606	T	20150723	JP 2015-505034	20130315
US 20150293100	A1	20151015	US 2014-14391085	20141007
MX 2014012233	A	20150617	MX 2014-12233	20141009

PRIORITY APPLN. INFO.:

EP 2012-382139	A	20120409
US 2012-61621949	P	20120409
US 2012-61724807	P	20121109
US 2012-61732174	P	20121130
US 2012-61732175	P	20121130

WO 2013-IB1204 W 20130315

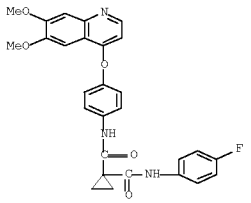
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to a method for the prognosis of bone metastasis in triple neg. (including basal-like) breast cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level. The invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of triple neg. (including basal-like) breast cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.

IT 849217-68-1, CAbozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for the prognosis and treatment of cancer metastasis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 285 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1549396 CAPLUS Full-text

DOCUMENT NUMBER: 159:577130

TITLE: Preparation of spirobicyclyl substituted pyrazolyl pyridinamine compounds as tyrosine kinase inhibitors for treating hyperproliferative disorders

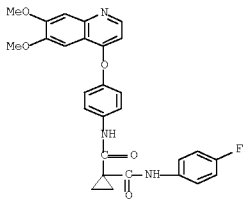
INVENTOR(S): Xi, Ning; Li, Minxiong; Zhou, Xuan; Wu, Yanjun

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 90pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 286 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1459937 CAPLUS Full-text

DOCUMENT NUMBER: 159:472093

TITLE: Preparation of substituted pyrazolylpyridinamine compounds as protein tyrosine kinase modulators for treatment of hyperproliferative disorders

INVENTOR(S): Xi, Ning; Wang, Tingjin; Yi, Lei

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 141pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013138210	A1	20130919	WO 2013-US30096	20130311

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61610473 P 20120314
US 2012-61617626 P 20120329

OTHER SOURCE(S): CASREACT 159:472093; MARPAT 159:472093

GI

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013148537	A1	20131003	WO 2013-US33633	20130325

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61617626 P 20120329

OTHER SOURCE(S): CASREACT 159:577130; MARPAT 159:577130

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides spirobicyclic compds. of general formula I (wherein R1-R6 are independently H, D, or F; each X and Y is independently (un)substituted C6-10aryl or (un)substituted 5-10 membered heteroaryl; Z is (un)substituted C5-12spirobicyclyl or (un)substituted -(C1-4alkylene)-(C5-12spirobicyclyl)-, with provisos), pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Synthetic procedures for preparing I are exemplified. For example, II was prepared in a 12-step synthesis that culminated in reaction of intermediates III and IV. II inhibited ALK kinase and c-Met kinase with IC50 values of 15 and 9 nM, resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of spirobicyclyl substituted pyrazolyl pyridinamine compds. as tyrosine kinase inhibitors for treating hyperproliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

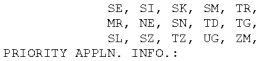
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides substituted pyrazolylpyridinamine compds. of formula I as protein tyrosine kinase modulators capable of regulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion for use in the treatment of hyperproliferative disorders. Compds. of formula I [wherein each R1, R2, R3, R4, R5, and R6 are independently H, D, or F; Z is substituted C3-7 heterocyclyl, substituted (C1-4 alkylene)-(C3-7 heterocyclyl), (un)substituted C5-12 fused bicyclyl, etc.;] stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, or pharmaceutically acceptable salts or prodrugs thereof are claimed and prepared For example, II was prepared by the reaction of 4-iodo-1-(4-((tetrahydro-2H-pyran-2-yl)oxy)tetrahydrofuran-3-yl)-1H-pyrazole with III followed by removal of the tetrahydro-2H-pyran and deprotection of the amine group to afford II in 80% yield. Pharmacodynamic and pharmacokinetic assays were performed on II. II inhibited ALK kinase and c-Met kinase with IC50 of 5 nM and 4 nM resp., demonstrated 82% inhibition of glioblastoma tumor growth when dosed orally at 60 mg/kg to mice, and exhibited a half-life of 35.37 min in human microsomes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolylpyridinamine compds. as protein tyrosine kinase modulators for treatment of hyperproliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

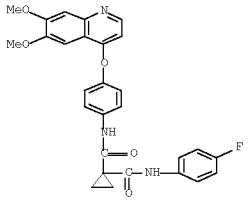
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 287 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1270627 CAPLUS Full-text
DOCUMENT NUMBER: 159:384885
TITLE: Epithelial membrane protein 2 (EMP2) regulates angiogenesis in cancer cells through induction of VEGF
INVENTOR(S): Wadehra, Madhuri; Braun, Jonathan; Gordon, Lynn K.
PATENT ASSIGNEE(S): University of California, USA; United States Dept. of Veterans Affairs
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

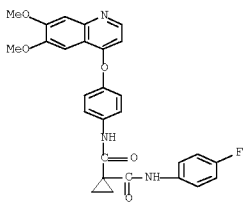
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013119693	A1	20130815	WO 2013-US24968	20130206
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2863986	A1	20130815	CA 2013-2863986	20130206
AU 2013203424	A1	20130822	AU 2013-203424	20130206
EP 2812354	A1	20141217	EP 2013-747090	20130206
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015508066	T	20150316	JP 2014-555854	20130206
US 20150079089	A1	20150319	US 2014-14376724	20140805

PRIORITY APPLN. INFO.: US 2012-61595617 P 20120206
WO 2013-US24968 W 20130206
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose the targeting of epithelial membrane protein 2 (EMP2) for the treatment and prevention of endometrial cancer. In one example, EMP2 expression directly correlated with VEGF protein levels as well as with secreted protein expression by endometrial adenocarcinoma cells. Ribozyme-mediated reduction of EMP2 resulted in undetectable levels of VEGF.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with anti-EMP2 antibodies for treatment of uterine cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 288 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1255893 CAPLUS Full-text
DOCUMENT NUMBER: 159:660795
TITLE: Ponatinib is a potent inhibitor of wild-type and drug-resistant gatekeeper mutant RET kinase
AUTHOR(S): Mologni, Luca; Redaelli, Sara; Morandi, Andrea; Plaza-Menacho, Ivan; Gambacorti-Passerini, Carlo
CORPORATE SOURCE: Dept. of Health Sciences, University of Milano-Bicoccavia Cadore, Monza, 20900, Italy
SOURCE: Molecular and Cellular Endocrinology (2013), 377(1-2), 1-6
CODEN: MCEND6; ISSN: 0303-7207
DIGITAL OBJECT ID: 10.1016/j.mce.2013.06.025
PUBLISHER: Elsevier Ireland Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB RET kinase is aberrantly activated in thyroid cancers and in rare cases of lung and colon cancer, and has been validated as a mol. target in these tumors. Vandetanib was recently approved for the treatment of medullary thyroid cancer. However, vandetanib is ineffective in vitro against RET mutants carrying bulky aminoacids at position 804, the gatekeeper residue, similarly to drug-resistant BCR-ABL mutants in chronic myeloid leukemia. Ponatinib is a multi-target kinase inhibitor that was recently approved for treatment-refractory Philadelphia-pos. leukemia. We show here potent inhibition of oncogenic RET by ponatinib, including the drug-insensitive V804M/L mutants. Ponatinib inhibited the growth of RET+ and BCR-ABL+ cells with similar potency, while not affecting RET-neg. cells. Both in biochem. and in cellular assays ponatinib compared favorably with known RET inhibitors, such as vandetanib, cabozantinib, sorafenib, sunitinib and motesanib, used as reference compds. We suggest that ponatinib should be considered for the treatment of RET+ tumors, in particular those expressing vandetanib-resistant V804M/L mutations.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multi-target tyrosine kinase inhibitor ponatinib exposure inhibited both wild-type and drug-resistant gatekeeper mutant RET kinase activity and inhibited growth of RET+ and BCR-ABL+ human cancer but not RET-cancer or normal cell)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

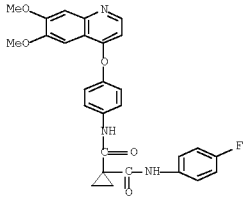


OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 289 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1254595 CAPLUS Full-text
DOCUMENT NUMBER: 159:353569
TITLE: Combination therapy comprising selective VEGFR-2 inhibitors and MEK inhibitors
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 106pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2626066	A1	20130814	EP 2012-154880	20120210
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

PRIORITY APPLN. INFO.: EP 2012-154880 20120210
AB The present invention relates to a combination therapy comprising selective inhibitors of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase and inhibitors of MAP kinase kinase (MEK). Accordingly, a pharmaceutical composition is provided that comprises a selective inhibitor of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase or a pharmaceutically acceptable salt, solvate and/or hydrate thereof, and an inhibitor or a pharmaceutically acceptable salt, solvate and/or hydrate thereof, for use in medicine, especially in the treatment of cancer, like lung cancer, such as non-small cell lung cancer, lung adenocarcinoma or small cell lung cancer. Also a method for identifying patients that are particularly susceptible to such a combination therapy is subject of the present invention. The method comprises the evaluation of the expression level of VEGFR-2 and/or VEGF. An increase in said expression level indicates susceptibility to the combination therapy.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy comprising selective VEGFR-2 inhibitors and MEK inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 290 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:1227139 CAPLUS Full-text
DOCUMENT NUMBER: 159:329544
TITLE: Methods for predicting tumor response to targeted therapies with signal transduction pathway inhibitors using biomarkers
INVENTOR(S): Cohen, Jonathan M.; Derrien-Colemyn, Alexandrine Josephe; Gillespie, John Williams; Park, Soon Sik
PATENT ASSIGNEE(S): 20/20 Gene Systems, Inc., USA
SOURCE: PCT Int. Appl., 146pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013116735	A1	20130808	WO 2013-US24456	20130201
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,				

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140378500 A1 20141225 US 2014-14375827 20140731

PRIORITY APPLN. INFO.: US 2012-61593688 P 20120201
US 2012-61654400 P 20120601
US 2012-61660305 P 20120615
US 2012-61660692 P 20120616
US 2012-61665943 P 20120629
US 2012-61699760 P 20120911
US 2012-61699874 P 20120912
WO 2013-US24456 W 20130201

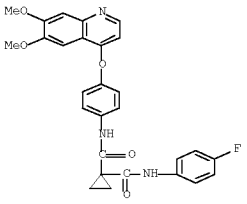
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A method for identifying cancer patients that are likely to be responders or non-responders to a signal transduction pathway inhibitor is described. The present invention is directed to methods and tests that help predict the likelihood that a tumor will respond to a targeted therapy so that those cancer patients most likely to benefit can receive that drug in a timely manner and those patients unlikely to benefit from a particular drug can instead be prescribed alternative therapies. The test comprises a panel of two or more biomarkers that are part of a signal transduction pathway. The biomarkers included in the panel, in combination, express differently in tumors that respond the drug from those that do not respond. The drugs to which these tests predict response may be designed or determined to target the signal transduction pathway of which the biomarker panel is associated Examples of such drugs are those that target angiogenesis pathways like VEGF or cellular growth pathways like mTOR. Alternatively, the drugs might target something other than the pathway with which the biomarkers are associated but activation of that pathway might otherwise limit or defeat the effectiveness of that drug. Examples of such drugs are those that block cellular receptors but for which activation of downstream signaling pathways nevertheless maintains cellular growth.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for predicting tumor response to targeted therapies with signal transduction pathway inhibitors using biomarkers)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 292 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1087476 CAPLUS Full-text

DOCUMENT NUMBER: 159:649618

TITLE: The novel c-Met inhibitor cabozantinib overcomes gemcitabine resistance and stem cell signaling in pancreatic cancer

AUTHOR(S): Hage, C.; Rausch, V.; Giese, N.; Giese, T.; Schoensiegel, F.; Labsch, S.; Nwaeburu, C.; Mattern, J.; Gladkich, J.; Herr, I.

CORPORATE SOURCE: Department of Experimental Medicine, Molecular OncoSurgery Group, University of Heidelberg and German Cancer Research Center, Heidelberg, Germany

SOURCE: Cell Death & Disease (2013), 4(May), e627
CODEN: CDDEA4; ISSN: 2041-4889

DIGITAL OBJECT ID: 10.1038/cddis.2013.158

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; (online computer file)

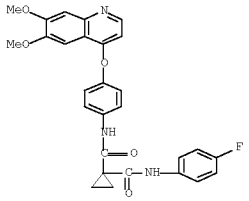
LANGUAGE: English

AB Pancreatic ductal adenocarcinoma (PDA) is one of the most lethal malignancies. Cancer stem cells (CSCs), which are not targeted by current therapies, may be the reason for pronounced therapy resistance. A new treatment option in phase II trials is cabozantinib that inhibits the pancreatic CSC surface marker and tyrosine kinase receptor c-Met. The purpose of this study was to evaluate the effect of cabozantinib to stem-like features and therapy resistance. Established PDA cell lines, a gemcitabine-resistant subclone, non-malignant pancreatic ductal cells and primary spheroidal cultures from patient tumors were analyzed by MTT-assay, flow cytometry, colony and spheroid formation assays, western blotting, qRT-PCR, antibody protein array, immunohistochem. and morphol. features. Cabozantinib inhibited viability and spheroid formation and induced apoptosis in malignant cells with minor effects in non-malignant cells. After long-term cabozantinib treatment, PDA cells had altered anti- and pro-apoptotic signaling, but still responded to cabozantinib, as apoptosis only slightly decreased and viability only slightly increased suggesting a low resistance-inducing potential of cabozantinib. In parallel, c-Met expression and the pluripotency transcription factor SOX2 were downregulated, which might counteract development of full therapy resistance in long-term treated subclones. In single-treatment studies, cabozantinib increased efficacy of gemcitabine. Most importantly, cabozantinib strongly induced apoptosis and reduced viability in PDA cell lines, which are completely resistant toward gemcitabine. In primary, CSC-enriched spheroidal cultures cabozantinib downregulated CSC markers SOX2, c-Met and CD133 and induced apoptosis. These findings suggest that the clin. use of cabozantinib may be more effective than current chemotherapeutics.

IT 849217-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel c-mesenchymal-epithelial transition factor inhibitor cabozantinib overcomes gemcitabine resistance and stem cell signaling in pancreatic cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 291 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:1191423 CAPLUS Full-text

DOCUMENT NUMBER: 159:508181

TITLE: Cabozantinib (XL184) for the treatment of locally advanced or metastatic progressive medullary thyroid cancer

AUTHOR(S): Viola, David; Cappagli, Virginia; Elisei, Rossella

CORPORATE SOURCE: Endocrinology Unit, Department of Clinical & Experimental Medicine, WHO Collaborating Center for the Study & Treatment of Thyroid Diseases & other Endocrine & Metabolic Disorders, University of Pisa, Via Paradisa 2, Pisa, 56124, Italy

SOURCE: Future Oncology (2013), 9(8), 1083-1092
CODEN: FOUNBN; ISSN: 1479-6694

DIGITAL OBJECT ID: 10.2217/fon.13.128

PUBLISHER: Future Medicine Ltd.

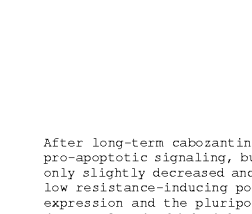
DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. Cabozantinib (XL184) is an oral multiple receptor tyrosine kinase inhibitor manufactured by Exelixis Inc., CA, USA. It mainly inhibits three tyrosine kinase receptors: MET, VEGFR2 and RET. In both preclin. and clin. studies it has been shown to inhibit tumor angiogenesis, invasiveness and metastases. The most frequent side effects are fatigue, diarrhea, decreased appetite, nausea, weight loss and palmar-plantar erythrodysesthesia. A Phase III clin. trial (EXAM study) of XL184 vs. placebo in advanced and progressive medullary thyroid cancer showed a 28 vs. 0% overall response rate and a progression-free survival of 11.2 vs. 4.0 mo (hazard ratio: 0.28; 95% CI: 0.19-0.40; $p < 0.0001$) in patients treated with cabozantinib and placebo, resp. The drug has been approved by the US FDA for the treatment of advanced/progressive metastatic medullary thyroid cancer in the USA. The EMA is now evaluating its approval in Europe.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of locally advanced or metastatic progressive medullary thyroid cancer)

RN 849217-68-1 CAPLUS



OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (24 CITINGS)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 293 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:948019 CAPLUS Full-text

DOCUMENT NUMBER: 159:312293

TITLE: Drug monographs: cabozantanib and omacetaxine

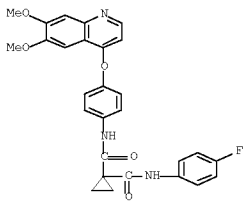
AUTHOR(S): Solimando, Dominic A., Jr.; Ho, Kristin V.; Waddell, J. Aubrey

CORPORATE SOURCE: Walter Reed National Military Medical Center, Bethesda, MD, USA

SOURCE: Hospital Pharmacy (2013), 48(5), 373-377
CODEN: HOPHAZ; ISSN: 0018-5787

DIGITAL OBJECT ID: 10.1310/hpj4805-373

PUBLISHER: Thomas Land Publishers, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The complexity of cancer chemotherapy requires pharmacists be familiar with the complicated regimens and highly toxic agents used. This column reviews various issues related to preparation, dispensing, and administration of antineoplastic therapy, and the agents, both com. available and investigational, used to treat malignant diseases. Questions or suggestions for topics should be addressed to Dominic A. Solimando, Jr, President, Oncol. Pharmacy Services, Inc, 4201 Wilson Blvd #110-545, Arlington, VA 22203, e-mail: OncRxSvc@aol.com; or J. Aubrey Waddell, Professor, University of Tennessee College of Pharmacy; Oncol. Pharmacist, Pharmacy Department, Blount Memorial Hospital, 907 E. Lamar Alexander Parkway, Maryville, TN 37804, e-mail: waddfour@charter.net.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug monographs of cabozantinib and omacetaxine)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

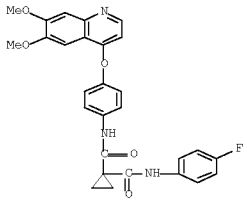


REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 294 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:909480 CAPLUS Full-text
DOCUMENT NUMBER: 159:736844
TITLE: Prostate cancer progression after androgen deprivation therapy: mechanisms of castrate resistance and novel therapeutic approaches
AUTHOR(S): Karantanos, T.; Corn, P. G.; Thompson, T. C.
CORPORATE SOURCE: Department of Genitourinary Medical Oncology-Research, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Oncogene (2013), 32(49), 5501-5511
CODEN: ONCNES; ISSN: 0950-9232
DIGITAL OBJECT ID: 10.1038/onc.2013.206
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Prostate cancer is the second-leading cause of cancer-related mortality in men in Western societies. Androgen receptor (AR) signaling is a critical survival pathway for prostate cancer cells, and androgen-deprivation therapy (ADT) remains the principal treatment for patients with locally advanced and metastatic disease. Although a majority of patients initially respond to ADT, most will eventually develop castrate resistance, defined as disease progression despite serum testosterone levels of <20 ng/dL. The recent discovery that AR signaling persists during systemic castration via intratumoral production of androgens led to the development of novel anti-androgen therapies including abiraterone acetate and enzalutamide. Although these agents effectively palliate symptoms and prolong life, metastatic castration-resistant prostate cancer remains incurable. An increased understanding of the mechanisms that underlie the pathogenesis of castrate resistance is therefore needed to develop novel therapeutic approaches for this disease. The aim of this review is to summarize the current literature on the biol. and treatment of castrate-resistant prostate cancer.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cabozantinib; prostate cancer progression after androgen deprivation therapy in relation to mechanisms of castrate resistance and novel therapeutic approaches)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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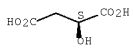
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CM 2

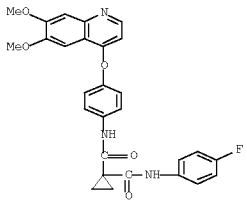
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



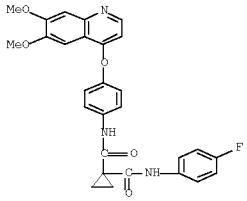
OS.CITING REF COUNT: 67 THERE ARE 67 CAPLUS RECORDS THAT CITE THIS RECORD (67 CITINGS)
REFERENCE COUNT: 158 THERE ARE 158 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 295 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:907853 CAPLUS Full-text
DOCUMENT NUMBER: 160:94029
TITLE: Response to Cabozantinib in Patients with RET Fusion-Positive Lung Adenocarcinomas
AUTHOR(S): Drilon, Alexander; Wang, Lu; Hasanovic, Adnan; Suehara, Yoshiyuki; Lipson, Doron; Stephens, Phil; Ross, Jeffrey; Miller, Vincent; Ginsberg, Michelle; Zakowski, Maureen F.; Kris, Mark G.; Ladanyi, Marc; Rizvi, Naiyer
CORPORATE SOURCE: Department of Medicine Thoracic Oncology Service, Lenox Hill Hospital, New York, NY, USA
SOURCE: Cancer Discovery (2013), 3(6), 630-635
CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID: 10.1158/2159-8290.CD-13-0035
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The discovery of RET fusions in lung cancers has uncovered a new therapeutic target for patients whose tumors harbor these changes. In an unselected population of non-small cell lung carcinomas (NSCLCs), RET fusions are present in 1%to2% of cases. This incidence increases substantially, however, in never-smokers with lung adenocarcinomas that lack other known driver oncogenes. Although preclin. data provide exptl. support for the use of RET inhibitors in the treatment of RET fusion-pos. tumors, clin. data on response are lacking. We report preliminary data for the first three patients treated with the RET inhibitor cabozantinib on a prospective phase II trial for patients with RET fusion-pos. NSCLCs (NCT01639508). Confirmed partial responses were observed in 2 patients, including one harboring a novel TRIM33-RET fusion. A third patient with a KIF5B-RET fusion has had prolonged stable disease approaching 8 mo (31 wk). All three patients remain progression-free on treatment.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response to cabozantinib in patients with RET fusion-pos. lung adenocarcinomas)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 83 THERE ARE 83 CAPLUS RECORDS THAT CITE THIS RECORD (85 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 296 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:884114 CAPLUS Full-text
DOCUMENT NUMBER: 161:430953
TITLE: Tumour angiogenesis: an elusive target in castration-resistant prostate cancer
AUTHOR(S): Galsky, Matthew D.; Oh, William K.
CORPORATE SOURCE: The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA
SOURCE: Lancet Oncology (2013), 14(8), 681-682
CODEN: LOANBN; ISSN: 1470-2045
DIGITAL OBJECT ID: 10.1016/S1470-2045(13)70239-0
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In this article, tumor angiogenesis an attractive target in castration-resistant prostate cancer is studied. Indeed, impressive single-agent activity has been reported with cabozantinib, a small mol. inhibitor of the tyrosine kinases MET and VEGFR2. The author reports on randomly allocated 1050 patients with castration-resistant prostate cancer to treatment with docetaxel plus prednisone with or without bevacizumab-the median overall survival for patients receiving bevacizumab was 22.6 mo compared with 21.5 mo for patients treated with placebo (hazard ratio 0.91, 95% CI 0.78-1.05; stratified log-rank p=0.181).
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on tumor angiogenesis as elusive target in castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

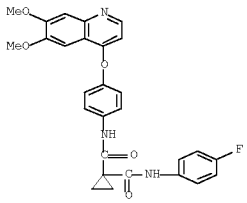


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 297 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:882495 CAPLUS Full-text
DOCUMENT NUMBER: 159:68803
TITLE: Targeting microRNA's miR-409-5p, miR-379 and miR-154* to treat prostate cancer bone metastasis and drug resistant lung cancer
INVENTOR(S): Chung, Leland W. K.; Josson, Sajni; Gururajan, Murali; Jain, Anjali
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 79pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013082499	A1	20130606	WO 2012-US67403	20121130
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2012345666	A1	20140619	AU 2012-345666	20121130
CN 104080461	A	20141001	CN 2012-80067969	20121130
EP 2785355	A1	20141008	EP 2012-854115	20121130
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2015504847	T	20150216	JP 2014-544946	20121130
US 20140323551	A1	20141030	US 2014-14360489	20140523
US 20160017331	A1	20160121	US 2015-14863828	20150924

PRIORITY APPLN. INFO.: US 2011-61565226 P 20111130
WO 2012-US67403 W 20121130
US 2014-14360489 A2 20140523
US 2014-62055215 P 20140925
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention describes methods of treating cancer, cancer metastasis, and drug resistant cancers using miRNA inhibitors; for example, inhibitors of miR-409-5p. Also described are methods of using the miRNA as biomarkers; for example, to predict responsiveness to a cancer drug, to detect a disease state of cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting microRNA's to treat prostate cancer bone metastasis and drug resistant lung cancer and combination with other treatments and use of microRNA's as biomarkers)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

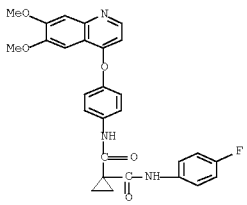


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

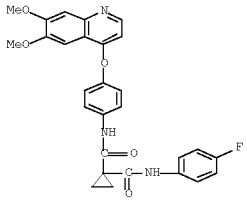
L8 ANSWER 298 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:873882 CAPLUS Full-text
DOCUMENT NUMBER: 159:100783
TITLE: Medical combination containing hepatocyte growth factor receptor inhibitor and Bcl-2 inhibitor for treating cancer
INVENTOR(S): Zhao, Lei; Wang, Limei
PATENT ASSIGNEE(S): Beijing Tianhe Ruitong Technology Development Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 25pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103127510	A	20130605	CN 2011-10389330	20111130
CN 103127510	B	20150325		

PRIORITY APPLN. INFO.: CN 2011-10389330 20111130
AB The title medical combination comprises a hepatocyte growth factor receptor (cMet) inhibitor and a Bcl-2 inhibitor. The medical combination can be used for preparing a drug for treating colon cancer, liver cancer, lung cancer, renal cancer, gastric cancer, brain tumor, sarcoma, neurospongioma, pancreas cancer, ovarian cancer or prostatic cancer. The medical combination has the advantages of good synergistic effects, high effects, low administration dosage and low side effects.
IT 849217-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical combination containing hepatocyte growth factor receptor inhibitor and Bcl-2 inhibitor for treating cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

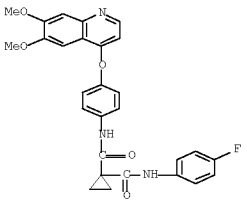


L8 ANSWER 299 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:869127 CAPLUS Full-text
DOCUMENT NUMBER: 159:436784
TITLE: A Dose-Ranging Study of Cabozantinib in Men with Castration-Resistant Prostate Cancer and Bone Metastases
AUTHOR(S): Lee, Richard J.; Saylor, Philip J.; Dror Michaelson, M.; Michael Rothenberg, S.; Smas, Malgorzata E.; Miyamoto, David T.; Gurski, Carol A.; Xie, Wanling; Maheswaran, Shyamala; Haber, Daniel A.; Goldin, Jonathan G.; Smith, Matthew R.
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Boston, MA, USA
SOURCE: Clinical Cancer Research (2013), 19(11), 3088-3094
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-0319
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Cabozantinib is an oral MET/VEGFR2 inhibitor. A recent phase II study of cabozantinib (100 mg daily) showed improved bone scans in subjects with metastatic castration-resistant prostate cancer (mCRPC), but adverse events (AE) caused frequent dose redns. This study was designed to determine the efficacy and tolerability of cabozantinib at lower starting doses. Exptl. Design: An adaptive design was used to determine the lowest active daily dose among 60, 40, and 20 mg. The primary endpoint was week 6 bone scan response, defined as ≥30% decrease in bone scan lesion area. The secondary endpoint was change in circulating tumor cells (CTC). Results: Among 11 evaluable subjects enrolled at 40 mg, there were 9 partial responses (PR), 1 complete response, and 1 stable disease (SD). Of 10 subjects subsequently enrolled at 20 mg, there were 1 PR, 5 SDs, and 4 with progressive disease. Among 13 subjects enrolled on the 40 mg expansion cohort, there were 6 PRs and 7 SDs. No subjects required dose reduction or treatment interruption at 6 or 12 wk; 3 subjects at dose level 0 discontinued due to AEs by 12 wk. At 40 mg, median treatment duration was 27 wk. 58% of subjects with ≥5 CTCs/7.5mL at baseline converted to <5. Conclusions: Cabozantinib 40 mg daily was associated with a high rate of bone scan response. Cabozantinib 40 mg daily was associated with better tolerability than previously reported for cabozantinib 100 mg daily. These observations informed the design of phase III studies of cabozantinib in mCRPC. Clin Cancer Res; 19(11); 3088-94. ©2013 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dose-ranging study of cabozantinib in men with castration-resistant prostate cancer and bone metastases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 300 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:847461 CAPLUS Full-text
DOCUMENT NUMBER: 159:357745
TITLE: The antiangiogenic ceiling in hepatocellular carcinoma: does it exist and has it been reached?
AUTHOR(S): Abou-Alfa, Ghassan K.; Venook, Alan P.
CORPORATE SOURCE: Section of Gastrointestinal Oncology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
SOURCE: Lancet Oncology (2013), 14(7), e283-e288
CODEN: LOANBN; ISSN: 1470-2045
DIGITAL OBJECT ID: 10.1016/S1470-2045(13)70161-X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The recommendation of sorafenib as std. of care in advanced hepatocellular carcinoma has lent support to the increased use of antiangiogenic therapies. However, in three phase 3 randomised trials that compared other antiangiogenics with sorafenib, results did not show superiority or non-inferiority of the new therapies. The 10-mo median overall survival shown in these studies for patients given sorafenib might be a ceiling for single-agent antiangiogenic therapy. Strategies to increase survival time include combination therapies that pair antiangiogenic treatment with biol. therapy or chemotherapy. The combination of sorafenib and erlotinib was not superior to sorafenib alone, which suggests no pos. interaction between antiangiogenics and tyrosine kinase inhibitors in the treatment of advanced hepatocellular carcinoma. A combination of sorafenib and doxorubicin is being assessed in a randomised phase 3 trial. Differences in patient outcome with sorafenib because of disease cause and the ethnic origin of patients suggest that sorafenib's multitarget capacity, including RAF kinase inhibition, might be important. MET inhibitors cabozantinib and tivantinib are drugs that might also bypass the so-called antiangiogenic ceiling and have led to selective treatment of patients that overexpress MET with these drugs. Although this intense period of research activity has not yet resulted in significant improvements in survival for patients with advanced hepatocellular carcinoma, we are certainly closer to a customised treatment, which should increase the antiangiogenic survival ceiling.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET inhibitors cabozantinib and tivantinib may be useful in treatment of patient with hepatocellular carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

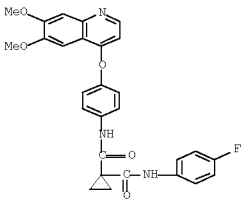
L8 ANSWER 301 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:761990 CAPLUS Full-text
DOCUMENT NUMBER: 158:704608
TITLE: Method of quantifying cancer treatment
INVENTOR(S): Holland, Jaymes
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 50pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

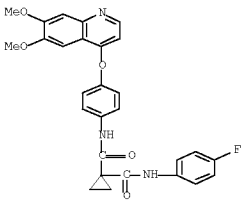
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013070903	A1	20130516	WO 2012-US64134	20121108
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
CA 2854664	A1	20130516	CA 2012-2854664	20121108
AU 2012335750	A1	20140605	AU 2012-335750	20121108
AR 88813	A1	20140710	AR 2012-104223	20121108
CN 104039226	A	20140910	CN 2012-80066413	20121108
EP 2775921	A1	20140917	EP 2012-795939	20121108
R:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO,			

RS, SE, SI, SK, SM, TR, BA, ME

JP 2015505360	T	20150219	JP 2014-541261		20121108
IN 2014CN03674	A	20150703	IN 2014-CN3674		20140515
PRIORITY APPLN. INFO.:			US 2011-61557362	P	20111108
			WO 2012-US64134	W	20121108

OTHER SOURCE(S): CASREACT 158:704608
AB This invention is directed to a method for quantifying cancer treatment response in patients with bone metastases using computer aided bone scan assessment, comprising: (a) obtaining a bone scan image; (b) normalizing the obtained bone scan image to identify normalized bone scan lesions; and (c) quant. assessing the normalized bone scan lesions using bone scan lesion area, bone scan intensity, or bone scan lesion count.
IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(quantifying cancer treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quantifying cancer treatment)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

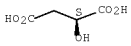
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CMF C28 H24 F N3 O5

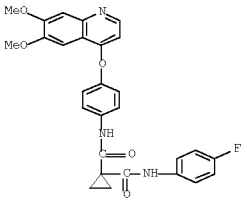
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quantifying cancer treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



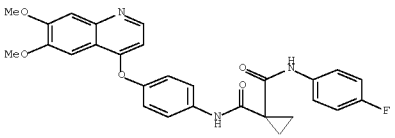
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 302 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:761969 CAPLUS Full-text
DOCUMENT NUMBER: 158:704607
TITLE: Dual inhibitor of Met and VEGF for treating cancer
INVENTOR(S): Aftab, Dana T.; Schimmoller, Frauke
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013070890	A1	20130516	WO 2012-US64116	20121108
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2854336	A1	20130516	CA 2012-2854336	20121108
AU 2012335737	A1	20140605	AU 2012-335737	20121108
IL 232421	A	20140630	IL 2012-232421	20121108
KR 2014088610	A	20140710	KR 2014-7015127	20121108
EP 2776033	A1	20140917	EP 2012-787328	20121108
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104159585	A	20141119	CN 2012-80066410	20121108
JP 2014532766	T	20141208	JP 2014-541256	20121108
MX 2014005458	A	20150416	MX 2014-5458	20140506
US 20140323522	A1	20141030	US 2014-14356927	20140508
ZA 2014003331	A	20151223	ZA 2014-3331	20140508
IN 2014CN04067	A	20151023	IN 2014-CN4067	20140530

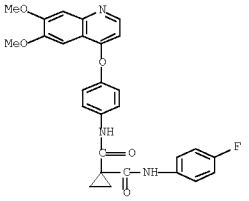
PRIORITY APPLN. INFO.: US 2011-61557358 P 20111108
WO 2012-US64116 W 20121108

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:704607; MARPAT 158:704607
GI



AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and bone metastases, with a dual inhibitor of MET and VEGF.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

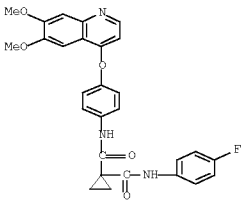


IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1

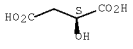
CMF C28 H24 F N3 O5



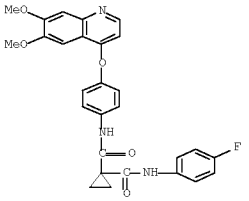
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



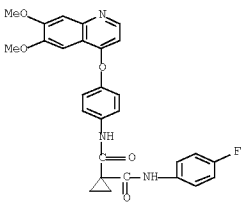
IT 849217-68-1, Cabozantinib 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

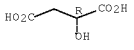
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 303 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:729332 CAPLUS Full-text
DOCUMENT NUMBER: 158:676742
TITLE: Fusion proteins with a C-terminal domain of the gene ret receptor and their use in cancer diagnosis
INVENTOR(S): Ju, Young-Seok; Seo, Jeong-Sun; Kim, Kun-Hee
PATENT ASSIGNEE(S): Macrogen Inc., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 61pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20130116280	A1	20130509	US 2012-13663565	20121030
WO 2013066047	A1	20130510	WO 2012-KR9056	20121031
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
KR 2014092846	A	20140724	KR 2014-7013826	20121031
EP 2773673	A1	20140910	EP 2012-845116	20121031
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2015504299	T	20150212	JP 2014-538724	20121031

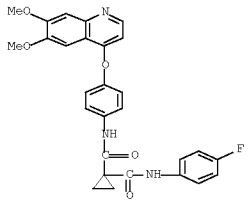
PRIORITY APPLN. INFO.: US 2011-61553483 P 20111031
US 2012-13663565 A 20121030
WO 2012-KR9056 W 20121031

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A fusion protein including N-terminal domain of a fusion partner at N-terminal and C-terminal domain of RET protein at C-terminal and the gene encoding are identified as diagnostic markers for cancers, especially lung cancers. The somatic mutation forming the chimeric gene was identified in a poorly differentiated lung adenocarcinoma. The adenocarcinoma did not show any of the most common lung cancer-associated mutations, but several discordant reads, indicating transposition events, were identified. Expression of the chimeric KIF5B-RET gene in NIH-3T3 resulted in a neoplastic phenotype. Growth of these cells could be inhibited by the ret kinase inhibitor cabozantinib.

IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as inhibitor of ret receptor fusion protein in cancer therapy; fusion proteins with C-terminal domain of gene ret receptor and their use in cancer diagnosis)

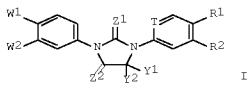
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 304 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:728614 CAPLUS Full-text
DOCUMENT NUMBER: 158:672026
TITLE: Methods using heteroaryl compounds for treatment of disorders involving androgen-, estrogen- and progesterone-receptors
INVENTOR(S): Protter, Andrew A.; Hung, David T.; Chakravarty, Sarvajit; Bernales, Sebastian
PATENT ASSIGNEE(S): Medivation Technologies, Inc., USA
SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013067131	A1	20130510	WO 2012-US62980	20121101
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2011-61554919 P 20111102
OTHER SOURCE(S): MARPAT 158:672026
GI

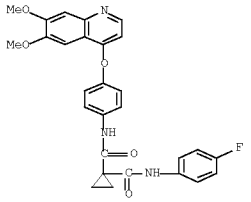


I

AB The disclosure describes compds. of formula I [W1 = CN, NO2, SO2R4; W2 = alkyl, alkenyl, alkynyl, halo; Z1 = S, O; Z2 = S, O, NR4; R4 = independently H, alkyl, aryl; Y1, Y2 = independently H, alkyl, alkenyl, aryl, arylalkyl, heterocyclic etc.; R1 = alkyl, cycloalkyl, heterocyclic etc.; R2 = independently H, halo, CN, alkyl etc.], or pharmaceutically acceptable salts thereof, useful for treating disorders involving androgen, estrogen, and/or progesterone receptors. In another embodiment of the invention the disorder is selected from the group consisting of neurodegenerative disorders, cancer, polyglutamate disease, rheumatoid arthritis, systemic hyperandrogenism, seborrhea, hirsutism, precocious puberty, polycystic ovary syndrome, acne, alopecia, benign prostatic hyperplasia, intrauterine fibroids, endometriosis, glaucoma, meningiomas, Kennedy's disease (KD) or X-linked spinal and bulbar muscular atrophy.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods using heteroaryl compds. for treatment of disorders involving androgen-, estrogen- and progesterone-receptors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 305 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:725439 CAPLUS Full-text
DOCUMENT NUMBER: 158:676739
TITLE: Fusion proteins with a C-terminal domain of the gene ret receptor and their use in cancer diagnosis
INVENTOR(S): Ju, Young-Seok; Seo, Jeong-Sun; Kim, Eun-Hee
PATENT ASSIGNEE(S): Macrogen Inc., S. Korea
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013066047	A1	20130510	WO 2012-KR9056	20121031
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20130116280	A1	20130509	US 2012-13663565	20121030
KR 2014092846	A	20140724	KR 2014-7013826	20121031
EP 2773673	A1	20140910	EP 2012-845116	20121031
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2015504299	T	20150212	JP 2014-538724	20121031

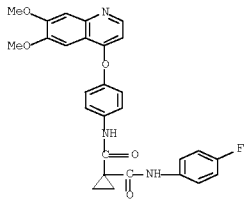
PRIORITY APPLN. INFO.: US 2011-61553483 P 20111031
US 2012-13663565 A 20121030
WO 2012-KR9056 W 20121031

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A fusion protein including N-terminal domain of a fusion partner at N-terminal and C-terminal domain of RET protein at C-terminal and the gene encoding are identified as diagnostic markers for cancers, especially lung cancers. The somatic mutation forming the chimeric gene was identified in a poorly differentiated lung adenocarcinoma. The adenocarcinoma did not show any of the most common lung cancer-associated mutations, but several discordant reads, indicating transposition events, were identified. Expression of the chimeric KIF5B-RET gene in NIH-3T3 resulted in a neoplastic phenotype. Growth of these cells could be inhibited by the ret kinase inhibitor cabozantinib.

IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as inhibitor of ret receptor fusion protein in cancer therapy; fusion proteins with C-terminal domain of gene ret receptor and their use in cancer diagnosis)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

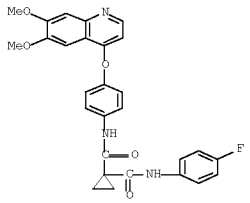


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 306 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:684015 CAPLUS Full-text
DOCUMENT NUMBER: 158:649640
TITLE: Free prostate specific antigen (PSA) antibodies as diagnostics, prognostics and therapeutics for prostate cancer
INVENTOR(S): Sawyers, Charles; Ulmert, David; Lewis, Jason; Evans, Michael; Lija, Hans
PATENT ASSIGNEE(S): Memorial Sloan-Kettering Cancer Center, USA
SOURCE: PCT Int. Appl., 103pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

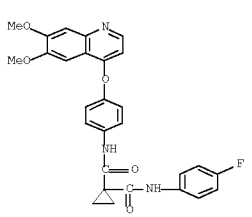
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013063312	A1	20130502	WO 2012-US61982	20121025
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2853705	A1	20130502	CA 2012-2853705	20121025
AU 2012328679	A1	20140612	AU 2012-328679	20121025
EP 2771688	A1	20140903	EP 2012-844178	20121025
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
CN 104040341	A	20140910	CN 2012-80063852	20121025
JP 2015502339	T	20150122	JP 2014-539018	20121025
US 20140308204	A1	20141016	US 2014-14353989	20140424
PRIORITY APPLN. INFO.:			US 2011-61551195 P	20111025
			WO 2012-US61982 W	20121025

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose the use of antibodies to free prostate-specific antigen (fPSA) in the diagnosis, prognosis, and therapeutic monitoring of prostate cancer. In one example, tumor localization of labeled anti-fPSA antibody is shown to be reduced by the antiandrogen MDV3100.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibodies to free PSA antigen therapy monitoring of)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 307 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:647172 CAPLUS Full-text
DOCUMENT NUMBER: 159:188392
TITLE: Emerging targeted therapies for castration-resistant prostate cancer
AUTHOR(S): Adamo, Vincenzo; Noto, Laura; Franchina, Tindara; Chiofalo, Giuseppe; Picciotto, Maria; Toscano, Giuseppe; Caristi, Nicola
CORPORATE SOURCE: Integrated Therapies in Oncology Unit, Department of Human Pathology, University of Messina, Messina, 98125, Italy
SOURCE: Frontiers in Cancer Endocrinology (2012), 3(May), 73
CODEN: FCERD9
DIGITAL OBJECT ID: 10.3389/fendo.2012.00073
PUBLISHER: Frontiers Media S.A.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Until recently, few therapeutic options were available for patients with castration-resistant prostate cancer (CRPC). Since 2010, four new mols. with a demonstrated benefit (sipuleucel-T, cabazitaxel, abiraterone and denosumab) have been approved in this setting and to-date several other agents are under investigation in clin. trials. The purpose of this review is to present an update of targeted therapies for CRPC. Presented data are obtained from literature and congress reports updated until Dec. 2011. Targeted therapies in advanced phases of clin. development include novel androgen signaling inhibitors, inhibitors of alternative signaling pathways, anti-angiogenic agents, inhibitors that target the bone microenvironment and immunotherapeutic agents. Radium-223 and MDV3100 demonstrated a survival advantage in phase III trials and the road for their introduction in clin. practice is rapidly ongoing. Results are also awaited for phase III studies currently underway or planned with new drugs given as monotherapy (TAK-700, cabozantinib, tasquinimod, PROSTVAC-VF, ipilimumab) or in combination with docetaxel (custirsen, aflibercept, dasatinib, zibotentan). The optimal timing, combination and sequencing of emerging therapies remain unknown and require further investigation. Addnl., the identification of novel markers of response and resistance to these therapies may better individualize treatment for patients with CRPC.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emerging targeted therapies for castration-resistance prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

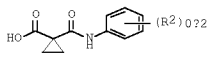


OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

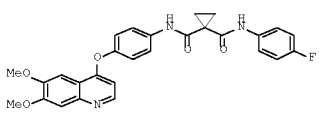
L8 ANSWER 308 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:644308 CAPLUS Full-text
DOCUMENT NUMBER: 158:620790
TITLE: Process for preparing quinoline derivatives
INVENTOR(S): Wilson, Jo Ann; Naganathan, Sriram; Pfeiffer, Matthew; Andersen, Neil G.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013059788	A1	20130425	WO 2012-US61320	20121022
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2852771	A1	20130425	CA 2012-2852771	20121022
AU 2012325768	A1	20140522	AU 2012-325768	20121022
IL 232139	A	20140528	IL 2012-232139	20121022
AR 88483	A1	20140611	AR 2012-103944	20121022
KR 2014088874	A	20140711	KR 2014-7012435	20121022
EP 2768796	A1	20140827	EP 2012-783763	20121022
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2014530880	T	20141120	JP 2014-537359	20121022
CN 104395284	A	20150304	CN 2012-80054241	20121022
ZA 2014002579	A	20150325	ZA 2014-2579	20140409
MX 2014004583	A	20141006	MX 2014-4583	20140415
US 20140256938	A1	20140911	US 2014-14353251	20140421
IN 2014CN02971	A	20150703	IN 2014-CN2971	20140421
PRIORITY APPLN. INFO.:			US 2011-61549312 P	20111020
			WO 2012-US61320 W	20121022

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:620790; MARPAT 158:620790
GI



I



II

AB The invention is directed to processes for prepg. compds. of formula I (R2 is H, F, Cl and Br) by activation of 1,1-cyclopropanedicarboxylic acid with thionyl chloride followed by amidation with substituted aniline derivative Example compound II L-malate was prepared by chlorination of 6,7-dimethoxyquinolin-4-ol followed by etherification of 4-chloro-6,7-dimethoxyquinoline with 4-aminophenol; the resulting 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine underwent acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropanecarbonyl chloride to give compound II, which underwent addition of L-malic acid to give the desired product.

IT 1140909-48-3P

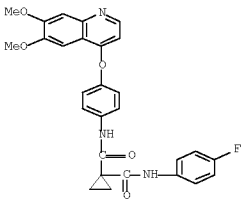
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing quinoline derivs.)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

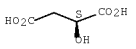
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

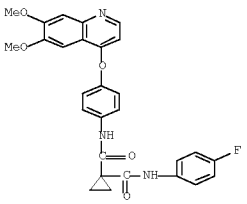


IT 849217-68-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing quinoline derivs.)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 309 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:564369 CAPLUS Full-text

DOCUMENT NUMBER: 159:419448

TITLE: Lessons learned and questions unanswered from use of multitargeted kinase inhibitors in medullary thyroid cancer

AUTHOR(S): Sherman, Steven I.

CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Oral Oncology (2013), 49(7), 707-710
CODEN: EJCCER; ISSN: 1368-8375

DIGITAL OBJECT ID: 10.1016/j.oraloncology.2013.03.442

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

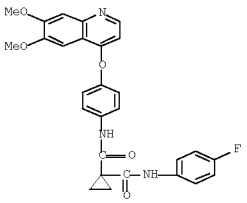
AB To review studies of novel multitargeted kinase inhibitors studied in patients with medullary thyroid cancer (MTC). Search of relevant refs. in PubMed and Google Scholar on "chemotherapy" and "medullary thyroid cancer". Multitargeted kinase inhibitors have revolutionized the role of chemotherapy for progressive MTC, providing for the first time tolerable therapeutic options that can improve outcomes in patients with progressive disease. Drugs thought to inhibit the RET kinase have advanced the furthest for this disease, but these agents also target the VEGF receptor along with other kinases that may be relevant to both beneficial and adverse effects. Vandetanib improved progression-free survival from 19.3 to 30.5 mo compared with placebo in patients with metastatic disease, whereas cabozantinib improved progression-free survival from 4.0 mo to 11.2 mo in a population with more aggressive disease. However, "cure" remains elusive, adverse events frequent, and exactly how such "targeted" agents actually function within MTC remains unclear. New approaches to clin. trial design and the preclin. development of targeted agents may be required to optimize the combination of maximum efficacy with minimal toxicity for patients with metastatic MTC.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of multitargeted kinase inhibitors in medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 310 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:522453 CAPLUS Full-text

DOCUMENT NUMBER: 159:125821

TITLE: Emerging therapies in metastatic castration-sensitive and castration-resistant prostate cancer

AUTHOR(S): MacVicar, Gary R.; Hussain, Maha H.

CORPORATE SOURCE: Division of Hematology/Oncology, Department of Internal Medicine, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

SOURCE: Current Opinion in Oncology (2013), 25(3), 252-260
CODEN: CUOOE8; ISSN: 1040-8746

DIGITAL OBJECT ID: 10.1097/CCO.0b013e32835ff161

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

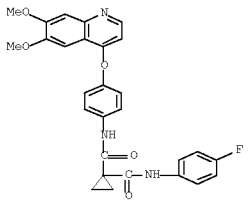
AB Purpose of review: Therapeutic options for men with metastatic prostate cancer are expanding. Here we discuss the scientific progress in this disease that led to approval of several agents in the last decade and highlight ongoing clin. investigation. Recent findings: In androgen-sensitive disease, trials are evaluating the role of intermittent androgen-deprivation therapy, early chemotherapy, and novel targeted and hormonal therapies. For chemotherapy-naive, metastatic castration-resistant prostate cancer (mCRPC), abiraterone is effective. Trials with addnl. agents targeting androgen receptor (AR) signaling, such as TAK-700 and enzalutamide, are ongoing. Other agents in development target the endothelin pathway, angiogenesis, AR chaperones, and immune mechanisms. Docetaxel with prednisone remains the standard first-line chemotherapeutic regimen as trials incorporating novel agents with docetaxel have been neg. Postdocetaxel, enzalutamide improves survival. Early results with cabozantinib are encouraging, and phase III studies are ongoing. Denosumab and radium-223 reduce the risk of skeletal-related events (SREs), but only radium-223 improves survival. Summary: Progress in understanding the disease biol. and mechanisms of castration resistance led to significant therapeutic advancements, particularly in the setting of mCRPC in which

several phase III trials, each incorporating agents with different mechanisms of action, have improved survival. As a result, new options exist, and the standard of care has changed significantly. Further advances are anticipated.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emerging therapies in metastatic castration-sensitive and castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 311 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:522113 CAPLUS Full-text

DOCUMENT NUMBER: 159:125816

TITLE: From Bevacizumab to Tasquinimod: Angiogenesis as a Therapeutic Target in Prostate Cancer

AUTHOR(S): Schweizer, Michael T.; Carducci, Michael A.

CORPORATE SOURCE: Prostate Cancer Research Program, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins, Baltimore, MD, USA

SOURCE: Cancer Journal (Philadelphia, PA, United States) (2013), 19(1), 99-106
CODEN: CAJOCB; ISSN: 1528-9117

DIGITAL OBJECT ID: 10.1097/PPO.0b013e31827e0b86

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review; (online computer file)

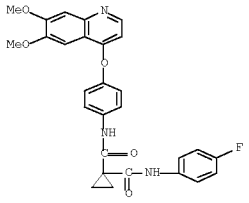
LANGUAGE: English

AB A review. It was first posited in the 1970s that angiogenesis may prove to be a useful target for anticancer therapies. Since then, a number of agents have been developed and tested across a range of tumor types; however, to date, there have unfortunately been more failures than successes. Prostate cancer (PCa) is no exception in this regard, and despite a strong preclin. rationale for targeting angiogenesis in men with PCa, there has yet to be an antiangiogenic therapy proven to prolong survival in this group of patients. Drugs have been developed to target a host of angiogenesis mediators. These include vascular endothelial growth factor (VEGF), the VEGF receptors, antiangiogenic factors (e.g., thrombospondin-1), and downstream mediators of angiogenesis (e.g., hypoxia-inducible factor-1α and MET). At present, there are 2 drugs being tested in the phase III setting for men with PCa: cabozantinib and tasquinimod. Cabozantinib, a dual VEGF receptor-2/MET inhibitor, has shown dramatic beneficial effects on radiog. evident bone metastases and pain in the phase II setting. There are currently 2 large phase III trials underway to further investigate cabozantinib's role in treating men with PCa. Both trials randomize subjects to cabozantinib vs. mitoxantrone: one is designed to evaluate overall survival, and the other, pain response durability. The other drug, tasquinimod, has a somewhat poorly understood mechanism of action. It is thought to exert an antiangiogenic effect through the inhibition of myeloid-derived suppressor cells, key to the support of an angiogenic environment, and down-regulation of hypoxia-inducible factor-1α. A phase II trial randomizing men to tasquinimod vs. placebo revealed a median progression-free survival advantage in the exptl. arm (7.6 vs. 3.3 mo with placebo; P = 0.0042). Based on these encouraging phase II results, a randomized, double-blind, placebo-controlled trial in men with metastatic castration-resistant PCa was launched. That trial is powered for a primary endpoint of progression-free survival and is expected to enroll 1200 men.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiogenesis as therapeutic target in prostate cancer and the role of various angiogenesis targeting drugs including bevacizumab and tasquinimod)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 312 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:522110 CAPLUS Full-text

DOCUMENT NUMBER: 159:125815

TITLE: Targeting MET and Vascular Endothelial Growth Factor Receptor Signaling in Castration-Resistant Prostate Cancer

AUTHOR(S): Lee, Richard J.; Smith, Matthew R.

CORPORATE SOURCE: Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA

SOURCE: Cancer Journal (Philadelphia, PA, United States) (2013), 19(1), 90-98
CODEN: CAJOCB; ISSN: 1528-9117

DIGITAL OBJECT ID: 10.1097/PPO.0b013e318281e280

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review; (online computer file)

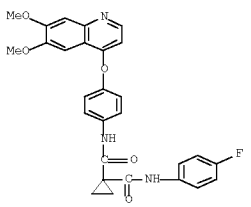
LANGUAGE: English

AB A review. Effective management of bone metastases in men with castration-resistant prostate cancer (CRPC) remains an important unmet medical need. MET and vascular endothelial growth factor receptor (VEGFR) are rational targets for intervention in CRPC. Clin. trials involving agents that inhibit one but not both pathways have reported modest activity and no improvement in overall survival. Cabozantinib is an oral multitargeted tyrosine kinase inhibitor that inhibits both MET and VEGFR-2. A phase II randomized discontinuation study involving subjects with CRPC demonstrated that cabozantinib therapy is associated with improvement in bone scans, bone turnover markers, and pain response, but with significant adverse events leading to dose reduction and treatment discontinuation. Lower doses of cabozantinib retain high levels of activity with less toxicity. Ongoing phase III clin. trials will define the role of cabozantinib in CRPC. We summarize the rationale for targeting MET and VEGFR pathways in CRPC and the clin. data available to date.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting MET and vascular endothelial growth factor receptor signaling in castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 313 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:470327 CAPLUS Full-text

DOCUMENT NUMBER: 158:493976

TITLE: Combinations comprising c-Met antagonists and B-raf antagonists for treatment of cancer

INVENTOR(S): Wilson, Timothy R.; Koeppen, Hartmut; Merchant, Mark; Settleman, Jeffrey

PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG

SOURCE: PCT Int. Appl., 148pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013043715	A1	20130328	WO 2012-US56106	20120919
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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CA 2846630	A1	20130328	CA 2012-2846630	20120919
US 20130078252	A1	20130328	US 2012-13622878	20120919
AU 2012312515	A1	20140313	AU 2012-312515	20120919
IL 231056	A	20140331	IL 2012-231056	20120919
AR 87918	A1	20140423	AR 2012-103446	20120919
KR 2014064971	A	20140528	KR 2014-7010162	20120919
CN 103930111	A	20140716	CN 2012-80055708	20120919
EP 2758055	A1	20140730	EP 2012-768982	20120919
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JP 2014534949	T	20141225	JP 2014-530956	20120919
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MX 2014002990	A	20140521	MX 2014-2990	20140313
US 20150125452	A1	20150507	US 2014-14535071	20141106

PRIORITY APPLN. INFO.:

US 2011-61536436	P	20110919
US 2011-61551328	P	20111025
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WO 2012-US56106	W	20120919

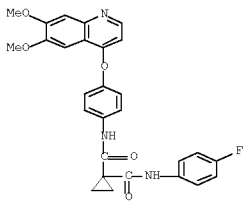
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides combination therapies for treating a pathol. condition, such as cancer, wherein a c-met antagonist (e.g. crizotinib, tivantinib, anti-HGF antibody, onartuzumab) is combined with a B-raf antagonist (e.g. vemurafenib), thereby providing significant antitumor activity. C-met expression was inversely correlated with sensitivity to vemurafenib treatment. In one aspect, provided are methods for treating a cancer patient who has increased likelihood of developing resistance to B-raf antagonist comprising administering an effective amount (in combination) of B-raf antagonist and c-met antagonist. In addition, patients with B-raf mutant melanoma who had higher levels of circulating hepatocyte growth factor (HGF) showed substantially reduced progression free survival and overall survival when treated with B-raf antagonist, relative to patients with lower circulating HGF levels treated with B-raf antagonist.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations comprising c-Met antagonists and B-raf antagonists for treatment of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 314 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:466384 CAPLUS Full-text

DOCUMENT NUMBER: 158:494085

TITLE: Method for treating osteoporosis

INVENTOR(S): Aftab, Dana T.; Clary, Douglas

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 73pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

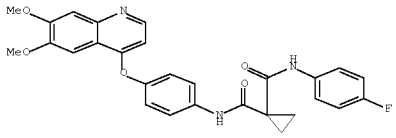
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013043840	A1	20130328	WO 2012-US56281	20120920
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IL 231495	A	20140430	IL 2012-231495	20120920
KR 2014069133	A	20140609	KR 2014-7009534	20120920
CN 103957915	A	20140730	CN 2012-80051094	20120920
EP 2758057	A1	20140730	EP 2012-770368	20120920
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JP 2014527984	T	20141023	JP 2014-531955	20120920
AR 87995	A1	20140430	AR 2012-103501	20120921
ZA 2014001728	A	20160127	ZA 2014-1728	20140310
MX 2014003027	A	20141024	MX 2014-3027	20140313
IN 2014CN02093	A	20141010	IN 2014-CN2093	20140319
US 20140228401	A1	20140814	US 2014-14346570	20140321
PRIORITY APPLN. INFO.:			US 2011-61538039 P	20110922
			WO 2012-US56281 W	20120920

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 158:494085; MARPAT 158:494085

GI



AB This invention is directed to the treatment of osteoporosis using N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide.

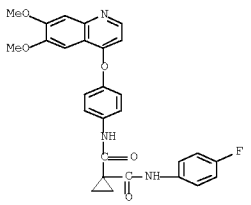
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for treating osteoporosis)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

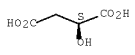
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



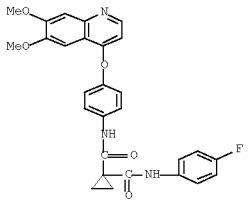
IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treating osteoporosis)

RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

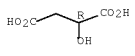
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

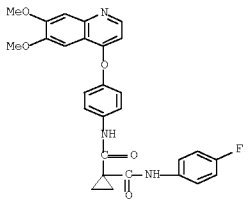
Absolute stereochemistry. Rotation (+).



IT 849217-68-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for treating osteoporosis)

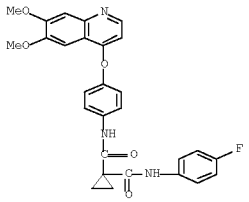
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 315 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:417299 CAPLUS Full-text
DOCUMENT NUMBER: 159:86304
TITLE: Pharmacokinetic evaluation of
AUTHOR(S): Karras, Spyridon; Pontikides, Nikolaos; Krassas, Gerasimos E.
CORPORATE SOURCE: Department of Endocrinology, Diabetes and Metabolism, Panagia General Hospital, Thessaloniki, Greece
SOURCE: Expert Opinion on Drug Metabolism & Toxicology (2013), 9(4), 507-515
CODEN: EODMAP; ISSN: 1742-5255
DIGITAL OBJECT ID: 10.1517/17425255.2013.780028
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Introduction: Conventional treatment modalities for thyroid cancer lead to complete remission in only one-third of patients with distant metastases. On the other hand, medullary thyroid cancer (MTC) and anaplastic thyroid cancer (ATC), although rare, are responsible for a significant percentage of thyroid cancer-related deaths. New treatments are needed to treat such patientsAreas covered: The aim of this review is to provide the latest information on , a new tyrosine kinase inhibitor (TKI) that is currently used mainly as a treatment of MTC. The authors collated data that were retrieved from a PubMed literature search.Expert opinion: CBZ targets multiple cell-signaling pathways involved in the mol. pathogenesis of thyroid cancer. These are namely VEGF receptor-2, hepatocyte growth factor receptor and rearranged during transfection receptor. Furthermore, it is a drug which may be used in cases where conventional therapies (mainly for MTC) are proved ineffective or have shown poor results with a good outcome. CBZ may also be administered alone or in combination with other drugs of the same family.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(understanding pharmacokinetics of cabozantinib may be useful in treatment of patient with medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

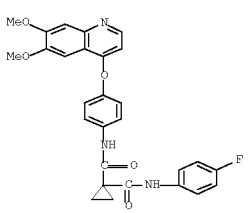


OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 316 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:414621 CAPLUS Full-text
DOCUMENT NUMBER: 159:53852
TITLE: Effects of dual targeting of tumor cells and stroma in human glioblastoma xenografts with a tyrosine kinase inhibitor against c-MET and VEGFR2
AUTHOR(S): Navis, Anna C.; Bourgonje, Annika; Wesseling, Pieter; Wright, Alan; Hendriks, Wiljan; Verrijp, Kiek; van der Laak, Jeroen A. W. M.; Heerschap, Arend; Leenders, William P. J.
CORPORATE SOURCE: Department of Pathology, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.
SOURCE: PLoS One (2013), 8(3), e58262
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0058262
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Anti-angiogenic treatment of glioblastoma with Vascular Endothelial Growth Factor (VEGF)- or VEGF Receptor 2 (VEGFR2) inhibitors normalizes tumor vessels, resulting in a profound radiol. response and improved quality of life. This approach however does not halt tumor progression by diffuse infiltration, as this phenotype is less angiogenesis dependent. Combined inhibition of angiogenesis and diffuse infiltrative growth would therefore be a more effective treatment approach in these tumors. The HGF/c-MET axis is important in both angiogenesis and cell migration in several tumor types including glioma. We therefore analyzed the effects of the c-MET- and VEGFR2 tyrosine kinase inhibitor cabozantinib (XL184, Exelixis) on c-MET pos. orthotopic E98 glioblastoma xenografts, which routinely present with angiogenesis-dependent areas of tumor growth, as well as diffuse infiltrative growth. In in vitro cultures of E98 cells, cabozantinib effectively inhibited c-MET phosphorylation, concomitant with inhibitory effects on AKT and ERK1/2 phosphorylation, and cell proliferation and migration. VEGFR2 activation in endothelial cells was also effectively inhibited in vitro. Treatment of BALB/c nu/nu mice carrying orthotopic E98 xenografts resulted in a significant increase in overall survival. Cabozantinib effectively inhibited angiogenesis, resulting in increased hypoxia in angiogenesis-dependent tumor areas, and induced vessel normalization. Yet, tumors ultimately escaped cabozantinib therapy by diffuse infiltrative outgrowth via vessel co-option. Of importance, in contrast to the results from in vitro expts., in vivo blockade of c-MET activation was incomplete, possibly due to multiple factors including restoration of the blood-brain barrier resulting from cabozantinib-induced VEGFR2 inhibition. In conclusion, cabozantinib is a promising therapy for c-MET pos. glioma, but improving delivery of the drug to the tumor and/or the surrounding tissue may be needed for full activity.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of dual targeting of tumor cells and stroma in human glioblastoma xenografts with tyrosine kinase inhibitor against c-MET and VEGFR2)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

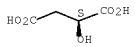
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CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

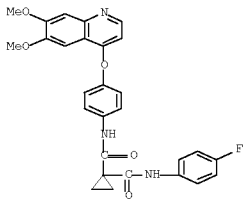
CRN 97-67-6
CMF C4 H6 O5



Absolute stereochemistry. Rotation (-).

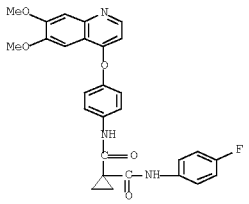
OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 317 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:378985 CAPLUS Full-text
DOCUMENT NUMBER: 159:193339
TITLE: Cellular signaling pathway alterations and potential targeted therapies for medullary thyroid carcinoma
AUTHOR(S): Giunti, Serena; Antonelli, Alessandro; Amorosi, Andrea; Santarpia, Libero
CORPORATE SOURCE: Department of Pathology, Centro Oncologico Fiorentino, Sesto Fiorentino, 50019, Italy
SOURCE: International Journal of Endocrinology (2013) 803171, 16 pp.
CODEN: IJENIG; ISSN: 1687-8345
DIGITAL OBJECT ID: 10.1155/2013/803171
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Parafollicular C-cell-derived medullary thyroid cancer (MTC) comprises 3% to 4% of all thyroid cancers. While cytotoxic treatments have been shown to have limited efficacy, targeted mol. therapies that inhibit rearranged during transfection (RET) and other tyrosine kinase receptors that are mainly involved in angiogenesis have shown great promise in the treatment of metastatic or locally advanced MTC. Multi-tyrosine kinase inhibitors such as vandetanib, which is already approved for the treatment of progressive MTC, and cabozantinib have shown distinct advantages with regard to rates of disease response and control. However, these types of tyrosine kinase inhibitor compds. are able to concurrently block several types of targets, which limits the understanding of RET as a specific target. Moreover, important resistances to tyrosine kinase inhibitors can occur, which limit the long-term efficacy of these treatments. Deregulated cellular signaling pathways and genetic alterations in MTC, particularly the activationof the RAS/mammalian target of rapamycin (mTOR) cascades and RET crosstalk signaling, are now emerging as novel and potentially promising therapeutic treatments for aggressive MTC.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cellular signaling pathway alterations and potential targeted therapies for medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 318 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:377358 CAPLUS Full-text
DOCUMENT NUMBER: 159:86211
TITLE: Cabozantinib as a Novel Therapy for Renal Cell Carcinoma
AUTHOR(S): Vaishampayan, Ulka
CORPORATE SOURCE: Wayne State University, Detroit, MI, 48201, USA
SOURCE: Current Oncology Reports (2013), 15(2), 76-82
CODEN: CORUAT; ISSN: 1534-6269
DIGITAL OBJECT ID: 10.1007/s11912-012-0289-x
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib/XL184 (Exelexis, Inc.) has demonstrated remarkable responses in kidney cancer. Preclin. results revealed VEGF, KIT and MET inhibition in a variety of solid tumors such as thyroid, ovarian, renal, lung, liver and prostate cancers. A phase II trial demonstrated efficacy in renal cancer with a 28 % objective response rate, stable disease rate of 62 % and median progression free survival of 14.7 mo. Predominant toxicities of fatigue and diarrhea were noted. Dramatic responses in bone metastases (three of four patients) make the agent especially valuable for palliation in a disease, where presence of bone metastases is a predictor of worse survival. Cabozantinib is an emerging novel agent with promising activity in advanced kidney cancer. Randomized trials are planned in comparison with standard VEGF inhibitor therapy. Defining the role of MET overexpression would help patient selection and enrich and enhance the future evaluation of this targeted novel agent.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as novel therapy may be useful for treatment of patient with renal cell carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

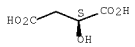


OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 319 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:359822 CAPLUS full-text
DOCUMENT NUMBER: 159:33929
TITLE: Treatment directed to signalling molecules in patients with advanced differentiated thyroid cancer
AUTHOR(S): Saez, Jose M. G.
CORPORATE SOURCE: Endocrinology and Nutrition Service, L'Hospitalet of Llobregat, Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (CIBERDEM), University Hospital of Bellvitge, Barcelona, Spain
SOURCE: Anti-Cancer Agents in Medicinal Chemistry (2013), 13(3), 483-495
CODEN: AAMCE4; ISSN: 1871-5206
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Mutation detection in samples from thyroid cancer with the addition of BRAF mutation, and also the detection of RAS, RET/PTC, and PAX8/PPARγ mutations, may also contribute to cancer diagnosis. On the other hand, the MAPK/ERK (mitogen-activated protein kinase/extracellular signal-regulated kinase signaling pathway) and PI3K/Akt (lipid kinase phoshoinositid-3-kinase signaling pathway) play an important role in the transmission of cell signals. The genes, coding the signaling cascade proteins (RET, RAS, BRAF, PI3K, PTEN, AKT), are mutated or aberrantly expressed in thyroid cancer derived from follicular thyroid cells. Genetic and epigenetic alternations, concerning MAPK/ERK and PI3K/Akt signaling pathways, contribute to their activation and interaction as a consequence of malignant follicular cell transformation. The understanding of this mol. mechanism provides access to novel mol. prognostic and therapeutic strategies for inhibiting the oncogenic activity of the signaling pathways. This ability to investigate tumor biol. allows for the selection of different drugs. Nowadays the most relevant are treatments directed to tyrosine kinase receptors that bind for a wide variety of ligands and are frequently mutated and induce a constitutive activation such that a chimerical protein expression takes place in follicular cells in the domain of RET, as well as in other receptors. Many mols. such as: motesanib, sorafenib, vandetanib, sunitinib, XL-184, imatinib, axitinib, pazopanib, lenvatinib, combretastatin, gefitinib, cetuximab, bortezomib and thiazoldonedione have been developed. Some of them also can act in receptors of vascular endothelial growth factor and epidermal growth factor receptors. Information obtained through cytol. or biopsy samples permits the study of complex metabolic or genetic pathways, thus providing researchers with a high throughput tool for elucidating changes in the global expression patterns seen in tumor cells and allowing for different therapeutic strategies in thyroid cancer which take into account the predominant altered pathways observed in these samples.
IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment directed to signaling mols. in patients with advanced differentiated thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

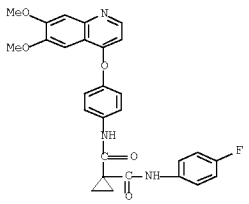
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CRN 849217-68-1
CMF C28 H24 F N3 O5



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 320 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2013:260769 CAPLUS full-text
DOCUMENT NUMBER: 158:690611
TITLE: Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial
AUTHOR(S): Smith, David C.; Smith, Matthew R.; Sweeney, Christopher; Elfiky, Aymen A.; Logothetis, Christopher; Corn, Paul G.; Vogelzang, Nicholas J.; Small, Eric J.; Harzstark, Andrea L.; Gordon, Michael S.; Vaishampayan, Ulka N.; Haas, Naomi B.; Spira, Alexander I.; Lara, Primo N., Jr.; Lin, Chia-Chi; Srinivas, Sandy; Sella, Avishay; Schoffski, Patrick; Scheffold, Christian; Weitzman, Aaron L.; Hussain, Maha
CORPORATE SOURCE: University of Michigan, Ann Arbor, USA
SOURCE: Journal of Clinical Oncology (2013), 31(4), 412-419
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.45.0494
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Cabozantinib (XL 184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. Patients and Methods: Patients received 100 mg of cabozantinib daily. Those with stable disease per RECIST at 12 wk were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 wk and progression-free survival (PFS) after random assignment. Results: One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 wk was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 wk (95% CI, 10.7 to 62.4 wk) with cabozantinib and 5.9 wk (95% CI, 5.4 to 6.6 wk) with placebo (hazard ratio, 0.12; P < .001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by ≥ 50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot



CM 2

CRN 97-67-6
CMF C4 H6 O5

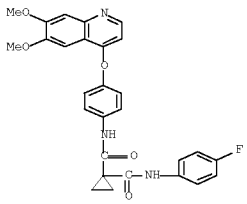
Absolute stereochemistry. Rotation (-).

syndrome (8%). Conclusion: Cabozantinib has clin. activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and redns. in bone turnover markers, pain, and narcotic use.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib improved progression-free survival, reduced soft tissue lesions, bone turnover markers, pain and narcotic use in patient with castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 135 THERE ARE 135 CAPLUS RECORDS THAT CITE THIS RECORD (135 CITINGS)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 321 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:260767 CAPLUS Full-text

DOCUMENT NUMBER: 160:42366

TITLE: Cabozantinib in prostate cancer: the beginning of a precision paradigm?

AUTHOR(S): Goodin, Susan; DiPaola, Robert S.

CORPORATE SOURCE: The Cancer Institute of New Jersey, University of Medicine and Dentistry of New Jersey Robert Wood Johnson Medical School, New Brunswick, NJ, USA

SOURCE: Journal of Clinical Oncology (2013), 31(4), 401-403
CODEN: JCONDN; ISSN: 0732-183X

DIGITAL OBJECT ID: 10.1200/JCO.2012.46.6185

PUBLISHER: American Society of Clinical Oncology

DOCUMENT TYPE: Journal; General Review

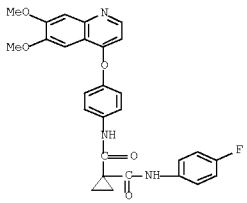
LANGUAGE: English

AB A review. The research of Smith et al. (2013) entitled, 'Cabozantinib in patients with advanced prostate cancer: Results of a phase II randomized discontinuation trial' is reviewed with commentary and refs. The authors presented data on a novel orally bioavailable tyrosine kinase inhibitor (TKI), cabozantinib, with activity against multiple targets including considerable activity in medullary thyroid cancer in a Phase III trial, including in heavily pretreated patients. Its novel combination of vascular endothelial growth factor and MET inhibition is believed to address the MET escape pathway, which is thought to be the cause of nonsustained tumor responses resulting from inhibition of vascular endothelial growth factor alone.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(profile of cabozantinib and potential in treatment of advanced medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 323 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1893113 CAPLUS Full-text

DOCUMENT NUMBER: 158:123654

TITLE: Methods of treating cancer using a chemotherapeutic agent with an agent that blocks the activity of hepatocyte growth factor or its cognate receptor c-MET.

INVENTOR(S): Golub, Todd; Straussman, Ravid

PATENT ASSIGNEE(S): The Broad Institute, Inc., USA; Dana-Farber Cancer Institute, Inc.

SOURCE: PCT Int. Appl., 104pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

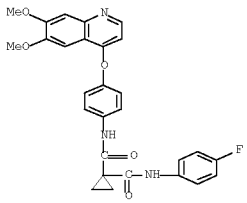
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012178038	A1	20121227	WO 2012-US43788	20120622

mesenchymal-epithelial transition factor (MET), also known as hepatocyte growth factor receptor, and the vascular endothelial growth factor receptor 2 (VEGFR2). They reported a reduction in uptake on bone scan with improvement in 68% of men (79 of 116) with bone metastasis and complete resolution in 14 patients.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 322 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2013:187940 CAPLUS Full-text

DOCUMENT NUMBER: 159:33573

TITLE: Profile of cabozantinib and its potential in the treatment of advanced medullary thyroid cancer

AUTHOR(S): Hart, Christopher D.; De Boer, Richard H.

CORPORATE SOURCE: Department of Oncology, Royal Melbourne Hospital, Parkville, Victoria, 3050, Australia

SOURCE: OncoTargets and Therapy (2013), 6, 1-7
CODEN: OTNHAZ; ISSN: 1178-6930

DIGITAL OBJECT ID: 10.2147/OTT.S27671

PUBLISHER: Dove Medical Press Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

AB A review. Medullary thyroid cancer is an uncommon malignancy for which until recently little effective treatment existed. It is often characterized by mutation and overexpression of the receptor tyrosine kinases RET (rearranged during transfection), VEGFR2 (vascular endothelial growth factor receptor 2) and MET (mesenchymal-epithelial transition factor), which make attractive targets for drug development. Cabozantinib is an orally bioavailable tyrosine kinase inhibitor which blocks MET, VEGFR2 and RET, and has shown

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140348819 A1 20141127 US 2014-14128916 20140819

PRIORITY APPLN. INFO.: US 2011-61501091 P1 20110624
WO 2012-US43788 W 20120622

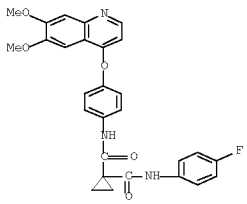
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods of treating cancer by preventing or reducing chemoresistance in a tumor by administering a chemotherapeutic agent together with another agent that blocks the activity of hepatocyte growth factor or its cognate receptor c-MET.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer treatment using a chemotherapeutic agent with an agent that blocks the activity of HGF or its cognate receptor c-MET)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

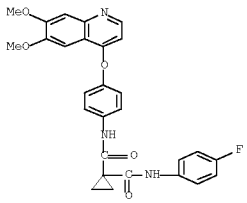


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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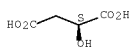
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

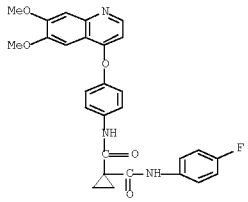
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



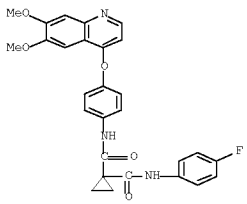
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 324 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1845709 CAPLUS Full-text
DOCUMENT NUMBER: 158:644003
TITLE: New agents in metastatic prostate cancer
AUTHOR(S): Choudhury, Atish D.; Kantoff, Philip W.
CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE: Journal of the National Comprehensive Cancer Network (2012), 10(11), 1403-1409
CODEN: JNCCA4; ISSN: 1540-1405
PUBLISHER: Harborside Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Discoveries of mol. mechanisms and therapeutic targets in metastatic castration-resistant prostate cancer (CRPC) have led to significant advancements in the development of effective agents in this setting, with diverse mechanisms of action. Within the past 2 years, 5 agents have been approved for the treatment of patients with metastatic CRPC (cabazitaxel, abiraterone, sipuleucel-T, denosumab, and enzalutamide), and another (Alpharadin) has shown overall survival benefit in a phase III trial. This article summarizes the phase III data showing clin. benefit from these agents, highlights other promising therapies in phase III studies as single agents (PROSTVAC-VF, ipilimumab, cabozantinib), discusses important unanswered questions regarding these therapies, and provides a schema for their use based on current regulatory approval and how this is likely to evolve as data from ongoing studies are reported. Although curative interventions in metastatic CRPC still do not exist, the hope is that optimization of therapeutic strategies can reduce the morbidity and mortality associated with this disease.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new agents in metastatic prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 325 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1765841 CAPLUS Full-text
DOCUMENT NUMBER: 158:670189
TITLE: Cabozantinib for the Treatment of Advanced Medullary Thyroid Cancer
AUTHOR(S): Nagilla, Madhavi; Brown, Rebecca L.; Cohen, Ezra E. W.
CORPORATE SOURCE: Section of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Chicago, Chicago, IL, 60645, USA
SOURCE: Advances in Therapy (2012), 29(11), 925-934
CODEN: ADTHE7; ISSN: 0741-238X
DIGITAL OBJECT ID: 10.1007/s12325-012-0060-6
PUBLISHER: Springer Healthcare Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Introduction Patients with advanced medullary thyroid cancer (MTC) have poor prognoses and limited treatment options. Improved knowledge about mol. aberrations associated with MTC and the availability of novel targeted tyrosine kinase inhibitors (TKIs) have led to new potential treatment modalities. Cabozantinib is an oral multitargeted TKI with activity against multiple receptors including RET, vascular endothelial growth factor receptor type 2 (VEGFR2), and MET that has been evaluated in MTC in the preclin. and clin. arenas. Methods This article reviews unmet clin. needs in advanced MTC. The authors consider novel agents that have been studied in MTC, with a focus on the investigational agent cabozantinib. Up-to-date clin. data of cabozantinib in MTC are discussed. Results Recent clin. evaluation suggests that cabozantinib is the first agent to prolong progression-free survival in patients with progressive MTC. These findings indicate that cabozantinib may be an effective therapy in advanced MTC. No improvement in overall survival has been demonstrated but data are not mature. Conclusion Cabozantinib may be an effective treatment option for patients with advanced MTC and is worthy of further evaluation.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for the treatment of advanced medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



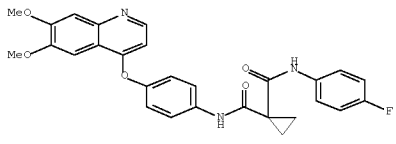
OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 326 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1630842 CAPLUS Full-text
DOCUMENT NUMBER: 157:699601
TITLE: Method of treating cancer and bone cancer pain
INVENTOR(S): Schwab, Gisela; Aftab, Dana T.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012151326	A1	20121108	WO 2012-US36191	20120502
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2834778	A1	20121108	CA 2012-2834778	20120502
AR 86242	A1	20131127	AR 2012-101544	20120502
AU 2012250759	A1	20131128	AU 2012-250759	20120502
IL 229094	A	20131231	IL 2012-229094	20120502
KR 2014025496	A	20140304	KR 2013-7031635	20120502
EP 2704717	A1	20140312	EP 2012-720754	20120502
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CN 103717221	A	20140409	CN 2012-80026424	20120502
JP 2014513129	T	20140529	JP 2014-509417	20120502
BR 112013028314	U2	20151103	BR 2013-212013028314	20120502
MX 2013012695	A	20140327	MX 2013-12695	20131030
ZA 2013008206	A	20140730	ZA 2013-8206	20131101
IN 2013KN03259	A	20140221	IN 2013-KN3259	20131105
US 20140179736	A1	20140626	US 2014-14115236	20140228
PRIORITY APPLN. INFO.:			US 2011-61481682 P	20110502
			US 2011-61557366 P	20111108
			WO 2012-US36191 W	20120502

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:699601; MARPAT 157:699601
GI

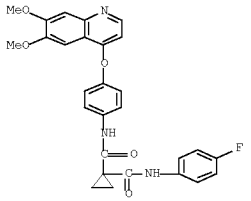


AB This invention is directed to the treatment of cancer, particularly lung cancer, breast cancer, melanoma, renal cell carcinoma, thyroid cancer that has metastasized to the bone. The invention is also directed to a method for treating bone cancer pain in an individual in need of such treatment comprising administering to the individual an effective amount of a compound of Formula I.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(method of treating cancer and bone cancer pain)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



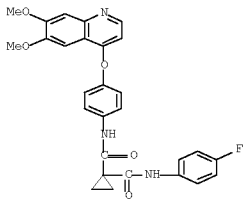
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cancer and bone cancer pain)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

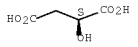
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



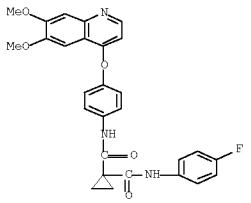
IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cancer and bone cancer pain)

RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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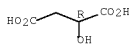
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 327 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1563334 CAPLUS Full-text

DOCUMENT NUMBER: 158:492390

TITLE: New developments in castrate-resistant prostate cancer

AUTHOR(S): Shore, N.; Mason, M.; de Reijke, Th. M.

CORPORATE SOURCE: Carolina Urologic Research Center, Atlantic Urology Clinics, Myrtle Beach, SC, USA

SOURCE: BJU International (2012), 109(Suppl. 6), 22-32
CODEN: BJINFO; ISSN: 1464-4096

DIGITAL OBJECT ID: 10.1111/j.1464-410X.2012.11217.x

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; General Review

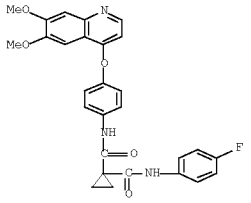
LANGUAGE: English

AB A review. Castrate-resistant prostate cancer (CRPC) occurs when disease progresses in the presence of castrate levels of androgens and remains sensitive to further hormonal manipulation. For many years the treatment of CRPC was limited to the use of docetaxel for metastatic disease. However, this has recently changed with the approval of several new agents. Sipuleucel-T, an immunotherapeutic vaccine, is now available in the US for patients with non-metastatic CRPC and abiraterone, an oral enzyme inhibitor of androgen biosynthesis, as well as cabazitaxel, a cytotoxic chemotherapeutic, have been approved for the treatment of metastatic CRPC. Also, denosumab, a s.c. antibody, is now an option for the treatment of patients with CRPC with bone metastases, in addition to zoledronic acid, an i.v. bisphosphonate. Further treatment advances for metastatic CRPC therapeutics are in late stage phase III development. These include therapies affecting the androgen receptor (MDV3100) as well as addnl. immune-based therapeutics, PROSTVAC and ipilimumab. A broad range of agents is also emerging under the term targeted therapies. The endothelin-A receptor antagonist zibotentan, the tyrosine kinase inhibitors dasatinib, sorafenib and cabozantinib, the anti-angiogenic agent aflibercept, and the clusterin inhibitor custirsen, are all currently being tested for efficacy in metastatic CRPC. The mechanism of action of these and other promising agents are discussed alongside current therapeutic options and their potential place in the treatment landscape for CRPC is considered.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new developments in castrate-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 328 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:1483426 CAPLUS Full-text

DOCUMENT NUMBER: 157:573884

TITLE: Methods for predicting and improving the survival of gastric cancer patients

INVENTOR(S): Kim, Phillip; Singh, Sharat

PATENT ASSIGNEE(S): Nestec SA, Switz.

SOURCE: PCT Int. Appl., 147pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012138785	A1	20121011	WO 2012-US32206	20120404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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CA 2831468	A1	20121011	CA 2012-2831468	20120404
AU 2012240242	A1	20131010	AU 2012-240242	20120404
IL 228579	A	20131128	IL 2012-228579	20120404
EP 2694972	A1	20140212	EP 2012-716858	20120404
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CN 103597354	A	20140219	CN 2012-80027365	20120404
CN 103597354	B	20160420		
JP 2014517259	T	20140717	JP 2014-503964	20120404
NZ 615738	A	20151127	NZ 2012-615738	20120404
SG 10201601301	A1	20160330	SG 2016-10201601301	20120404
MX 2013011431	A	20140606	MX 2013-11431	20130930
US 20140099300	A1	20140410	US 2013-14044792	20131002

PRIORITY APPLN. INFO.:
US 2011-61471678 P 20110404
US 2012-61590787 P 20120125
WO 2012-US32206 W 20120404

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides assays and methods for predicting the post-operative survival of a subject having an early stage gastric cancer after tumor surgery. The present invention also provides methods for treating a subject having an early stage gastric cancer by administering a combination therapy tailored to the signal transduction biomarkers that are activated in the cancer. In particular embodiments, the methods of the invention rely on the detection of the activation state or level of a specific combination of signal transducer analytes in a cancer cell obtained from the subject. Thus, the methods of the invention are particularly useful for predicting the survival or prognosis of a subject having an early stage gastric cancer and for guiding both pre- and post-operative treatment decisions by identifying subjects who would benefit from combination therapy as opposed to monotherapy.

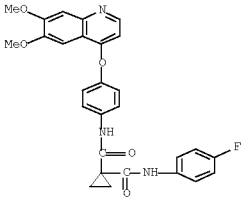
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cMET and HER as markers and drug targets for predicting survival of a subject having type I or II gastric cancer after tumor surgery)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

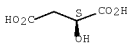
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 329 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1450760 CAPLUS Full-text
DOCUMENT NUMBER: 157:567006
TITLE: Method of treating cancer
INVENTOR(S): Aftab, Dana T.; Schimmoller, Frauke
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 17pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120252840	A1	20121004	US 2012-13438964	20120404
US 20150196545	A1	20150716	US 2015-14668312	20150325
US 20160051532	A1	20160225	US 2015-14933801	20151105

PRIORITY APPLN. INFO.:
US 2011-61471367 P 20110404
US 2012-13438964 A1 20120404
US 2015-14668312 A1 20150325

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

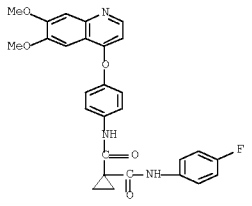
OTHER SOURCE(S): CASREACT 157:567006

AB This invention is directed to the treatment of cancer, particularly ocular melanoma, with a dual inhibitor of MET and VEGF such as Compound 1.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(method of treating cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



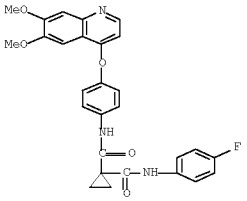
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

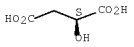
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



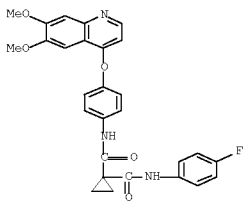
IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cancer)

RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

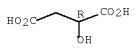
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



L8 ANSWER 330 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1270117 CAPLUS Full-text
DOCUMENT NUMBER: 157:438359
TITLE: Preparation of substituted quinoline compounds as protein tyrosine kinase modulators
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., USA; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120219522	A1	20120830	US 2012-13400586	20120221
US 9133162	B2	20150915		
CA 2820709	A1	20120907	CA 2012-2820709	20120221
CA 2820709	C	20160216		
WO 2012118632	A1	20120907	WO 2012-US25834	20120221

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,

MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

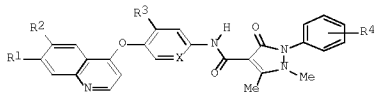
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

KR 2013095806	A	20130828	KR 2013-7015842	20120221
KR 1546693	B1	20150824		
EP 2680886	A1	20140108	EP 2012-752321	20120221
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JP 2014506925	T	20140320	JP 2013-556713	20120221
JP 5707518	B2	20150430		
ZA 2013003793	A	20140730	ZA 2013-3793	20120221
AU 2012223639	B2	20150319	AU 2012-223639	20120221
RU 2568258	C2	20151120	RU 2013-135662	20120221
MX 2013007278	A	20130913	MX 2013-7278	20130621
US 20150342945	A1	20151203	US 2015-14824096	20150812

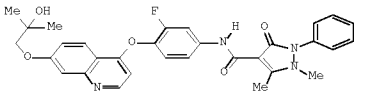
PRIORITY APPLN. INFO.:

US 2011-61447104	P	20110228
US 2012-13400586	A3	20120221
WO 2012-US25834	W	20120221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:438359; MARPAT 157:438359
GI



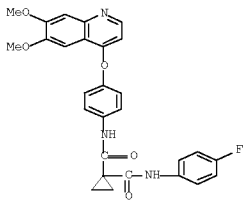
I



II

AB The present invention provides novel substituted quinoline compds. I [R1, R2 = H, alkoxy, hydroxyalkoxy; R3 = H, F; R4 = H, F, Cl, Br, I, etc.; X = CH or N, wherein at least one of R1 and R2 = hydroxyalkoxy], pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. Syntheses of exemplified compds. I were described. E.g., a multi-step synthesis of the pyrazolecarboxamide II, starting from 3-benzyloxybenzenamine, was provided. Exemplified compds. I were tested for their efficacy as inhibitors of receptor tyrosine kinases such as c-Met, VEGFR and Axl, and as antitumor agents (data given). The invention also provides pharmaceutically acceptable compns. comprising compds. I and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted quinoline compds. as protein tyrosine
kinase modulators)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 331 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1269771 CAPLUS Full-text
DOCUMENT NUMBER: 157:431629
TITLE: Methods for detecting cancer and/or determining response to therapeutic agent, and numerous circulating markers (including proteins, nucleic acids and vesicles) used in said methods
INVENTOR(S): Spetzler, David; Holterman, Daniel A.; Pawlowski, Traci; Tasinato, Andrea
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, S.A.R.L., Luxembourg
SOURCE: PCT Int. Appl., 695pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012115885	A1	20120830	WO 2012-US25741	20120217

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2827894	A1	20120830	CA 2012-2827894	20120217
AU 2012220872	A1	20130912	AU 2012-220872	20120217
CN 103492590	A	20140101	CN 2012-80019718	20120217
EP 2678448	A1	20140101	EP 2012-749642	20120217
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2014507160	T	20140327	JP 2013-555467	20120217
US 20140141986	A1	20140522	US 2014-14001016	20140207
AU 2015268602	A1	20160107	AU 2015-268602	20151209

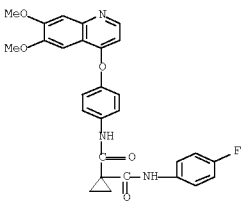
PRIORITY APPLN. INFO.:

US 2011-61445273	P	20110222
US 2011-61446313	P	20110224
US 2011-61471417	P	20110404
US 2011-61501680	P	20110627
US 2011-61523763	P	20110815
AU 2011-291599	A3	20110818
WO 2012-US25741	W	20120217

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods for detecting cancer, for detg. whether a cancer is responding to treatment, and /or for determining whether a cancer is likely to respond to treatment that involve detecting of circulating biomarkers. The invention relates that said circulating biomarkers can include nucleic acids, proteins, vesicles and/or microRNAs. The invention also relates that said biol. samples used in the disclosed methods include isolated extracellular microvesicle populations. The invention also provides kits comprising all reagents used in the disclosed methods. In the examples, the invention disclosed that specific biomarkers are elevated in specific types of cancer, which can used in diagnosis and in determining treatments.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for detecting cancer and/or determining response to therapeutic agent, and numerous circulating markers (including proteins, nucleic acids and vesicles) used in said methods)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

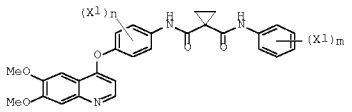


OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

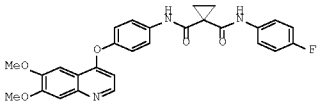
L8 ANSWER 332 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1201570 CAPLUS Full-text
DOCUMENT NUMBER: 157:382704
TITLE: Processes for preparing quinoline compounds and pharmaceutical compositions containing such compounds
INVENTOR(S): Wilson, Jo Ann
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012109510	A1	20120816	WO 2012-US24591	20120210
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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CA 2826751	A1	20120816	CA 2012-2826751	20120210
AU 2012214322	A1	20130829	AU 2012-214322	20120210
AR 85155	A1	20130911	AR 2012-100446	20120210
IL 227848	A	20130930	IL 2012-227848	20120210
CN 103459373	A	20131218	CN 2012-80017723	20120210
EP 2673262	A1	20131218	EP 2012-704492	20120210
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2014505109	T	20140227	JP 2013-553580	20120210
KR 2014044782	A	20140415	KR 2013-7023174	20120210
NZ 614130	A	20151030	NZ 2012-614130	20120210
MX 2013009116	A	20140131	MX 2013-9116	20130807
ZA 2013006072	A	20140430	ZA 2013-6072	20130813
IN 2013KN02666	A	20140103	IN 2013-KN2666	20130903
US 20140200242	A1	20140717	US 2014-13984559	20140320

PRIORITY APPLN. INFO.: US 2011-61441520 P 20110210
US 2011-61441527 P 20110210
WO 2012-US24591 W 20120210
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:382704; MARPAT 157:382704
GI

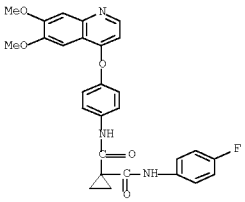


I



II

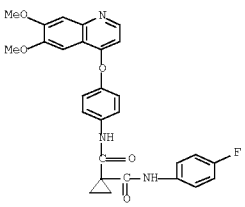
AB The invention is directed to processes for prepg. quinoline compds. of formula I wherein X1 is H, Br, Cl and F; X2 is H, Br, Cl and F; n is 1-2 and m is 1-2; and pharmaceutically acceptable salts thereof. Example compound II L-malate was prepared by chlorination of 6,7-dimethoxyquinolin-4-ol followed by etherification of 4-chloro-6,7-dimethoxyquinoline with 4-aminophenol; the resulting 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine underwent acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropanecarbonyl chloride to give compound II, which underwent addition of L-malic acid to give the desired product.
IT 849217-68-1
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for preparing quinoline derivs. and pharmaceutical compns. thereof)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparing quinoline derivs. and pharmaceutical compns. thereof)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

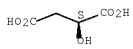
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

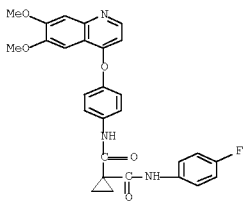


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 333 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1051547 CAPLUS Full-text
DOCUMENT NUMBER: 157:218520
TITLE: Molecular diagnostic methods for predicting brain metastasis of breast cancer
INVENTOR(S): Wong, Stephen T. C.; Zhao, Hong
PATENT ASSIGNEE(S): The Methodist Hospital Research Institute, USA
SOURCE: U.S. Pat. Appl. Publ., 53pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120184560	A1	20120719	US 2011-13245706	20110926

PRIORITY APPLN. INFO.: US 2010-61386186 P 20100924
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Disclosed are mol. diagnostic compns. and methods for predicting brain metastasis of breast cancer, as well as methods for drug repositioning to identify existing and new therapeutics for use in developing individualized, patient-specific treatment regimens for improving diagnoses and patient outcomes in individuals at risk for brain metastasis of breast cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. diagnostic methods for predicting brain metastasis of breast cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 334 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:1042874 CAPLUS Full-text
DOCUMENT NUMBER: 157:221701
TITLE: Bcl-2-like protein 11 (BIM) SRM/MRM assay
INVENTOR(S): Krizman, David B.; Hembrough, Todd; Thyparambil, Sheeno; Liao, Wei-Li
PATENT ASSIGNEE(S): Expression Pathology, Inc., USA
SOURCE: PCT Int. Appl., 28pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

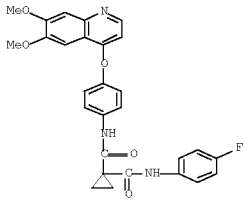
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012097276	A2	20120719	WO 2012-US21283	20120113
WO 2012097276	A3	20121129		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2824752	A1	20120719	CA 2012-2824752	20120113
AU 2012205337	A1	20130801	AU 2012-205337	20120113
IL 227471	A	20130829	IL 2012-227471	20120113
EP 2663863	A2	20131120	EP 2012-734572	20120113
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2014505251	T	20140227	JP 2013-549580	20120113
US 20130302334	A1	20131114	US 2013-13942574	20130715

PRIORITY APPLN. INFO.: US 2011-61432462 P 20110113
WO 2012-US21283 W 20120113

AB Specific peptides, and derived ionization characteristics of those peptides, from the Bcl-2-like protein 11 (BIM) are provided that are particularly advantageous for quantifying the BIM protein directly in biol. samples that have been fixed in formalin by the method of Selected Reaction Monitoring (SRM) mass spectrometry, or what can also be termed as Multiple Reaction Monitoring (MRM). Such biol. samples are chemical preserved and fixed where the biol. sample is selected from tissues and cells treated with formaldehyde containing agents/fixatives including formalin-fixed tissue/cells, formalin- fixed/paraffin embedded (FFPE) tissue/cells, FFPE tissue blocks and cells from those blocks, and tissue culture cells that have been formalin fixed and or paraffin embedded. A protein sample is prepared from the biol. sample using the Liquid Tissue reagents and protocol, and the BIM protein is quantitated in the Liquid Tissue sample by the method of SRM/MRM mass spectrometry by quantitating in the protein sample at least one or more of the peptides described. These peptides can be quantitated if they reside in a modified or an unmodified form. An example of a modified form of a BIM peptide is phosphorylation of a tyrosine, threonine, serine, and/or other amino acid residues within the peptide sequence. Samples were prepared with Liquid Tissue and digested with trypsin. Three peptides from BIM were found to be suitable for SRM/MRM assay.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(determination of cancer resistance to; BIM protein determination by determining BIM peptides by SRM/MRM mass spectrometry)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L8 ANSWER 335 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:924299 CAPLUS Full-text
DOCUMENT NUMBER: 157:122897
TITLE: Drug selection for therapy for malignancies involving c-Met signaling using antibody-based arrays
INVENTOR(S): Singh, Sharat; Hoe, Nicholas; Princen, Fred; Liu, Xinjun
PATENT ASSIGNEE(S): Prometheus Laboratories Inc., USA
SOURCE: PCT Int. Appl., 140pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012088337	A1	20120628	WO 2011-US66624	20111221
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2822283	A1	20120628	CA 2011-2822283	20111221
AU 2011348256	A1	20130711	AU 2011-348256	20111221
IL 227009	A	20130829	IL 2011-227009	20111221
EP 2656077	A1	20131030	EP 2011-805738	20111221
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 103384828	A	20131106	CN 2011-80068269	20111221
KR 2014002711	A	20140108	KR 2013-7019356	20111221
JP 2014503821	T	20140213	JP 2013-546392	20111221
NZ 612483	A	20150327	NZ 2011-612483	20111221
SG 10201510086	A1	20160128	SG 2015-10201510086	20111221
US 20140024548	A1	20140123	US 2013-13923316	20130620
MX 2013007429	A	20140131	MX 2013-7429	20130621

PRIORITY APPLN. INFO.: US 2010-61426948 P 20101223
US 2011-61438904 P 20110202
WO 2011-US66624 W 20111221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

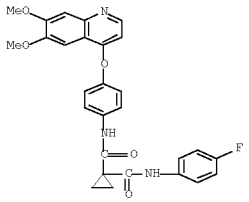
AB The present invention provides methods for selecting a suitable anticancer drug therapy, and for identifying and predicting response, for the treatment of a malignant cancer involving aberrant c-Met signaling. The present invention also provides methods for monitoring the status of a malignant cancer involving aberrant c-Met signaling and monitoring how a patient with the malignant cancer is responding to anticancer drug therapy. Information on the expression and/or activation states of components of signal transduction pathways (e.g., HER3 and/or c-Met signal transduction pathway components) derived from practice of the present invention can be used for malignant cancer diagnosis, prognosis, and in the design of cancer treatments for malignancies involving aberrant c-Met signaling. Certain embodiments comprise administering a cMet inhibitor alone or a cMet inhibitor in combination with a pathway-directed therapy based upon the differences between the expression and/or activation levels of cMet protein and/or HER3 protein in the sample compared to the control protein and/or control sample.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for therapy for malignancies involving aberrant c-Met signaling using antibody-based arrays)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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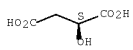
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 336 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:706472 CAPLUS Full-text
DOCUMENT NUMBER: 156:628365

TITLE: Cancer cell-derived receptor activator of the NF-KB ligand drives bone and soft tissue metastases
INVENTOR(S): Chu, Gina C. Y.; Chung, Leland W. K.; Zhau, Haiyen E.; Wang, Ruoxiang
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012064967	A2	20120518	WO 2011-US60204	20111110
WO 2012064967	A3	20120705		

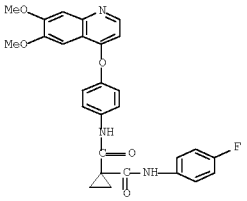
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 20130263297	A1	20131003	US 2013-13889135	20130507

PRIORITY APPLN. INFO.:
US 2010-61412360 P 20101110
US 2011-61442679 P 20110214
WO 2011-US60204 A2 20111110
US 2012-61718626 P 20121025
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention relates to metastases. More specifically, the invention relates to compns. and methods for the inhibition of metastases of cancer cells, such as prostate cancer cells, to bones and soft tissue. The present invention also relates to the treatment of cancer, including but not limited to prostate cancer. Also provided are animal models for studying cancer metastasis; particularly, prostate cancer metastasis.
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer cell-derived receptor activator of the NF-KB ligand drives bone and soft tissue metastases)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

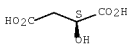
CRN 849217-68-1
CMF C28 H24 F N3 O5



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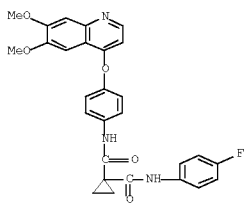
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



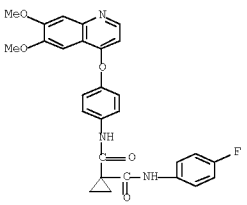
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L8 ANSWER 337 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:560657 CAPLUS Full-text
DOCUMENT NUMBER: 158:122090
TITLE: Recent advances in the molecular pathogenesis and targeted therapies of medullary thyroid carcinoma
AUTHOR(S): Almeida, Madson Q.; Hoff, Ana O.
CORPORATE SOURCE: Instituto do Cancer da Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil
SOURCE: Current Opinion in Oncology (2012), 24(3), 229-234
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e328351c71a
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: This review will focus on the recent advances in mol. pathogenesis and targeted therapies for medullary thyroid carcinoma (MTC). Unlike hereditary MTC in which rearranged during transfection (RET) mutations are the most important precipitating events, in sporadic MTC the genetic or mol. biomarkers are yet to be established. Recent findings: Targeted mol. therapies that inhibit RET and other tyrosine kinase receptors involved in angiogenesis have shown great promise in the treatment of metastatic or locally advanced MTC and are under investigation. In addition, the recent findings of H-RAS mutations in 56% of RET-neg. sporadic MTC and the activation of the mammalian target of rapamycin (mTOR) intracellular signaling pathway in hereditary MTC suggests that addnl. or alternative genetic events are important for MTC pathogenesis. Summary: Recently, vandetanib (ZD6474), an inhibitor of vascular endothelial growth factor receptor (VEGFR) 2 and VEGFR 3, RET, and epidermal growth factor receptor (EGFR), was approved for the treatment of adults with symptomatic or progressive MTC. Significant advantages for vandetanib over placebo were seen in terms of response rate, disease control rate, and biochem. response in a phase III study. Furthermore, cabozantinib (XL184), an inhibitor of VEGFR 1 and VEGFR 2, hepatocyte growth factor receptor (MET), and RET, was associated with partial response and stable disease in 29 and 41%, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vandetanib and cabozantinib was effective in treatment of patient with medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 338 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:508891 CAPLUS Full-text
DOCUMENT NUMBER: 158:93453
TITLE: Novel Molecular Targets for the Therapy of Castration-Resistant Prostate Cancer
AUTHOR(S): Agarwal, Neeraj; Sonpavde, Guru; Sternberg, Cora N.
CORPORATE SOURCE: Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA
SOURCE: European Urology (2012), 61(5), 950-960
CODEN: EUURAV; ISSN: 0302-2838
DIGITAL OBJECT ID: 10.1016/j.eururo.2011.12.028
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Improved understanding of mechanisms underlying metastatic castration-resistant prostate cancer (mCRPC) progression has led to the recognition of multiple mol. targets and advances in the therapeutic landscape. The addition of abiraterone acetate, sipuleucel-T, cabazitaxel, and denosumab to the therapeutic armamentarium and the impending addition of MDV-3100 and radium-223 underscore the importance of androgen pathway inhibition, immunotherapy, tubulin antagonism, and pathophysiol. of bone metastasis. Review the next generation of mol. targets in mCRPC. Medline databases were searched for >100 original articles published as of Oct. 18, 2011, with the search terms metastatic castration-resistant prostate cancer, targeted therapy, biol. agents, and immunotherapy. Proceedings from the last 5 yr of conferences of the American Society of Clin. Oncol., American Urol. Association, European Society of Medical Oncol., and the European Association of Urol. were also searched. We included novel and promising drugs that have reached clin. trial evaluation. The major findings were addressed in an evidence-based fashion. Prospective trials and important preclin. data were analyzed.mCRPC is a disease with multiple mol. drivers. Mol. pathways being targeted in ongoing phase 3 trials are androgen signaling (MDV3100, TAK700), immunoregulatory pathways (ipilimumab, Prostvac-VF-TRICOM), Src (dasatinib), Met (cabozantinib), clusterin (custirsen), and angiogenesis (aflibercept, tasquinimod). The strides made in identifying multiple other novel mol. targets offer potential opportunities for further improving outcomes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(knowledge on novel mol. targets like Met signaling pathway using drugs like cabozantinib could be more beneficial in patient with metastatic castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



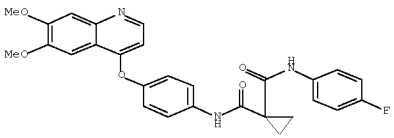
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REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 339 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:495814 CAPLUS Full-text
DOCUMENT NUMBER: 156:469436
TITLE: Dual inhibitors of Met and VEGF for the treatment of castration- resistant prostate cancer and osteoblastic bone metastases
INVENTOR(S): Smith, David; Hussain, Maha
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

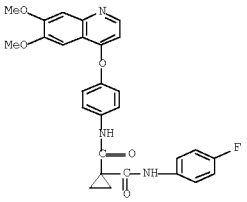
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WO 2012044572	A1	20120405	WO 2011-US53233	20110926
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AU 2011307304	A1	20130502	AU 2011-307304	20110926
IL 225507	A	20130530	IL 2011-225507	20110926
EP 2621481	A1	20130807	EP 2011-764655	20110926
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2013537916	T	20131007	JP 2013-530386	20110926
CN 103402505	A	20131120	CN 2011-80056580	20110926
KR 2014025304	A	20140304	KR 2013-7010372	20110926
MX 2013003594	A	20130801	MX 2013-3594	20130327
ZA 2013002422	A	20131223	ZA 2013-2422	20130404
IN 2013KN00998	A	20130906	IN 2013-KN998	20130409
US 20140057943	A1	20140227	US 2013-13876290	20131105

PRIORITY APPLN. INFO.: US 2010-61386959 P 20100927
US 2011-61481671 P 20110502
WO 2011-US53233 W 20110926
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:469436; MARPAT 156:469436
GI



AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and osteoblastic bone metastases, with a dual inhibitor of MET and VEGF.

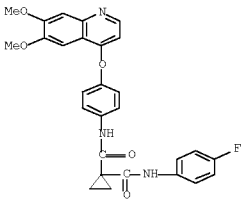
IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

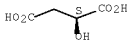
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

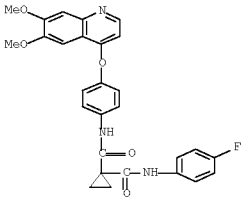
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3P
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

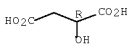
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 340 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:495788 CAPLUS Full-text
DOCUMENT NUMBER: 156:469435
TITLE: Dual inhibitors of Met and VEGF for the treatment of castration resistant prostate cancer and osteoblastic bone metastases
INVENTOR(S): Smith, David; Hussain, Maha
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012044577	A1	20120405	WO 2011-US53245	20110926
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,				

MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2812744	A1	20120405	CA 2011-2812744		20110926
AU 2011307309	A1	20130502	AU 2011-307309		20110926
EP 2621483	A1	20130807	EP 2011-764657		20110926
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR					
JP 2013537918	T	20131007	JP 2013-530392		20110926
CN 103391773	A	20131113	CN 2011-80056999		20110926
US 20140057908	A1	20140227	US 2013-13876306		20131108
PRIORITY APPLN. INFO.:			US 2010-61386971	P	20100927
			US 2010-61386983	P	20100927
			US 2010-61386993	P	20100927
			WO 2011-US53245	W	20110926

OTHER SOURCE(S): CASREACT 156:469435; MARPAT 156:469435

AB This invention discloses compds. directed at the treatment of cancer, particularly castration- resistant prostate cancer and osteoblastic bone metastases, with a dual inhibitor of MET and VEGF.

IT 1140909-48-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

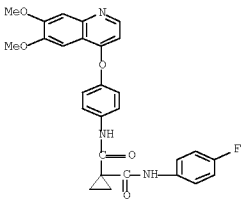
RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1

CMF C28 H24 F N3 O5

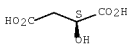


CM 2

CRN 97-67-6

CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



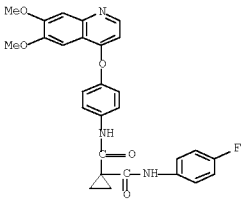
IT 849217-68-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 341 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2012:425741 CAPLUS Full-text

DOCUMENT NUMBER: 156:412018

TITLE: Methods of using C-met modulators as Anticancer agents

INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-Ming; Forsyth, Timothy Patrick; Khoury, Richard George; Leahy, James William; Mac, Morrison B.; Mann, Larry W.; Nuss, John M.; Parks, Jason Jevious; Wang, Yong; Xu, Wei; Simeone, Diane

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 25pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

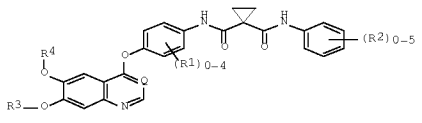
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20120070368	A1	20120322	US 2011-13087094		20110414
US 20150202196	A1	20150723	US 2014-14518733		20141020
PRIORITY APPLN. INFO.:			US 2010-61325095	P	20100416
			US 2011-13087094	B1	20110414

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 156:412018; MARPAT 156:412018

GI



I

AB Disclosed are methods of treating cancer by administering a compd. of Formula I (wherein R1, R2 = independently, halo; R3, R4 = independently, (C1-C6)-alkyl; Q = CH, N) in combination with gemcitabine (GEM).

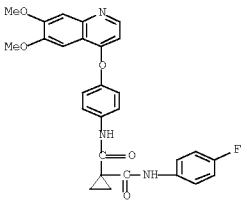
IT 849217-68-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(c-met modulators as antitumor agents)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1365530-43-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(c-met modulators as antitumor agents)

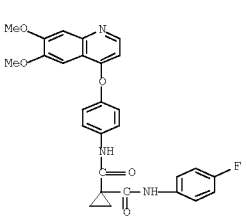
RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1

CMF C28 H24 F N3 O5

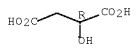


CM 2

CRN 636-61-3

CMF C4 H6 O5

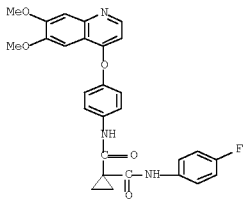
Absolute stereochemistry. Rotation (+).



L8 ANSWER 342 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:373163 CAPLUS Full-text
DOCUMENT NUMBER: 157:622817
TITLE: Multi-targeted tyrosine kinase inhibitors in clinical development: focus on XL-184 (cabozantinib)
AUTHOR(S): Bowles, D. W.; Kessler, E. R.; Jimeno, A.
CORPORATE SOURCE: Division of Medical Oncology, University of Colorado Denver, Aurora, CO, USA
SOURCE: Drugs of Today (2011), 47(11), 857-868
CODEN: MDACAP; ISSN: 1699-3993
DIGITAL OBJECT ID: 10.1358/dot.2011.47.11.1688487
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. XL-184 (cabozantinib) is a novel, small-mol., multi-targeted receptor tyrosine kinase inhibitor with particular activity against hepatocyte growth factor receptor (tyrosine-protein kinase Met), vascular endothelial growth factor receptor 2 (VEGFR-2) and proto-oncogene tyrosine-protein kinase receptor Ret. There is ample evidence of Met, VEGFR-2 and Ret signaling in several tumor types. Preclin. data suggest that XL-184 has activity in tumors derived from both epithelial and mesenchymal origins. Phase I and II clin. studies support significant antitumor activity, particularly in medullary thyroid cancer and cancers metastatic to the bone. This review will evaluate XL-184's preclin. pharmacol., pharmacokinetics, drug interactions and clin. activity in phase I through phase III studies.
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(focus on XL-184 (cabozantinib) is a novel multi-targeted tyrosine kinase inhibitors in clin. development)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

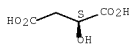
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

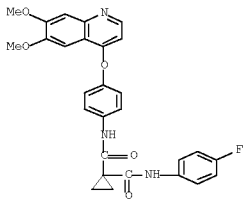
L8 ANSWER 343 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:345887 CAPLUS Full-text
DOCUMENT NUMBER: 156:388076
TITLE: C-met biomarker in treatment efficacy and prognosis
INVENTOR(S): Patel, Premal; Peterson, Amy C.; Yauch, Robert L.; Zha, Jiping
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 134pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012031027	A1	20120308	WO 2011-US50069	20110831
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2808236	A1	20120308	CA 2011-2808236	20110831
US 20120089541	A1	20120412	US 2011-13223173	20110831
AU 2011295919	A1	20130307	AU 2011-295919	20110831
IL 224962	A	20130430	IL 2011-224962	20110831
EP 2612151	A1	20130710	EP 2011-754597	20110831
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 103221825	A	20130724	CN 2011-80051781	20110831
KR 2013103734	A	20130924	KR 2013-7008025	20110831
JP 2013537966	T	20131007	JP 2013-526209	20110831
ZA 2013001175	A	20140430	ZA 2013-1175	20110831
SG 10201408229	A1	20150227	SG 2014-10201408229	20110831
MX 2013002084	A	20130509	MX 2013-2084	20130221
IN 2013DN01711	A	20141024	IN 2013-DN1711	20130225
AU 2013202759	A1	20130502	AU 2013-202759	20130406
US 20140037625	A1	20140206	US 2013-14046867	20131004
AU 2016200630	A1	20160218	AU 2016-200630	20160202

PRIORITY APPLN. INFO.:

US 2010-61378911	P	20100831
US 2010-61389922	P	20101005
US 2010-61390995	P	20101007
US 2010-61420703	P	20101207
US 2011-61487527	P	20110518
US 2011-61492338	P	20110601
US 2011-61503489	P	20110630
AU 2011-295919	A3	20110831
US 2011-13223173	B1	20110831
WO 2011-US50069	W	20110831
AU 2013-202759	A3	20130406

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose the use of c-met as a biomarker for patient selection and patient prognosis in cancer. In a clin. trial, combination treatment with MetMAb (onartuzumab) and erlotinib provided a clin. meaningful benefit to patients with non-small cell lung cancer (NSCLC) that expressed high levels of c-met biomarker. The results showed that the efficacy, as evaluated by progression free survival (PFS) and overall survival (OS), was pos. especially when compared to PFS and OS data for erlotinib treatment alone. The addition of MetMAb to erlotinib nearly doubled the progression free and overall survival in patients with NSCLC that expressed high levels of c-met biomarker. The clin. trial data also showed that treatment with MetMAb in combination with erlotinib increased the risk of progression and death in patients with NSCLC that expressed low levels of c-met biomarker.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Met receptor as biomarker for combination therapy efficacy and cancer prognosis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

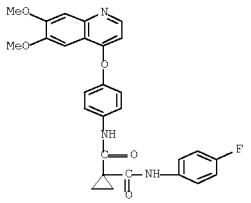
L8 ANSWER 344 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:340365 CAPLUS Full-text
DOCUMENT NUMBER: 156:380310
TITLE: Synergistic drug combination for the treatment of cancer
INVENTOR(S): Gusenbauer, Simone; Ullrich, Axel
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 111pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2425830	A1	20120307	EP 2010-75382	20100903
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BA, ME, RS				

PRIORITY APPLN. INFO.: EP 2010-75382 20100903
AB The invention relates to synergistic drug combinations and the use of said drug combinations for the treatment of proliferative diseases such as cancer. Combination of drugs include e.g. chlorethamine, cyclophosphamide, trofosfamide, daunorubicin, doxorubicin, mitomycin C.
IT 1140909-48-3, X1184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic drug combination for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

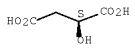
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 345 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:265414 CAPLUS Full-text
DOCUMENT NUMBER: 156:357951
TITLE: Circulating biomarkers for disease
INVENTOR(S): Spetzler, David; Holterman, Daniel; Pawlowski, Traci; Kuslich, Christine
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, Luxembourg
SOURCE: PCT Int. Appl., 639pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012024543	A1	20120223	WO 2011-US48327	20110818
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2808417	A1	20120223	CA 2011-2808417	20110818
AU 2011291599	A1	20130307	AU 2011-291599	20110818
AU 2011291599	B2	20150910		
EP 2606353	A1	20130626	EP 2011-818814	20110818
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2013540995	T	20131107	JP 2013-526012	20110818
US 20140148350	A1	20140529	US 2013-13817383	20130520
US 20150301055	A1	20151022	US 2015-14789729	20150701
AU 2015268602	A1	20160107	AU 2015-268602	20151209

PRIORITY APPLN. INFO.:

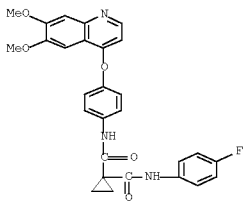
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US 2010-61379670	P	20100902
US 2010-61381305	P	20100909
US 2010-61383305	P	20100915
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US 2010-61393823	P	20101015
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US 2010-61421851	P	20101210
US 2010-61423557	P	20101215
US 2010-61428196	P	20101229
US 2011-61471417	P	20110404
US 2010-61321392	P	20100406
US 2010-61321407	P	20100406
US 2010-61322690	P	20100409
US 2010-61332174	P	20100506
US 2010-61334547	P	20100513
US 2010-61348214	P	20100525
US 2010-61348685	P	20100526
US 2010-61354125	P	20100611
US 2010-61355387	P	20100616
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US 2010-61357517	P	20100622
US 2010-61362674	P	20100708
US 2010-61364785	P	20100715
US 2010-61370088	P	20100802
WO 2011-US31479	A	20110406
AU 2011-291599	A3	20110818
WO 2011-US48327	W	20110818
US 2013-13639756	A2	20130424
US 2013-13817383	A1	20130520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Biomarkers can be assessed for diagnostic, therapy-related or prognostic methods to identify phenotypes, such as a condition or disease, or the stage or progression of a disease. Circulating biomarkers from a bodily fluid can be used in profiling of physiol. states or determining phenotypes. These include nucleic acids, protein, and circulating structures such as vesicles. Biomarkers can be used for theranostic purposes to select candidate treatment regimens for diseases, conditions, disease stages, and stages of a condition, and can also be used to determine treatment efficacy. The biomarkers can be circulating biomarkers, including vesicles and microRNA. Various anti-DLL4 antibodies were tethered to beads and used to capture vesicles in blood samples from subjects with breast cancer, colorectal cancer or normal subjects. The bead captured vesicles were detected with fluorescently-labeled antibodies against the tetraspanins CD9, CD63, and CD81. The median fluorescence intensity of the captured and labeled vesicles was measured using laser detection. There were noticeable differences both among normals and breast cancer plasma as well as between the avs. of normals and cancer patients.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DLL4, vesicle, and microRNA circulating biomarkers for disease diagnosis, therapy, prognosis, or theranostics)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



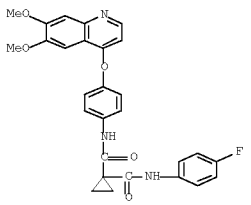
OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 346 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:155432 CAPLUS Full-text
DOCUMENT NUMBER: 157:565304
TITLE: Drug development to overcome resistance to EGFR inhibitors in lung and colorectal cancer
AUTHOR(S): Dienstmann, Rodrigo; De Dosso, Sara; Felip, Enriqueta; Tabernero, Josep
CORPORATE SOURCE: Medical Oncology Department, Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, 08035, Spain
SOURCE: Molecular Oncology (2012), 6(1), 15-26
CODEN: MOONC3; ISSN: 1574-7891
DIGITAL OBJECT ID: 10.1016/j.molonc.2011.11.009
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Epidermal growth factor receptor (EGFR) is a validated target in different human malignancies. EGFR tyrosine kinase inhibitors (TKIs) are known to contribute considerably to the extension of progression-free survival in EGFR-mutant non-small cell lung cancer and monoclonal antibodies (mAbs) targeting EGFR have also improved the efficacy outcomes in KRAS wild-type colorectal cancer. Nevertheless, a significant percentage of lung and colorectal cancer patients do not respond to anti-EGFR agents and secondary resistance after initial benefit is a challenging reality faced by clinicians. Extensive preclin. work on the potential mechanisms of resistance to EGFR inhibitors in different disease settings has guided the development of second-generation irreversible EGFR TKIs, more efficient anti-EGFR mAbs, and combination strategies with agents targeting other receptors and downstream effectors. In order to elucidate the role of the multiple therapeutic strategies under investigation to overcome EGFR inhibitors-resistance, rational drug development based on stringent preclin. data, biomarker validation and proper selection of patients in the ongoing clin. trials are of paramount importance. Preliminary results of clin. trials evaluating these approaches will be discussed in this manuscript, with emphasis on TKIs in lung cancer and mAbs in advanced colorectal cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug development to overcome resistance to EGFR inhibitors in lung and colorectal cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



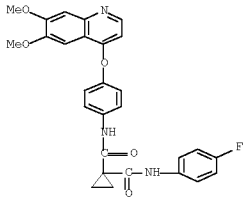
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RECORD (20 CITINGS)
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 347 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:99813 CAPLUS Full-text
DOCUMENT NUMBER: 157:249246
TITLE: HGF/c-MET targeted therapeutics: novel strategies for cancer medicine
AUTHOR(S): Yap, Timothy A.; Sandhu, Shahneen K.; Alam, Salma M.; de Bono, Johann S.
CORPORATE SOURCE: The Royal Marsden NHS Foundation Trust, Sutton, Surrey, SM2 5PT, UK
SOURCE: Current Drug Targets (2011), 12(14), 2045-2058
CODEN: CDTUAU; ISSN: 1389-4501
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The hepatocyte growth factor/mesenchymal-epithelial transition factor (HGF/c-MET) receptor tyrosine kinase (RTK) pathway plays a pleotropic role in cell proliferation, migration, invasion, angiogenesis and survival. Although it has critical physiol. functions in embryonic development and tissue repair, this signaling cascade is frequently deregulated in a wide range of tumors. Aberrant HGF/c-MET signaling, driven by various mechanisms, including constitutive activation and over-expression, has multifunctional effects in oncogenesis and is implicated in the acquisition of an aggressive phenotype with metastatic potential. The central role of c-MET activity in cancer progression, as well as disparities between quiescent HGF/c-MET signaling in normal tissue and overexpression in tumor may provide a degree of tumor selectivity for therapeutic intervention, making HGF or c-MET inhibition an attractive proposition in oncol. This review focuses on the underlying oncogenic role of aberrant HGF/c-MET signaling in malignant progression, as well as recent preclin. and clin. data on the different strategies employed in inhibiting HGF/c-MET function.
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapies targeting hepatocyte growth factor/mesenchymal-epithelial transition factor signaling involved in cell proliferation, migration, invasion, angiogenesis and survival may be useful for treatment of patient with cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

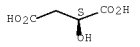
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 134 THERE ARE 134 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 348 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:94602 CAPLUS Full-text
DOCUMENT NUMBER: 156:167648
TITLE: Administration of hypoxia activated prodrugs and antiangiogenic agents for the treatment of cancer
INVENTOR(S): Hart, Charles; Curd, John; Kroll, Stewart; Sun, Jessica
PATENT ASSIGNEE(S): Threshold Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012009288	A2	20120119	WO 2011-US43594	20110711
WO 2012009288	A9	20120419		

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ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

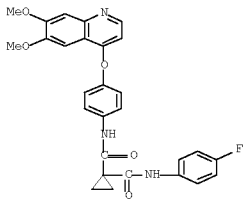
CA 2803675	A1	20120119	CA 2011-2803675	20110711
KR 2013045341	A	20130503	KR 2013-7002206	20110711
EP 2593139	A2	20130522	EP 2011-807356	20110711
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JP 2013531038	T	20130801	JP 2013-519747	20110711
MX 2012014428	A	20130305	MX 2012-14428	20121210
ZA 2013000692	A	20130925	ZA 2013-692	20130125
US 20140010805	A1	20140109	US 2013-13809135	20130724

PRIORITY APPLN. INFO.:
US 2010-61363610 P 20100712
US 2011-61470412 P 20110331
US 2011-61470812 P 20110401
WO 2011-US43594 W 20110711

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Administration of a hypoxia activated prodrug in combination with an antiangiogenic agent is useful for treating cancer. Hypoxia activated prodrug is selected from the group consisting of TH-281, TH-302, and TH-308. The antiangiogenic agent is selected from the group consisting of an anti-VEGF antibody, a VEGF-trap, an anti-VEGFR antibody, a VEGFR inhibitor, thalidomide etc.
IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of hypoxia activated prodrugs and antiangiogenic agents for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

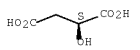
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L8 ANSWER 349 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:90800 CAPLUS Full-text
DOCUMENT NUMBER: 156:186804
TITLE: C-met modulator pharmaceutical compositions comprising N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide
INVENTOR(S): Wilson, Jo Ann
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 40pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012009722	A1	20120119	WO 2011-US44378	20110718

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SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

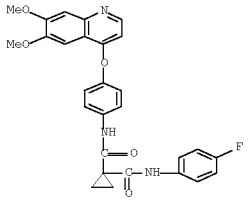
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AR 82252	A1	20121121	AR 2011-102584		20110718
AU 2011278950	A1	20130307	AU 2011-278950		20110718
IL 224189	A	20130324	IL 2011-224189		20110718
EP 2593090	A1	20130522	EP 2011-740764		20110718
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CN 103221035	A	20130724	CN 2011-80044602		20110718
JP 2013531045	T	20130801	JP 2013-519870		20110718
KR 2013137586	A	20131217	KR 2013-7003043		20110718
NZ 607118	A	20150529	NZ 2011-607118		20110718
IN 2013KN00112	A	20130705	IN 2013-KN112		20130114
MX 2013000567	A	20130501	MX 2013-567		20130115
ZA 2013000458	A	20130925	ZA 2013-458		20130117
US 20130337015	A1	20131219	US 2013-13810537		20130826
PRIORITY APPLN. INFO.:			US 2010-61365253	P	20100716
			US 2010-61370843	P	20100805
			WO 2011-US44378	W	20110718

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:186804

AB Pharmaceutical compns. and unit dosage forms comprising N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (I) are disclosed. Thus, 6,7-dimethoxyquinolin-4-ol was converted to 4-chloro-6.7-dimethoxyquinoline followed by reaction with 4-aminphenol to give 4-(6,7-dimethoxy-quinolin-4-yloxy)-phenylamine. This was further allowed to react with 1-(4-fluorophenylcarbamoyl)cyclopropanecarbonyl chloride to give I. A tablet composition comprised 31.68% along with excipients such as microcryst. cellulose 38.85, lactose, HPC, and Croscarmellose sodium.

IT 849217-68-1 1140909-48-3, Cabozantinib S-malate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-met modulator pharmaceutical compns. comprising dimethoxyquinolinyloxyphenyl(fluorophenyl)cyclopropanedicarboxamide)

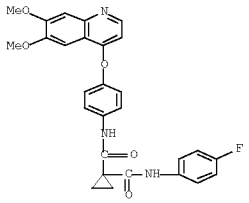
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CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

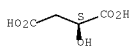
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

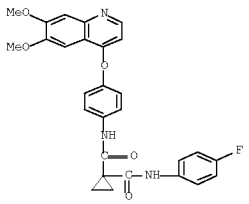


IT 1235470-36-6 1235470-38-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C-met modulator pharmaceutical compns. comprising dimethoxyquinolinyloxyphenyl(fluorophenyl)cyclopropanedicarboxamide)

RN 1235470-36-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

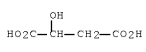
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CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

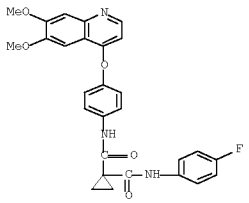
CRN 6915-15-7
CMF C4 H6 O5



RN 1235470-38-8 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

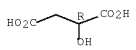
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 350 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2012:10093 CAPLUS Full-text
DOCUMENT NUMBER: 157:152076
TITLE: In the clinic: ongoing clinical trials evaluating c-MET-inhibiting drugs
AUTHOR(S): Sharma, Neelesh; Adjei, Alex A.
CORPORATE SOURCE: Department of Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA
SOURCE: Therapeutic Advances in Medical Oncology (2011), 3(Suppl. 1), S37-S50
CODEN: TAMOB8; ISSN: 1758-8340
DIGITAL OBJECT ID: 10.1177/1758834011423403
PUBLISHER: Sage Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The c-MET (mesenchymal-epithelial transition factor) pathway is dysregulated in many human cancers and promotes tumor growth, invasion and dissemination. The c-MET receptor tyrosine kinase can be activated via gene mutation, gene amplification, protein overexpression and/or a Ligand-dependent autocrine/paracrine loop. Abnormalities in c-MET signaling have been reported to correlate with poor clin. outcomes and drug

resistance in patients with cancer. Significant progress has been made in advancement of c-MET pathway inhibitors through to clin. trials. A robust pipeline of high-quality inhibitors targeting different aspects of c-MET activation is currently being explored in phase I, II and III clin. trials across multiple tumor types. Preliminary data demonstrate promising clin. activity with these agents, along with an acceptable toxicity profile. In this manuscript, the pharmacol. profile of drugs targeting the c-MET pathway and available data from ongoing clin. trials of these drugs are discussed.

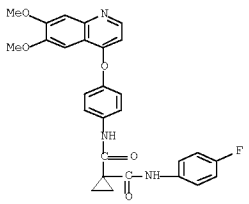
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ongoing clin. trials evaluating mesenchymal-epithelial transition factor-inhibiting drugs)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

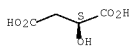
CRN 849217-68-1
CMF C28 H24 F N3 O5



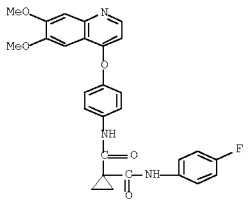
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)



OS.CITING REF COUNT: 216 THERE ARE 216 CAPLUS RECORDS THAT CITE THIS RECORD (217 CITINGS)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 352 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:1503311 CAPLUS Full-text
DOCUMENT NUMBER: 155:694113
TITLE: Replication-competent retroviral vectors carrying expression cassettes for cytosine deaminase variants
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Perez, Omar D.; Logg, Christopher R.
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 207pp., Cont.-in-part of Appl. No. PCT/US2009/058512.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20110287020	A1	20111124	US 2011-13072704	20110326
US 8829173	B2	20140909		
WO 2010036986	A2	20100401	WO 2009-US58512	20090926
WO 2010036986	A3	20100701		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
CN 105274125	A	20160127	CN 2015-10505943	20090926
WO 2011126864	A2	20111013	WO 2011-US30402	20110329
WO 2011126864	A3	20120419		
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EP 2547353	A2	20130123	EP 2011-766479	20110329
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JP 2013523754	T	20130617	JP 2013-502771	20110329
US 20130130986	A1	20130523	US 2013-13638490	20130116
AU 2013205006	A1	20130516	AU 2013-205006	20130413
AU 2013205006	B2	20160218		
US 20160053232	A1	20160225	US 2014-14477741	20140904
JP 2015119712	A	20150702	JP 2015-4923	20150114
JP 2015186479	A	20151029	JP 2015-97980	20150513

PRIORITY APPLN. INFO.:

US 2008-61100666	P	20080926
US 2008-61120618	P	20081208
US 2009-61186823	P	20090613
WO 2009-US58512	A2	20090926
US 2010-61318728	P	20100329
AU 2009-303690	A3	20090926
CN 2009-80147509	A3	20090926
JP 2011-529291	A3	20090926
JP 2011-529292	A3	20090926
US 2011-13072704	A1	20110326
WO 2011-US30402	W	20110329

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods of delivering cytosine deaminase variants for prodrug activation using retroviral expression vectors are described. The vector includes the viral gag, pol, and env genes with the cytosine deaminase gene being coexpressed using an internal ribosome entry site. Vectors were derived from the prior art pACE-GFPemd vector. The envelope protein of the virus is amphotropic and excess viral sequences outside the long terminal repeats were removed. The resulting vector was named pACE-emdGFP. The vector was stable in storage and replicated efficiently in mammalian cells and could be used to deliver a range of therapeutic genes. The Saccharomyces cerevisiae cytosine deaminase gene was modified to give a codon usage suitable for mammalian cells and to improve thermostability of the enzyme. Use of these vectors results in high intracellular copy nos. for the therapeutic gene and these cells can be superinfected by the vector.

IT 1140909-48-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in cancer therapy with retroviral gene therapy vectors; replication-competent retroviral vectors carrying expression cassettes for cytosine deaminase variants)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 351 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2011:1586879 CAPLUS Full-text
DOCUMENT NUMBER: 156:655505
TITLE: Cabozantinib (XL184), a Novel MET and VEGFR2 Inhibitor, Simultaneously Suppresses Metastasis, Angiogenesis, and Tumor Growth
AUTHOR(S): Yakes, F. Michael; Chen, Jason; Tan, Jenny; Yamaguchi, Kyoko; Shi, Yongchang; Yu, Peiwen; Qian, Fawn; Chu, Felix; Bentzien, Frauke; Cancilla, Belinda; Orf, Jessica; You, Andrew; Laird, A. Douglas; Engst, Stefan; Lee, Lillian; Lesch, Justin; Chou, Yu-Chien; Joly, Alison H.
CORPORATE SOURCE: Exelixis, Inc., South San Francisco, CA, 94083, USA
SOURCE: Molecular Cancer Therapeutics (2011), 10(12), 2298-2308
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-11-0264
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The signaling pathway of the receptor tyrosine kinase MET and its ligand hepatocyte growth factor (HGF) is important for cell growth, survival, and motility and is functionally linked to the signaling pathway of VEGF, which is widely recognized as a key effector in angiogenesis and cancer progression. Dysregulation of the MET/VEGF axis is found in a number of human malignancies and has been associated with tumorigenesis. Cabozantinib (XL184) is a small-mol. kinase inhibitor with potent activity toward MET and VEGF receptor 2 (VEGFR2), as well as a number of other receptor tyrosine kinases that have also been implicated in tumor pathobiol., including RET, KIT, AXL, and FLT3. Treatment with cabozantinib inhibited MET and VEGFR2 phosphorylation in vitro and in tumor models in vivo and led to significant redns. in cell invasion in vitro. In mouse models, cabozantinib dramatically altered tumor pathol., resulting in decreased tumor and endothelial cell proliferation coupled with increased apoptosis and dose-dependent inhibition of tumor growth in breast, lung, and glioma tumor models. Importantly, treatment with cabozantinib did not increase lung tumor burden in an exptl. model of metastasis, which has been observed with inhibitors of VEGF signaling that do not target MET. Collectively, these data suggest that cabozantinib is a promising agent for inhibiting tumor angiogenesis and metastasis in cancers with dysregulated MET and VEGFR signaling. Mol Cancer Ther; 10(12); 2298-308.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib inhibited proliferation of human, mouse and rat cancer cell and suppressed metastasis, angiogenesis, tumor growth via inhibiting MET and VEGFR2 protein phosphorylation in mouse and rat xenografted with cancer)

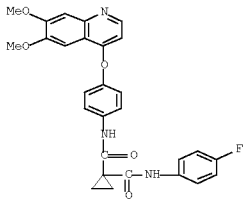
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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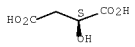
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

L8 ANSWER 353 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:1304241 CAPLUS Full-text
DOCUMENT NUMBER: 155:559702
TITLE: Detection of circulating mRNA, microRNA, protein and vesicle markers in disease diagnosis and selection of therapies
INVENTOR(S): Kuslich, Christine; Poste, George; Klass, Michael; Spetzler, David; Pawlowski, Traci
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, Luxembourg
SOURCE: PCT Int. Appl., 584pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011127219	A1	20111013	WO 2011-US31479	20110406
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2795776	A1	20111013	CA 2011-2795776	20110406
AU 2011237669	A1	20121101	AU 2011-237669	20110406
IL 222232	A	20121129	IL 2011-222232	20110406
EP 2556172	A1	20130213	EP 2011-766687	20110406
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CN 103025890	A	20130403	CN 2011-80027541	20110406
KR 2013043104	A	20130429	KR 2012-7028831	20110406
JP 2013526852	T	20130627	JP 2013-503934	20110406
IN 2012DN09454	A	20160101	IN 2012-DN9454	20121101
US 20140162888	A1	20140612	US 2013-13639756	20130424
US 20150301055	A1	20151022	US 2015-14789729	20150701
JP 2016028584	A	20160303	JP 2015-176236	20150908
AU 2015268602	A1	20160107	AU 2015-268602	20151209

PRIORITY APPLN. INFO.:		
US 2010-61321392	P	20100406
US 2010-61321407	P	20100406
US 2010-61322690	P	20100409
US 2010-61332174	P	20100506
US 2010-61334547	P	20100513
US 2010-61348214	P	20100525
US 2010-61348685	P	20100526
US 2010-61354125	P	20100611
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US 2010-61356974	P	20100621
US 2010-61357517	P	20100622
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US 2010-61370088	P	20100802
US 2010-61379670	P	20100902
US 2010-61381305	P	20100909
US 2010-61383305	P	20100915
US 2010-61391504	P	20101008
US 2010-61393823	P	20101015
US 2010-61411890	P	20101109
US 2010-61413377	P	20101112
US 2010-61416560	P	20101123
US 2010-61274124	P	20100301
US 2010-61374951	P	20100818
US 2010-61414870	P	20101117
US 2010-61421851	P	20101210
US 2010-61423557	P	20101215
US 2010-61428196	P	20101229
JP 2012-556185	A3	20110301
US 2011-61471417	P	20110404
WO 2011-US31479	W	20110406
AU 2011-291599	A3	20110818
WO 2011-US48327	A	20110818
US 2013-13639756	A2	20130424
US 2013-13817383	A1	20130520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

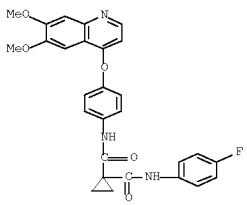
AB Biomarkers can be assessed for diagnostic, therapy-related or prognostic methods to identify phenotypes, such as a condition or disease, or the stage or progression of a disease. Circulating biomarkers from a bodily fluid can be used in profiling of physiol. states or determining phenotypes. These include nucleic acids, protein, and circulating structures such as vesicles. Biomarkers can be used for theranostic purposes to select candidate treatment regimens for diseases, conditions, disease stages, and stages of a condition, and can also be used to determine treatment efficacy. The biomarkers can be circulating biomarkers, including microvesicles and their protein content and microRNAs.

IT 1140909-48-3, XL184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selection for cancer therapy; detection of circulating mRNA, microRNA, protein and vesicle markers in disease diagnosis)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

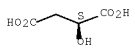
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 354 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:1016190 CAPLUS Full-text
DOCUMENT NUMBER: 156:353197
TITLE: Biologically targeted therapies for thyroid cancers
AUTHOR(S): Sherman, Steven I.
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders Division of Internal Medicine, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Thyroid Cancer (2011), 329-349. Editor(s): Carpi, Angelo; Mechanick, Jeffrey I. CRC Press: Boca Raton, Fla.
CODEN: 69OKVM; ISBN: 978-1-4398-6221-6
DIGITAL OBJECT ID: 10.1201/b10945-21
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review. Systemic chemotherapies for advanced or metastatic thyroid carcinomas have been of only limited effectiveness. For patients with differentiated thyroid epithelial or medullary thyroid carcinomas unresponsive to conventional treatments, novel therapies are needed to improve disease outcomes. Multiple novel therapies primarily targeting angiogenesis have entered clin. trials for metastatic thyroid carcinoma. Partial response rates up to 30% have been reported in single agent studies, but prolonged disease stabilization is more commonly seen. The most successful agents target the vascular endothelial growth factor receptors, with potential targets including the mutant kinases associated with papillary and medullary oncogenesis. Two drugs approved for other malignancies, sorafenib and sunitinib, have had promising preliminary results reported, and are being used selectively for patients who do not qualify for clin. trials. Addnl. agents targeting tumor vasculature, nuclear receptors, epigenetic abnormalities, and the immune response to neoplasia have also been investigated. Randomized trials for several agents are under way that may lead to eventual drug approval for thyroid cancer. Treatment for patients with metastatic or advanced thyroid carcinoma now emphasizes clin. trial opportunities for novel agents with considerable promise. Alternative options now exist for use of these mol. targeted therapies, especially tyrosine kinase inhibitors, which are well tolerated and may prove worthy of regulatory approval for this disease.

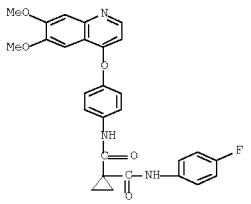
IT 1140909-48-3, XL 184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. targeted therapies for thyroid cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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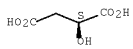
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

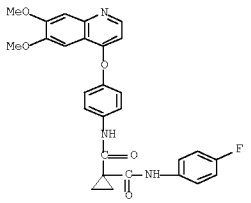


REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 355 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:991678 CAPLUS Full-text
DOCUMENT NUMBER: 156:440657
TITLE: Activity of XL184 (cabozantinib), an oral tyrosine kinase inhibitor, in patients with medullary thyroid cancer
AUTHOR(S): Kurzrock, Razelle; Sherman, Steven I.; Ball, Douglas W.; Forastiere, Arlene A.; Cohen, Roger B.; Mehra, Ranee; Pfister, David G.; Cohen, Ezra E. W.; Janisch, Linda; Nauling, Forlisa; Hong, David S.; Ng, Chaan S.; Ye, Lei; Gagel, Robert F.; Frye, John; Muller, Thomas; Ratain, Mark J.; Salgia, Ravi
CORPORATE SOURCE: The University of Texas MD Anderson Cancer Center, Houston, USA
SOURCE: Journal of Clinical Oncology (2011), 29(19), 2660-2666
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2010.32.4145
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: XL184 (cabozantinib) is a potent inhibitor of MET, vascular endothelial growth factor receptor 2 (VEGFR2), and RET, with robust antiangiogenic, antitumor, and anti-invasive effects in preclin. models. Early observations of clin. benefit in a phase I study of cabozantinib, which included patients with medullary thyroid cancer (MTC), led to expansion of an MTC-enriched cohort, which is the focus of this article. Patients and Methods: A phase I dose-escalation study of oral cabozantinib was conducted in patients with advanced solid tumors. Primary end points included evaluation of safety, pharmacokinetics, and maximum-tolerated dose (MTD) determination Addnl. end points included RECIST (Response Evaluation Criteria in Solid Tumors) response, pharmacodynamics, RET mutational status, and biomarker analyses. Results: Eighty-five patients were enrolled, including 37 with MTC. The MTD was 175 mg daily. Dose-limiting toxicities were grade 3 palmar plantar erythrodysesthesia (PPE), mucositis, and AST, ALT, and lipase elevations and grade 2 mucositis that resulted in dose interruption and reduction Ten (29%) of 35 patients with MTC with measurable disease had a confirmed partial response. Overall, 18 patients experienced tumor shrinkage of 30% or more, including 17 (49%) of 35 patients with MTC with measurable disease. Addnl., 15 (41%) of 37 patients with MTC had stable disease (SD) for at least 6 mo, resulting in SD for 6 mo or longer or confirmed partial response in 68% of patients with MTC. Conclusion: Cabozantinib has an acceptable safety profile and is active in MTC. Cabozantinib may provide clin. benefit by simultaneously targeting multiple pathways of importance in MTC, including MET, VEGFR2, and RET. A global phase III pivotal study in MTC is ongoing (ClinicalTrials.gov number NCT00215605).
IT 1140909-48-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activity of cabozantinib, an oral tyrosine kinase inhibitor, in patients with medullary thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

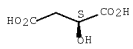
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

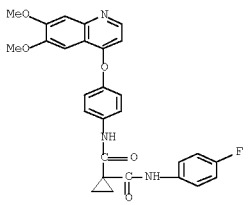


OS.CITING REF COUNT: 162 THERE ARE 162 CAPLUS RECORDS THAT CITE THIS RECORD (163 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 356 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:945715 CAPLUS Full-text
DOCUMENT NUMBER: 156:301829
TITLE: Current status of molecularly targeted drugs for the treatment of advanced thyroid cancer
AUTHOR(S): Takami, Hiroshi E.
CORPORATE SOURCE: Department of Surgery, Teikyo University School of Medicine, Tokyo, 173-8605, Japan
SOURCE: Endocrine Journal (Kyoto, Japan) (2011), 58(3), 151-153
CODEN: ENJOEO; ISSN: 0918-8959
DIGITAL OBJECT ID: 10.1507/endocrj.K11E-076
PUBLISHER: Japan Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The prognosis of almost all thyroid cancers is good, but some patients have indications for these molecularly targeted drugs. Some of these drugs, i.e., vandetanib, XL-184, sorafenib, motesanib, axitinib, and pazopanib, are clearly useful clin.
IT 1140909-48-3, XL-184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(current status of molecularly targeted drugs for the treatment of advanced thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

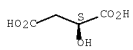
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 357 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:724271 CAPLUS Full-text
DOCUMENT NUMBER: 155:290943
TITLE: The effects of four different tyrosine kinase inhibitors on medullary and papillary thyroid cancer cells
AUTHOR(S): Verbeek, Hans H. G.; Alves, Maria M.; de Groot,

Jan-Willem B.; Osinga, Jan; Plukker, John T. M.; Links, Thera P.; Hofstra, Robert M. W.
CORPORATE SOURCE: Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, 9700 RB, Neth.
SOURCE: Journal of Clinical Endocrinology and Metabolism (2011), 96(6), E991-E995
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2010-2381
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Medullary and papillary thyroid carcinoma (MTC and PTC) are 2 types of thyroid cancer that can originate from activating mutations or rearrangements in the RET gene. Therapeutic options are limited in recurrent disease, but because RET is a tyrosine kinase (TK) receptor involved in cellular growth and proliferation, treatment with a TK inhibitor might be promising. Several TK inhibitors were tested in clin. trials, but it is unknown which inhibitor is most effective and whether there is any specificity for particular RET mutations. We aimed to compare the effect of 4 TK inhibitors (axitinib, sunitinib, vandetanib, and XL184) on cell proliferation, RET expression and autophosphorylation, and ERK activation in cell lines expressing a MEN2A (MTC-TT), a MEN2B (MZ-CRC-1) mutation, and a RET/PTC (TPC-1) rearrangement. The 3 cell lines were cultured and treated with the 4 TK inhibitors. Effects on cell proliferation and RET and ERK expression and activation were determined XL184 and vandetanib most effectively inhibited cell proliferation, RET autophosphorylation in combination with a reduction of RET expression, and ERK phosphorylation in MTC-TT and MZ-CRC-1, resp. TPC-1 cells showed a decrease in RET autophosphorylation after treatment with XL184, but no effect was observed on ERK activation. There is indeed specificity for different RET mutations, with XL184 being the most potent inhibitor in MEN2A and PTC and vandetanib the most effective in MEN2B in vitro. No TK inhibitor was superior for all the cell lines tested, indicating that mutation-specific therapies could be beneficial in treating MTC and PTC.

IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Tyr kinase inhibitors effect on medullary and papillary thyroid cancer related to RET mutation, rearrangement, and ERK)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
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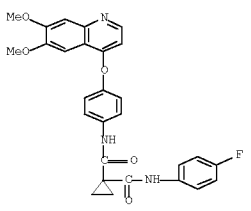
androgen deprivation therapy. Denosumab is shown to support bone mineral d. in hormonal sensitive PCa patients. Targeting of androgen-dependent pathways in CRPC postchemotherapy has been shown to improve survival with the lyase inhibitor abiraterone, and lead to prostate-specific antigen and objective responses with an androgen receptor antagonist (MDV3100). However, the addition of bevacizumab to docetaxel/prednisone in treating metastatic CRPC failed to provide a survival benefit. Cabazitaxel in metastatic CRPC postdocetaxel did demonstrate a survival benefit. Provenge, an autologous dendritic cell-based vaccine, demonstrated a reduction in the risk of death in metastatic CRPC. Other immunotherapy agents, including Prostvac and ipilimumab are under investigation. We also discuss the receptor tyrosine kinase inhibitor XL184 and poly (ADP-ribose) polymerase inhibitors which are in early clin. trials. Summary: Recent advances in androgen targeting, chemotherapy, immunotherapy, and other targeted therapies have led to significant improvements in the care of CRPC patients.

IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel agents and new therapeutics in castration-resistant prostate cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

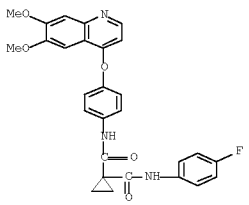
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CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

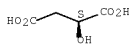
Absolute stereochemistry. Rotation (-).



CM 2

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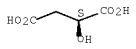
Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 358 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:461207 CAPLUS Full-text
DOCUMENT NUMBER: 156:46100
TITLE: Novel agents and new therapeutics in castration-resistant prostate cancer
AUTHOR(S): Wu, Yichao; Rosenberg, Jonathan E.; Taplin, Mary-Ellen
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SOURCE: Current Opinion in Oncology (2011), 23(3), 290-296
CODEN: COONE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e3283449400
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Purpose of review: This review highlights recent therapeutic advances in systemic therapies for prostate cancer (PCa). Recent findings: Progress in PCa therapeutics has been made during the past year with the approval of a vaccine therapy, second-line chemotherapy, and reported survival advantage for a CYP (17,20) lyase inhibitor in castration-resistant prostate cancer (CRPC). This report will summarize the recently reported and expected data for PCa trials including an evaluation of intermittent vs. continuous

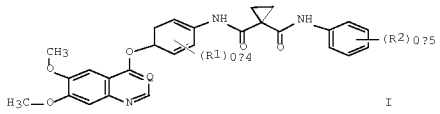


OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 359 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:174316 CAPLUS Full-text
DOCUMENT NUMBER: 154:225400
TITLE: C-met modulators as antitumor agents
INVENTOR(S): Aftab, Dana T.; Mueller, Thomas; Weitzman, Aaron; Holland, Jaymes
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011017639	A1	20110210	WO 2010-US44749	20100806
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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CA 2770100	A1	20110210	CA 2010-2770100	20100806
AU 2010279234	A1	20120301	AU 2010-279234	20100806
KR 2012059540	A	20120608	KR 2012-7006111	20100806
EP 2461810	A1	20120613	EP 2010-742985	20100806
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CN 102647985	A	20120822	CN 2010-80045677	20100806
JP 2013501731	T	20130117	JP 2012-523982	20100806
IL 217889	A	20130228	IL 2010-217889	20100806
NZ 598055	A	20140530	NZ 2010-598055	20100806
IL 238849	A	20150630	IL 2010-238849	20100806
NZ 624643	A	20151127	NZ 2010-624643	20100806
IN 2012MN00278	A	20120824	IN 2012-MN278	20120203
ZA 2012000842	A	20121128	ZA 2012-842	20120203
MX 2012001654	A	20120314	MX 2012-1654	20120207
US 20120282179	A1	20121108	US 2012-13389266	20120712

US 20160000772 A1 20160107 US 2015-14699683 20150429
PRIORITY APPLN. INFO.: US 2009-61232382 P 20090807
IL 2010-217889 A3 20100806
NZ 2010-598055 A3 20100806
WO 2010-US44749 W 20100806
US 2012-13389266 B1 20120712
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 154:225400; MARPAT 154:225400
GI



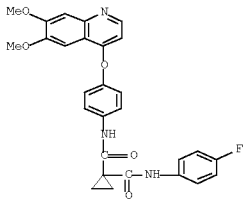
I

AB Methods of treating cancer by administering a compd. of Formula I (wherein R1 = halo; R2 = halo; Q = CH, N; n = 0-4; m = 0-5) or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments are described.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(methods of using c-met modulators)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



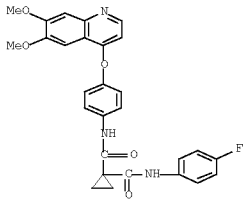
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of using c-met modulators)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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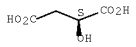
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 360 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:111410 CAPLUS Full-text
DOCUMENT NUMBER: 155:346258
TITLE: Antiangiogenic agents in the treatment of recurrent or newly diagnosed glioblastoma: analysis of single-agent and combined modality approaches
AUTHOR(S): Beal, Kathryn; Abrey, Lauren E.; Gutin, Philip H.
CORPORATE SOURCE: Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Radiation Oncology (2011), 6, 2
CODEN: ROANCM; ISSN: 1748-717X
URL: http://www.ro-journal.com/content/pdf/1748-717X-6-2.pdf

DIGITAL OBJECT ID: 10.1186/1748-717X-6-2
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Surgical resection followed by radiotherapy and temozolomide in newly diagnosed glioblastoma can prolong survival, but it is not curative. For patients with disease progression after frontline therapy, there is no standard of care, although further surgery, chemotherapy, and radiotherapy may be used. Antiangiogenic therapies may be appropriate for treating glioblastomas because angiogenesis is critical to tumor growth. In a large, noncomparative phase II trial, bevacizumab was evaluated alone and with irinotecan in patients with recurrent glioblastoma; combination treatment was associated with an estimated 6-mo progression-free survival (PFS) rate of 50.3%, a median overall survival of 8.9 mo, and a response rate of 37.8%. Single-agent bevacizumab also exceeded the predetd. threshold of activity for salvage chemotherapy (6-mo PFS rate, 15%), achieving a 6-mo PFS rate of 42.6% (p<0.0001). On the basis of these results and those from another phase II trial, the US Food and Drug Administration granted accelerated approval of single-agent bevacizumab for the treatment of glioblastoma that has progressed following prior therapy. Potential antiangiogenic agents - such as cilengitide and XL184 - also show evidence of single-agent activity in recurrent glioblastoma. Moreover, the use of antiangiogenic agents with radiation at disease progression may improve the therapeutic ratio of single-modality approaches. Overall, these agents appear to be well tolerated, with adverse event profiles similar to those reported in studies of other solid tumors. Further research is needed to determine the role of antiangiogenic therapy in frontline treatment and to identify the optimal schedule and partnering agents for use in combination therapy.

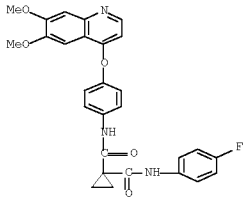
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiangiogenic agents in the treatment of recurrent or newly diagnosed glioblastoma)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

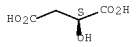
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 361 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2011:80577 CAPLUS Full-text
DOCUMENT NUMBER: 154:174225
TITLE: Drug selection for gastric cancer therapy using antibody-based arrays
INVENTOR(S): Singh, Sharat; Kim, Phillip; Liu, Xinjun; Ybarrondo, Belen
PATENT ASSIGNEE(S): Prometheus Laboratories Inc., USA
SOURCE: PCT Int. Appl., 189pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011008990	A1	20110120	WO 2010-US42182	20100715

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP,

KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2768013	A1	20110120	CA 2010-2768013		20100715
AU 2010273319	A1	20120223	AU 2010-273319		20100715
AU 2010273319	B2	20150122			
EP 2454598	A1	20120523	EP 2010-800567		20100715
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JP 2012533738	T	20121227	JP 2012-520794		20100715
JP 5795311	B2	20151014			
US 20110281748	A1	20111117	US 2011-13014674		20110126
US 20130237436	A9	20130912			
US 20120270745	A1	20121025	US 2012-13354257		20120119
AU 2013202682	A1	20130502	AU 2013-202682		20130405
AU 2013202682	B2	20150716			
JP 2016001187	A	20160107	JP 2015-159663		20150812
PRIORITY APPLN. INFO.:			US 2009-61225866	P	20090715
			US 2009-61265218	P	20091130
			US 2010-61325000	P	20100416
			US 2006-61007527	P	20060921
			US 2007-60913087	P	20070420
			AU 2007-299774	A3	20070920
			WO 2007-US79002	A1	20070920
			US 2008-46381	A2	20080311
			JP 2012-520794	A3	20100715
			WO 2010-US42182	W	20100715
			US 2011-13014674	A2	20110126
			US 2011-61436945	P	20110127
			US 2011-61467950	P	20110325

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

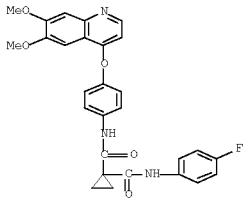
AB The present invention provides methods for selecting a suitable anticancer therapy, and for identifying and predicting response for the treatment of a gastric cancer. The present invention provides compns. and methods for detecting the status (e.g., expression and/or activation levels) of components of signal transduction pathways in tumor cells (e.g., gastric tumor cells). Information on the expression and/or activation states of components of signal transduction pathways (e.g., HER2 and/or c-Met signal transduction pathway components) derived from practice of the present invention can be used for gastric cancer diagnosis, prognosis, and in the design of gastric cancer treatments. The compns. and methods of the present invention advantageously provide accurate prediction, selection, and monitoring of cancer patients (e.g., gastric cancer patients) most likely to benefit from targeted therapy by performing pathway profiling on easily accessible tumor cells using multiplexed, antibody-based proximity assays.

IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for gastric cancer therapy using antibody-based arrays for detecting the status of signal transduction pathways)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

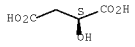
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 362 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:1570396 CAPLUS Full-text
DOCUMENT NUMBER: 155:177406
TITLE: Targeting RET Receptor Tyrosine Kinase Activation in Cancer
AUTHOR(S): Phay, John E.; Shah, Manisha H.
CORPORATE SOURCE: Department of Surgery, Division of Surgical Oncology, Department of Internal Medicine, and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA

SOURCE: Clinical Cancer Research (2010), 16(24), 5936-5941
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-09-0786
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

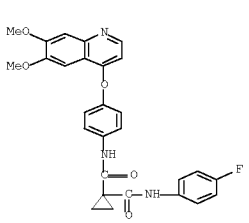
AB A review. After ligand binding induces dimerization, the RET receptor tyrosine kinase activates multiple signal transduction pathways. Constitutively activating mutations and chromosomal rearrangements are the primary oncogenic event in a significant number of medullary thyroid cancers (MTC) and papillary thyroid cancers (PTC), resp. When specific germline mutations in RET are identified early, prophylactic thyroidectomy can be timed to remove at-risk tissue in patients with multiple endocrine neoplasia 2 (MEN2) syndromes who would otherwise develop MTC. Conventional therapy for progressive metastatic MTC is limited. Small-mol. tyrosine kinase inhibitors can target multiple kinases at nanomolar concns., including RET, and have shown efficacy against a variety of malignancies. Initial clin. evidence suggests that several of these inhibitors, including sorafenib, vandetanib, motesanib, sunitinib, and XL-184, may have some benefit in treating progressive MTC. Although initial success seen in these trials seems to be modest, it represents a major breakthrough in the treatment of patients with widespread metastatic MTC. Clin Cancer Res; 16(24); 5936-41.

IT 1140909-48-3, XL-184,
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(role of RET receptor tyrosine kinase activation in cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

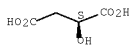
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 50 THERE ARE 50 CAPLUS RECORDS THAT CITE THIS RECORD (50 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 363 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:1240526 CAPLUS Full-text
DOCUMENT NUMBER: 153:595314
TITLE: Tyrosine kinase inhibitors in thyroid cancer
AUTHOR(S): Illouz, Frederic
CORPORATE SOURCE: Service EDN, Centre de reference des pathologies de la receptivite hormonale, CHU d'Angers, Fr.
SOURCE: Correspondances en Metabolismes, Hormones, Diabetes et Nutrition (2010), 14(7), 210-214
CODEN: CMHDBH; ISSN: 2100-9619
PUBLISHER: Edimark SAS
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

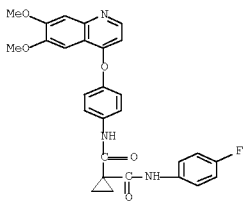
AB A review.

IT 1140909-48-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitors in thyroid cancer therapy)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

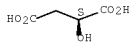
CRN 849217-68-1
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 364 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:1003327 CAPLUS Full-text
DOCUMENT NUMBER: 153:278035
TITLE: Treatment of lung cancer with a PARP inhibitor in combination with a growth factor inhibitor
INVENTOR(S): Sherman, Barry M.; Bradley, Charles; Ossovskaya, Valeria S.
PATENT ASSIGNEE(S): BiPar Sciences, Inc., USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

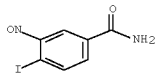
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010091140	A1	20100812	WO 2010-US23137	20100204

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AR 75239	A1	20110316	AR 2010-100305	20100204
AU 2010210636	A1	20110922	AU 2010-210636	20100204
KR 2011113648	A	20111017	KR 2011-7020246	20100204
EP 2393364	A1	20111214	EP 2010-739097	20100204
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CN 102307475	A	20120104	CN 2010-80006536	20100204
JP 2012516895	T	20120726	JP 2011-549246	20100204
IL 214366	A	20130131	IL 2010-214366	20100204
MX 2011008221	A	20110817	MX 2011-8221	20110804
IN 2011CN06195	A	20121012	IN 2011-CN6195	20110829
US 20120130144	A1	20120524	US 2011-13146865	20111222

PRIORITY APPLN. INFO.: US 2009-61149977 P 20090204
WO 2010-US23137 W 20100204

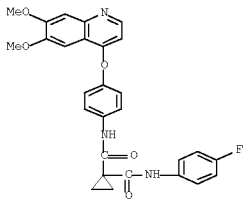
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 153:278035
GI



AB In one aspect, the present invention provides a method of treating lung cancer, comprising administering to a subject at least one PARP inhibitor in combination with at least one growth factor inhibitor. In another aspect, the present invention provides a method of treating non-small cell lung cancer comprising administering to a subject at least one PARP inhibitor in combination with at least one growth factor inhibitor.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of lung cancer with a PARP inhibitor in combination with a growth factor inhibitor)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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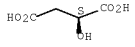
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

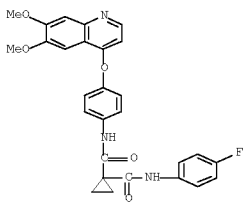


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
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L8 ANSWER 365 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:944155 CAPLUS Full-text
DOCUMENT NUMBER: 155:230334
TITLE: Patients with advanced head and neck cancers have similar progression-free survival on phase I trials and their last food and drug administration-approved treatment
AUTHOR(S): Garrido-Laguna, Ignacio; Janku, Filip; Falchook, Gerald S.; Fu, Siqing; Hong, David S.; Naing, Aung; Aaron, Joanne; Wang, Xuemei; Kies, Merrill; Kurzrock, Razelle
CORPORATE SOURCE: Departments of Investigational Cancer Therapeutics (Phase I Clinical Trials Program), The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Clinical Cancer Research (2010), 16(15), 4031-4037
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-10-0672
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: To compare clin. outcomes of metastatic head and neck cancer patients treated in phase I clin. trials with clin. outcomes of those patients who had their last Food and Drug Administration (FDA)-approved therapy in the setting of metastatic disease. Exptl. Design: We retrospectively reviewed the outcomes of 61 consecutive patients with head and neck tumors treated in 36 phase I trials at The University of Texas M.D. Anderson Cancer Center between July 2004 and Sept. 2009. Results: The most common histol. was head and neck squamous cell carcinoma (62%). Median age was 55 years (range, 26-80). Eastern Cooperative Oncol. Group performance status was 0 to 1 for 95% of patients. Fifty-nine patients had received FDA-approved drugs as the backbone of their last systemic therapy before inclusion in phase I trials (median, 2 systemic therapies). Progression-free survival (PFS) on phase I trials was not inferior to PFS on their last FDA-approved therapies (12 vs. 10.7 wk, log-rank P = 0.87). Fifty-three patients were evaluable for response by Response Evaluation Criteria in Solid Tumors criteria. Four (7%) had partial responses and 16 (26%) had stable disease for ≥4 mo. In univariate anal., number of metastatic sites, lactate dehydrogenase (LDH) levels at baseline, and Royal Marsden Hospital prognosis scores were significant predictors of survival. Only LDH was significant in multivariate anal. (hazard ratio, 6.35; P ≤ 0.0001). Conclusions: For patients with heavily pretreated advanced head and neck tumors, PFS on phase I trials is not inferior to PFS with their last FDA-approved therapy. The only significant predictor of survival in the multivariate anal. was baseline LDH.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(patients with advanced head and neck cancers have similar progression-free survival on phase I trials and their last food and drug administration-approved treatment)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

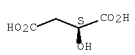
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



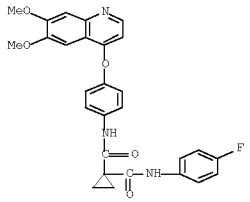
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L8 ANSWER 366 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:928655 CAPLUS Full-text
DOCUMENT NUMBER: 154:425137
TITLE: XL-184, a MET, VEGFR-2 and RET kinase inhibitor for the treatment of thyroid cancer, glioblastoma multiforme and NSCLC
AUTHOR(S): Zhang, Ying; Guessous, Fadila; Kofman, Alex; Schiff, David; Abounader, Roger
CORPORATE SOURCE: Department of Microbiology, University of Virginia, Charlottesville, VA, 22903, USA
SOURCE: IDrugs (2010), 13(2), 112-121
CODEN: IDRUFN; ISSN: 2040-3410
URL:
http://www.biomedcentral.com/content/pdf/cd-1071541.pdf

PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. XL-184 (BMS-907351), under development by Exelixis Inc and Bristol-Myers Squibb Co, is a pan-tyrosine kinase inhibitor for the potential oral treatment of medullary thyroid cancer, glioblastoma multiforme and NSCLC. The prinicipal targets of XL-184 are MET, VEGFR-2 and RET, but the drug is also reported to display inhibitory activity against KIT, FLT3 and TEK. Preclin. studies demonstrated that XL-184 potently inhibited multiple receptor tyrosine kinases in various cancer cell lines and animal xenograft models, and that the drug exhibited significant oral bioavailability and blood-brain barrier penetration. A phase I clin. trial in patients with advanced solid malignancies indicated that XL-184 accumulated dose-dependently in the plasma and had a long terminal half-life. A phase II trial in patients with progressive or recurrent glioblastoma revealed modest but promising median progression-free survival. Toxicity and side effects for the drug have generally been of low-to-moderate severity. At the time of publication, three addnl. trials of XL-184 were recruiting patients, including a phase I trial in combination with standard of care in patients with glioblastoma, a phase I/II trial in combination with erlotinib in patients with NSCLC, and a phase III trial in patients with medullary thyroid cancer.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL-184, a MET, VEGFR-2 and RET kinase inhibitor for the treatment of thyroid cancer, glioblastoma multiforme and NSCLC)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

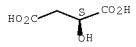
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 48 THERE ARE 48 CAPLUS RECORDS THAT CITE THIS RECORD (48 CITINGS)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 367 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:912816 CAPLUS Full-text
DOCUMENT NUMBER: 153:204211

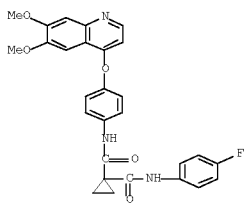
TITLE: Preparation of malate salts of N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide and crystalline forms thereof for the treatment of cancer.
INVENTOR(S): St Clair Brown, Adrian; Lamb, Peter; Gallagher, William P.
PATENT ASSIGNEE(S): Exelixis, Inc., USA; Bristol-Meyers Squibb Company
SOURCE: PCT Int. Appl., 72pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010083414	A1	20100722	WO 2010-US21194	20100115
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2758030	A1	20100722	CA 2010-2758030	20100115
AR 75025	A1	20110302	AR 2010-100098	20100115
AU 2010204619	A1	20110901	AU 2010-204619	20100115
EP 2387563	A1	20111123	EP 2010-701175	20100115
EP 2387563	B1	20130306		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
KR 2012013301	A	20120214	KR 2011-7018924	20100115
CN 102388024	A	20120321	CN 2010-80012656	20100115
JP 2012515220	T	20120705	JP 2011-546390	20100115
JP 5677318	B2	20150225		
IL 214086	A	20130131	IL 2010-214086	20100115
PT 2387563	E	20130325	PT 2010-701175	20100115
ES 2402524	T3	20130506	ES 2010-701175	20100115
NZ 594594	A	20131129	NZ 2010-594594	20100115
EA 19959	B1	20140730	EA 2011-70941	20100115
TW I447108	B	20140801	TW 2010-101140	20100115
IL 234097	A	20140930	IL 2010-234097	20100115
NZ 618004	A	20150626	NZ 2010-618004	20100115
ZA 2011005167	A	20120328	ZA 2011-5167	20110713
MX 2011007620	A	20111104	MX 2011-7620	20110715
IN 2011KN03402	A	20121102	IN 2011-KN3402	20110811
US 20120035212	A1	20120209	US 2011-13145054	20111020
US 8877776	B2	20141104		
HK 1164305	A1	20131108	HK 2012-104893	20120518
AU 2013203780	A1	20130502	AU 2013-203780	20130411
US 20150057310	A1	20150226	US 2014-14340871	20140725
JP 2015096543	A	20150521	JP 2014-264071	20141226

PRIORITY APPLN. INFO.: US 2009-61145421 P 20090116
AU 2010-204619 A3 20100115
IL 2010-214086 A3 20100115
JP 2011-546390 A3 20100115
NZ 2010-594594 A3 20100115
WO 2010-US21194 W 20100115
US 2011-13145054 A3 20111020
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 153:204211
AB N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide malate salts were prepared Thus, 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid (preparation given) was stirred with (COCl)2 in THF/DMF at ≤30° and the mixture was added to 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine (preparation given) and K2CO3 in THF/H2O followed by addition of H2O and stirring for 10 h to give N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide. The latter in EtOH was treated with malic acid in H2O followed by addition of C, thiol silica, heating to 78°, and addition of H2O followed by filtration, addition of Me2CHOH, cooling, and filtration to give N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide malate.
IT 1235470-36-6
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)
RN 1235470-36-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

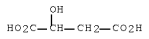
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

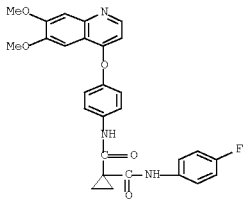
CRN 6915-15-7
CMF C4 H6 O5



IT 1235470-37-7P 1235470-38-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)
RN 1235470-37-7 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

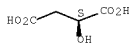
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

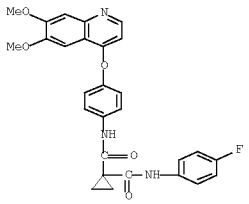
Absolute stereochemistry. Rotation (-).



RN 1235470-38-8 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

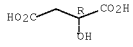
CRN 849217-68-1
CMF C28 H24 F N3 O5



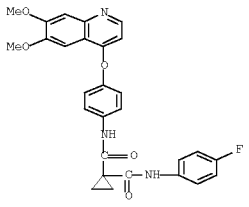
CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



IT 849217-68-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



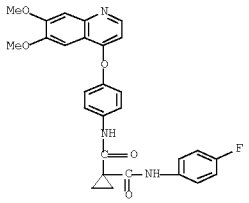
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 368 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:726266 CAPLUS Full-text
DOCUMENT NUMBER: 153:633557
TITLE: Targeted therapy for thyroid cancer: an updated review of investigational agents
AUTHOR(S): Deshpande, Hari A.; Gettinger, Scott N.; Sosa, Julie A.
CORPORATE SOURCE: Yale Cancer Center, New Haven, CT, 06520, USA
SOURCE: Current Opinion in Investigational Drugs (BioMed Central) (2010), 11(6), 661-668
CODEN: COIDAZ; ISSN: 2040-3429
URL: http://www.biomedcentral.com/content/pdf/cd-1102161.pdf

PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The treatment of thyroid cancer is evolving. The mol. mechanisms of carcinogenesis for many thyroid cancers have been investigated, and have yielded targets for potential therapies. These targets include VEGFR in the treatment of all thyroid cancers, BRAF in the treatment of papillary thyroid cancer, and RET in the treatment of medullary thyroid cancer (MTC). Many promising drugs that target one or more of these proteins are currently being evaluated, including sorafenib and sunitinib, both of which are still under development for the treatment of thyroid cancer but which have been approved for use in other malignancies. In addition, compds. such as vandetanib (AstraZeneca plc) and XL-184 (Bristol-Myers Squibb Co/Exelixis Inc) have demonstrated activity in early-phase clin. trials of MTC and are being tested further in randomized trials.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL-184 targeting vascular endothelial growth factor receptor, RET and BRAF protein may be effective in patient with thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

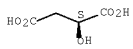
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

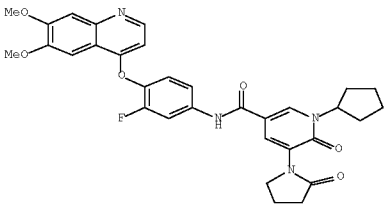
L8 ANSWER 369 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:439254 CAPLUS Full-text
DOCUMENT NUMBER: 152:422278
TITLE: Methods for the treatment of cancer
INVENTOR(S): Johns, Terrance
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 139pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010039248	A1	20100408	WO 2009-US5421	20090930
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2009300328	A1	20100408	AU 2009-300328	20090930
CA 2738583	A1	20100408	CA 2009-2738583	20090930
EP 2349328	A1	20110803	EP 2009-740207	20090930
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
JP 2012504606	T	20120223	JP 2011-530051	20090930
MX 2011003363	A	20110427	MX 2011-3363	20110329
US 20110229469	A1	20110922	US 2011-13122106	20110613
JP 2015107974	A	20150611	JP 2014-256872	20141219
AU 2015201812	A1	20150430	AU 2015-201812	20150410

PRIORITY APPLN. INFO.:
US 2008-61101971 P 20081001
AU 2009-300328 A3 20090930
JP 2011-530051 A3 20090930
WO 2009-US5421 W 20090930

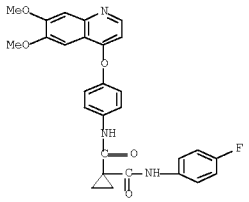
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 152:422278
GI



AB Methods for treating cancer with at least one HGF-Met inhibitor and at least one EGFR inhibitor are provided.
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

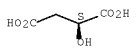
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 370 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:402977 CAPLUS Full-text
DOCUMENT NUMBER: 152:423197
TITLE: Recombinant replication-competent retroviral vectors expressing therapeutic products for treatment of proliferative disorders
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas; Perez, Omar
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

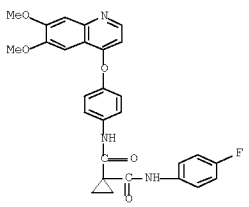
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010036986	A2	20100401	WO 2009-US58512	20090926
WO 2010036986	A3	20100701		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 2344648	A2	20110720	EP 2009-816967	20090926
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
CN 102227503	A	20111026	CN 2009-80147515	20090926
CN 102227503	B	20151021		
JP 2012503987	T	20120216	JP 2011-529292	20090926
JP 5684130	B2	20150311		
ZA 2011002115	A	20120725	ZA 2011-2115	20090926
CN 105274125	A	20160127	CN 2015-10505943	20090926
PH 12011500630	B1	20151211	PH 2011-12011500630	20110325
US 20110287020	A1	20111124	US 2011-13072704	20110326
US 8829173	B2	20140909		
AU 2013205006	A1	20130516	AU 2013-205006	20130413
AU 2013205006	B2	20160218		
US 20160053232	A1	20160225	US 2014-14477741	20140904
JP 2015119712	A	20150702	JP 2015-4923	20150114
JP 2015186479	A	20151029	JP 2015-97980	20150513

PRIORITY APPLN. INFO.:
US 2008-61100666 P 20080926
US 2008-61120618 P 20081208
US 2009-61186823 P 20090613
AU 2009-303690 A3 20090926
CN 2009-80147509 A3 20090926
JP 2011-529291 A3 20090926
JP 2011-529292 A3 20090926
WO 2009-US58512 W 20090926
US 2010-61318728 P 20100329
US 2011-13072704 A1 20110326

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Recombinant replication-competent retroviral (RCR) vectors are provided comprising: a retroviral gag protein; a retroviral pol protein; a retroviral envelop, a retroviral polynucleotide comprising long terminal repeat (LTR) sequence at the 3' end of the retroviral polynucleotide sequence; a mammalian-suitable promoter sequence at the 5' end of the retroviral polynucleotide, a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous polynucleotide; and cis-acting sequences necessary for reverse transcription, packaging and integration in a target cell. The RCR maintains higher replication competency after 6 passages compared to a pACE vector. The heterologous polynucleotide may encode modified cytosine deaminase (thermostabilized and codon optimized), single-chain antibody to CTLA-4, microRNAs miR-128-1 and miR-128-2, γ-interferon, interleukin 2, or other therapeutic proteins of interest. The disclosure further relates to cells and vector expressing or comprising such modified CDs and methods of using such modified CDs in the treatment of disease and disorders, and in particular cell proliferative disorders such as cancer.
IT 1140909-48-3, XL 184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy with; recombinant replication-competent retroviral vectors expressing therapeutic products for treatment of proliferative disorders)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

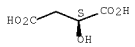
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L8 ANSWER 371 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2010:55413 CAPLUS Full-text
DOCUMENT NUMBER: 152:163651
TITLE: Methods for diagnosis, prognosis and treatment
INVENTOR(S): Fantl, Wendy J.; Rosen, David B.; Cesano, Alessandra; Putta, Santosh K.; Nolan, Garry P.; Cohen, Aileen C.; Evenson, Erik
PATENT ASSIGNEE(S): Nodality, Inc., USA
SOURCE: PCT Int. Appl., 201pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010006291	A1	20100114	WO 2009-US50295	20090710
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2304436	A1	20110406	EP 2009-790295	20090710
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
US 20150017119	A1	20150115	US 2014-14279905	20140516

PRIORITY APPLN. INFO.: US 2008-61079766 P 20080710
US 2008-61085789 P 20080801
US 2008-61104666 P 20081010
US 2008-61120320 P 20081205
US 2009-460029 A3 20090710
WO 2009-US50295 W 20090710
US 2012-13473829 A1 20120517

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

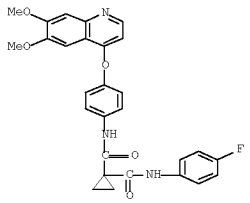
AB The present invention provides an approach for the detn. of the activation states of a plurality of proteins in single cells. This approach permits the rapid detection of heterogeneity in a complex cell population based on activation states, expression markers and other criteria, and the identification of cellular subsets that exhibit correlated changes in activation within the cell population. Moreover, this approach allows the correlation of cellular activities or properties. In addition, the use of modulators of cellular activation allows for characterization of pathways and cell populations. Several exemplary diseases that can be analyzed using the invention include AML, MDS, and MPN.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hematopoietic cell flow cytometry anal. and pathway stimulation for diagnosing, prognosing, therapy and progression of acute leukemia, myelodysplastic syndrome and myeloproliferative syndrome)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

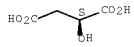
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 372 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:1534585 CAPLUS Full-text
DOCUMENT NUMBER: 153:76060
TITLE: Antiangiogenic strategies for treatment of malignant gliomas
AUTHOR(S): Chi, Andrew S.; Norden, Andrew D.; Wen, Patrick Y.
CORPORATE SOURCE: Stephen E. and Catherine Pappas Center for Neuro-Oncology, Department of Neurology, Division of Hematology and Oncology, Dana-Farber/Harvard Cancer Center, Harvard Medical School, Massachusetts General Hospital Cancer Center, USA
SOURCE: Neurotherapeutics (2009), 6(3), 513-526
CODEN: NEURNV; ISSN: 1933-7213
DIGITAL OBJECT ID: 10.1016/j.nurt.2009.04.010
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

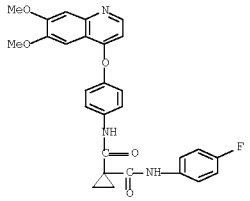
AB A review. Numerous antiangiogenic agents with diverse mechanisms of action are currently under investigation for the treatment of patients with glioblastoma (GBM), a diagnosis that continues to carry a poor prognosis despite maximal conventional therapy. Early clin. trials suggest that antiangiogenic drugs, which target the blood vessels of these highly angiogenic tumors, may have clin. benefit in GBM patients. Antiangiogenic agents have potent antiedema and steroid-sparing effects in patients, and emerging data suggest that these drugs may modestly improve progression-free survival. Although these early results are encouraging, several issues arise regarding the use and efficacy of these agents. Interpretation of the radiog. changes that occur after treatment with antiangiogenic agents presents a major challenge. Still lacking are reliable radiog. and biol. markers that can predict which patients will benefit from treatment and that accurately indicate response and progression during therapy. In addition, most patients treated with antiangiogenic drugs eventually progress, and the mechanisms by which tumors escape from therapy are only beginning to be understood. Larger prospective trials that incorporate correlative biomarker studies will be required to address these challenges. Here, we summarize the clin. experience with antiangiogenic therapy in patients with malignant gliomas (MG), review the major issues concerning the use and development of these agents, and discuss strategies that may build upon the initial gains observed with antiangiogenic agents.

IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiangiogenic agent XL 184 may show clin. utility in treatment of patient with malignant glioblastoma)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

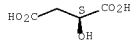
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 373 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:1435911 CAPLUS Full-text
DOCUMENT NUMBER: 151:565112
TITLE: Combinations VEGF(R) inhibitors and hepatocyte growth factor (c-met) inhibitors for the treatment of cancer
INVENTOR(S): Burgess, Theresa L.; Coxon, Angela; Dussault, Isabelle; Kaplan-Lefko, Paula; Polverino, Anthony J.; Beaupre, Darrin
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

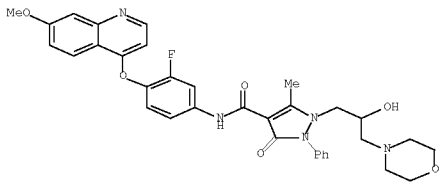
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009140549	A1	20091119	WO 2009-US44034	20090514
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,				

FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2009246263	A1	20091119	AU 2009-246263		20090514
AU 2009246263	B2	20140821			
CA 2723617	A1	20091119	CA 2009-2723617		20090514
EP 2288383	A1	20110302	EP 2009-747630		20090514
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, RS					
JP 2011520908	T	20110721	JP 2011-509721		20090514
JP 5699075	B2	20150408			
MX 2010012290	A	20110221	MX 2010-12290		20101110
US 20110104161	A1	20110505	US 2011-992359		20110111
US 20140243339	A1	20140828	US 2014-14194431		20140228
PRIORITY APPLN. INFO.:			US 2008-61127753	P	20080514
			WO 2009-US44034	W	20090514
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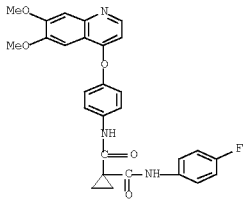
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 151:565112
GI



AB This invention is in the field of pharmaceutical agents and specifically relates to compds., compns., uses and methods for treating cancer, by combining VEGF(R) inhibitors and inhibitors of HGF/SF:c-Met. E.g., enhanced activity was observed when AMG 706 (Motesanib) was combined with Amgen Compound 3 [N-[4-[4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)-2-fluorophenoxy]pyridin-2-yl]morpholine-4-carboxamide] compared to either single agent alone when tested on human gastric adenocarcinoma cancer cells.
IT 1140909-48-3, XL 184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations VEGF(R) inhibitors and hepatocyte growth factor inhibitors for cancer treatment)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

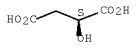
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

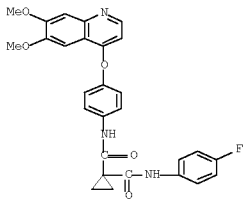


OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 374 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:1001773 CAPLUS Full-text
DOCUMENT NUMBER: 152:349858
TITLE: Novel treatment of medullary thyroid cancer
AUTHOR(S): Sugawara, Masahiro; Geffner, David L.; Martinez, Dorothy; Hershman, Jerome M.
CORPORATE SOURCE: aEndocrinology and Diabetes Division, Veterans Affairs Greater Los Angeles Medical Center, Department of Medicine, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA
SOURCE: Current Opinion in Endocrinology, Diabetes and Obesity (2009), 16(5), 367-372
CODEN: COEDFK; ISSN: 1752-296X
DIGITAL OBJECT ID: 10.1097/MED.0b013e3283304f0c
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: Metastatic medullary thyroid cancer (MTC) is an incurable disease once metastasis becomes unresectable. Many therapeutic drugs and methods have been tried to circumvent this difficulty. We review currently published treatments and hope for future developments of more effective treatment methods. Recent findings: Motesanib, vandetanib, axitinib (tyrosine kinase inhibitors), and XL184 (multikinase inhibitor) have been shown to achieve partial response or stable disease state of metastatic MTC. Sunitinib and sorafenib, currently available tyrosine kinase inhibitors, can also be tried for patients with MTC. However, these medications are not curative and do not improve survival rate. Only carcinoembryonic antigen-I-iodine-based radioimmunotherapy improved survival of a subset of patients with a very aggressive type of MTC. Drugs currently available for possible use of MTC treatment include bortezomib (proteasome inhibitor), valproic acid (histone deacetylase inhibitor), capecitabine (5-fluorouracil prodrug), and indomethacin (NSAID), although clin. studies have yet to be done. Cardiac natriuretic hormones and an extract of the plant Cautleya gracilis are new agents to be studied for MTC. Summary: Kinase inhibitors are the first drugs showing some efficacy in MTC. To improve survival, unconventional drugs or other therapies with or without kinase inhibitors need to be considered.
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multikinase inhibitors like XL184 was effective in patient with metastatic thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

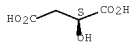
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



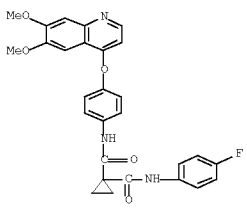
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REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 375 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:378374 CAPLUS Full-text
DOCUMENT NUMBER: 153:495871
TITLE: EGFR agonist: irreversible EGFR-TKI and c-Met inhibitors combination
AUTHOR(S): Yadoya, Takehito; Takahashi, Toshiaki; Yamamoto, Nobuyuki
CORPORATE SOURCE: Dep. of Respiratory Diseases, Shizuoka Cancer Center, Shizuoka, Japan
SOURCE: Mebio Oncology (2009), 6(1), 23-31
CODEN: MOENAJ; ISSN: 1349-2179
PUBLISHER: Mejikarubyusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review discussing (1) resistant mechanism to reversible epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), (2) irreversible EGFR-TKIs HKI-272, BIBW-2992, PF-299804 and CI-1033 and (3) c-Met inhibitors AMG-102, XL-184, XL-880 and ARQ-197.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(epidermal growth factor receptor agonist and the combination of irreversible EGFR-TKI and c-Met inhibitors)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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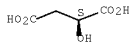
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

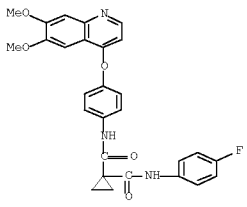


L8 ANSWER 376 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:239386 CAPLUS Full-text
DOCUMENT NUMBER: 150:275539
TITLE: Methods for diagnosis, prognosis and methods of treatment
INVENTOR(S): Fantl, Wendy J.; Putta, Santosh K.; Perez, Omar D.; Francis-Lang, Helen L.; Cohen, Aileen C.
PATENT ASSIGNEE(S): Nodality, Inc., USA
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

(methods for diagnosis, prognosis and treatment of diseases)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

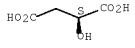
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

L8 ANSWER 377 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2009:140345 CAPLUS Full-text
DOCUMENT NUMBER: 150:214411
TITLE: Pyrimidine derivatives as JAK-2 inhibitors in combination with other agents and their preparation and use in the treatment of diseases
INVENTOR(S): Lamb, Peter
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 854pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009025847	A2	20090226	WO 2008-US9975	20080821
WO 2009025847	A3	20090611		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2008289442	A1	20090226	AU 2008-289442	20080821
CA 2696402	A1	20090226	CA 2008-2696402	20080821
US 20090098594	A1	20090416	US 2008-229476	20080821
EP 2179037	A2	20100428	EP 2008-795509	20080821
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CN 101802182	A	20100811	CN 2008-80107737	20080821
JP 2010536371	T	20101202	JP 2010-521884	20080821
EP 2860247	A1	20150415	EP 2014-189449	20080821
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IN 2010DN01966	A	20100820	IN 2010-DN1966	20100319
US 20120309029	A1	20121206	US 2012-13493857	20120611
US 9182385	B2	20151110		
US 20160097770	A1	20160407	US 2015-14825486	20150813

PRIORITY APPLN. INFO.:
US 2007-60957160 P 20070821
US 2008-61048920 P 20080429
EP 2008-795509 A3 20080821
US 2008-229476 A1 20080821
WO 2008-US9975 W 20080821
US 2012-13493857 A1 20120611

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB This invention is directed to methods and compns. for diagnosis, prognosis and for determining methods of treatment. The physiol. status of cells present in a sample (e.g. clin. sample) can be used in diagnosis or prognosis of a condition (e.g. chronic lymphocytic leukemia), in patient selection for therapy, to monitor treatment and to modify or optimize therapeutic regimens. The physiol. status of a cell can be determined by comparing the intracellular status of one or more activation elements (e.g. the phosphorylation status of a signaling mol.) in a cell (e.g. a cancer cell) to that of another cell (e.g. a normal cell). The physiol. status of a cell can be further classified by adding one or more modulators (e.g. an inhibitor or activator) to the cell in question. In some embodiments, the invention is directed to methods of determining a phenotypic profile of a population of cells.

IT 1140909-48-3, XL 184
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

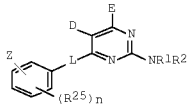
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009017838	A2	20090205	WO 2008-US9360	20080731
WO 2009017838	A3	20090702		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				

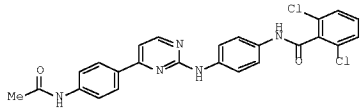
PRIORITY APPLN. INFO.:
US 2007-60962776 P 20070801

OTHER SOURCE(S): CASREACT 150:214411; MARPAT 150:214411

GI



I



II

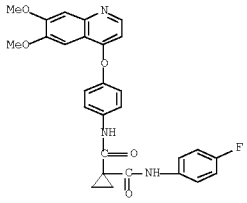
AB A method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a JAK-2 compound of formula I, or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of formula I and a pharmaceutically acceptable carrier, in combination with an active agent selected from of a Raf inhibitor, an EGFR inhibitor, a VEGFR inhibitor, a ErbB2 inhibitor, a BCR-Abl, inhibitor, a Flt3 inhibitor, a Src inhibitor, a c Kit inhibitor, an Akt inhibitor, a Ret inhibitor, an IFG1R inhibitor, an m-Tor inhibitor, a PI3K inhibitor, a PI3Kalpha inhibitor, wherein the mammal is in need of the treatment. Compds. of formula I wherein D and E are independently H, halo, CF3, heterocycloalkyl and alkyl; D and E taken together to form a 5- to

7-membered heteroaryl, and 5- to 7-membered heterocycloalkyl; L is a bond, O and NH; Z is alkoxy, cycloalkyl, and (un)substituted heteroaryl; Z and R25 taken together for form a 5- to 6-membered heterocycloalkyl, 5- to 6-membered heteroaryl, 5- to 6-membered cycloalkyl, etc.; each R25 is independently alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, etc.; R1 is H; R2 is (un)substituted aryl, (un)substituted heteroaryl, alkyl, etc.; n is 0 - 4; and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by acylation of 2-(4-aminophenylamino)-5-(4-acetylaminophenyl)pyrimidine with 2,6-dichlorobenzoyl chloride. All the invention compds. were evaluated for their JAK-2 inhibitory activity (some data given).

IT 849217-68-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as JAK-2 inhibitors in combination with other agents useful in treatment of diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L8 ANSWER 378 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2008:1282443 CAPLUS Full-text
DOCUMENT NUMBER: 149:486836
TITLE: Methods for treating cancer resistant to ErbB therapeutics
INVENTOR(S): Janne, Pasi A.; Engelman, Jeffrey; Cantley, Lewis C.
PATENT ASSIGNEE(S): Dana Farber Cancer Institute, USA; Beth Israel Deaconess Medical Center; Massachusetts General Hospital
SOURCE: PCT Int. Appl., 96pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008127710	A2	20081023	WO 2008-US4804	20080411
WO 2008127710	A3	20081204		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
AU 2008239594	A1	20081023	AU 2008-239594	20080411
AU 2008239594	B2	20131024		
CA 2683559	A1	20081023	CA 2008-2683559	20080411
EP 2076289	A2	20090708	EP 2008-742861	20080411
EP 2076289	B1	20141112		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
JP 2010523680	T	20100715	JP 2010-503084	20080411
ES 2529790	T3	20150225	ES 2008-742861	20080411
EP 2851091	A1	20150325	EP 2014-189064	20080411
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR				
US 20120225870	A1	20120906	US 2010-450826	20100318
US 8715665	B2	20140506		
AU 2013203111	A1	20130502	AU 2013-203111	20130409
AU 2013203111	B2	20151008		
US 20140296100	A1	20141002	US 2014-14256418	20140418
JP 2014141530	A	20140807	JP 2014-97474	20140509

PRIORITY APPLN. INFO.:
US 2007-60923384 P 20070413
AU 2008-239594 A3 20080411
EP 2008-742861 A3 20080411
JP 2010-503084 A3 20080411
WO 2008-US4804 W 20080411
US 2010-450826 A1 20100318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided herein are methods for treating cancer that is resistant to treatment with an anti- ErbB therapeutic agent and which is associated with an activating MET gene mutation or a MET gene amplification. The methods involve administering to a subject a combination of an anti- ErbB therapeutic and an anti-MET therapeutic. Also provided are methods for reducing ErbB mediated signaling or PI3 kinase mediated signaling in a cancer cell.

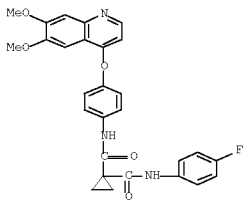
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treating cancer resistant to ErbB therapeutics using combination of anti-Met receptor agent and anti-ErbB receptor agent in relation to activation mutation or gene amplification)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

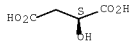
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L8 ANSWER 379 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN
ACCESSION NUMBER: 2008:771167 CAPLUS Full-text
DOCUMENT NUMBER: 149:104583
TITLE: N-Acylazetidine derivatives as MEK inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer
INVENTOR(S): Lamb, Peter
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 534pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

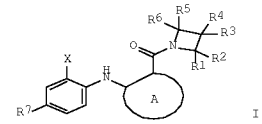
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008076415	A1	20080626	WO 2007-US25751	20071214
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2007334402	A1	20080626	AU 2007-334402	20071214
AU 2007334402	B2	20140213		
CA 2671982	A1	20080626	CA 2007-2671982	20071214
CA 2671982	C	20160126		
US 20080166359	A1	20080710	US 2007-2340	20071214
US 7999006	B2	20110816		
EP 2101759	A1	20090923	EP 2007-853418	20071214
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
CN 101605540	A	20091216	CN 2007-80051355	20071214
JP 2010513288	T	20100430	JP 2009-541420	20071214
JP 5311673	B2	20131009		
CN 105106199	A	20151202	CN 2015-10422958	20071214
AU 2013204026	A1	20130516	AU 2013-204026	20130411
JP 2013151569	A	20130808	JP 2013-102016	20130514

PRIORITY APPLN. INFO.:
US 2006-60875412 P 20061214
AU 2007-334402 A3 20071214
CN 2007-80051355 A3 20071214
JP 2009-541420 A3 20071214
WO 2007-US25751 W 20071214

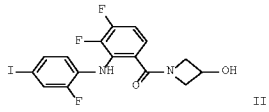
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 149:104583; MARPAT 149:104583

GI



I



II

AB The invention provides methods of treating cancer by administering a compound of formula I, or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments. Compds. of formula I wherein ring A is (un)substituted (hetero)arylene; X is (halo)alkyl, halo and haloalkoxy; R1, R2, R3, R4, R5 and R6 are independently H, halo, NO2, NH2 and derivs., OH and derivs., NHSO2H and derivs., CN, SH and derivs., etc.; R7 is H, halo and alkyl; and their pharmaceutically acceptable salts and solvates thereof are claimed. Example compound II was prepared by amidation of 3,4-difluoro-2-[(2-fluoro-4- iodophenyl)amino]benzoic acid with azetidin-3-ol hydrochloride. All the invention compds. were evaluated for their MEK inhibitory activity (some data given).

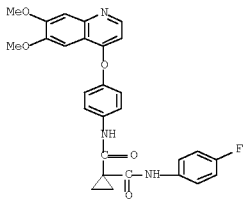
IT 849217-68-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of N-acylazetidine derivs. as MEK inhibitors useful in the mono- and combination therapy of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 380 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2008:699999 CAPLUS Full-text

DOCUMENT NUMBER: 149:30417

TITLE: Antibodies and inhibitory nucleic acids for targeing HIF-1α and for diagnosing/treating tumor or metastasis

INVENTOR(S): Huang, L. Eric

PATENT ASSIGNEE(S): University of Utah Research Foundation, USA

SOURCE: PCT Int. Appl., 157pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008070616	A2	20080612	WO 2007-US86264	20071203
WO 2008070616	A3	20090430		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
US 20100074897	A1	20100325	US 2009-517132	20090710
PRIORITY APPLN. INFO.:			US 2006-60868188 P	20061201
			WO 2007-US86264 W	20071203

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed are compns. and methods related to HIF-1α (hypoxia-inducible factor 1α). The compns. and methods comprise use of HIF-1α inhibitors for reducing tumor growth or metastatic tumor growth. The HIF-1α inhibitor is an antibody (including monoclonal, human and humanized antibody), small mol., siRNA, shRNA, or antisense polynucleotide.

IT 1140909-48-3, XL 184

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

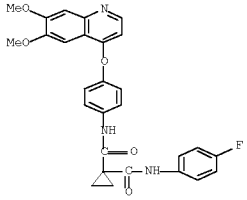
(antibodies and inhibitory nucleic acids for targeing HIF-1α and for diagnosing/treating tumor or metastasis)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

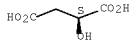
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L8 ANSWER 381 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2007:671771 CAPLUS Full-text

DOCUMENT NUMBER: 147:93969

TITLE: Combination of anti-angiopoietin 2 human monoclonal antibody and of VEGF-A, KDR and/or FLT1 antagonist for treating cancer

INVENTOR(S): Brown, Jeffrey Lester; Emery, Stephen Charles; Blakey, David Charles

PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited

SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007068895	A1	20070621	WO 2006-GB4611	20061212
WO 2007068895	A9	20080612		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
AU 2006324477	A1	20070621	AU 2006-324477	20061212
CA 2633211	A1	20070621	CA 2006-2633211	20061212
KR 2008073766	A	20080811	KR 2008-7015745	20061212
KR 1371773	B1	20140307		
EP 1962903	A1	20080903	EP 2006-820476	20061212
EP 1962903	B1	20130313		
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CN 101370519	A	20090218	CN 2006-80052740	20061212
CN 101370519	B	20130724		
JP 2009521412	T	20090604	JP 2008-545075	20061212
JP 5179373	B2	20130410		
NZ 569787	A	20110729	NZ 2006-569787	20061212
EP 2518083	A2	20121031	EP 2011-167374	20061212
EP 2518083	A3	20121205		
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ES 2411505	T3	20130705	ES 2006-820476	20061212
CN 103341168	A	20131009	CN 2013-10251494	20061212
AR 58359	A1	20080130	AR 2006-105550	20061215
NO 2008002448	A	20080710	NO 2008-2448	20080528
IN 2008DN04540	A	20090320	IN 2008-DN4540	20080528
MX 2008007686	A	20080627	MX 2008-7686	20080613
US 20090123474	A1	20090514	US 2008-97384	20080613
HK 1121674	A1	20131011	HK 2008-112903	20081125
US 20110097321	A1	20110428	US 2010-890101	20100924

AU 2011201326	A1	20110414	AU 2011-201326		20110323
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AU 2012202120	A1	20120503	AU 2012-202120		20120412
US 20120288497	A1	20121115	US 2012-13472862		20120516
JP 2012211155	A	20121101	JP 2012-131988		20120611
US 20140023654	A1	20140123	US 2013-13952997		20130729
PRIORITY APPLN. INFO.:			US 2005-60750551	P	20051215
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			JP 2008-545075	A3	20061212
			WO 2006-GB4611	W	20061212
			US 2008-97384	B1	20080613
			US 2010-890101	A1	20100924
			AU 2011-201326	A3	20110323
			US 2012-13472862	A1	20120516

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to agents which possess anti-angiogenic activity and are accordingly useful in methods of treatment of disease states associated with angiogenesis in the animal or human body. More specifically the invention concerns a combination of a monoclonal antibody against human anglopoietin 2 (anti-Ang-2) and an antagonist of the biol. activity of VEGF-A, and/or KDR receptor, and/or FLT1, and uses of such antagonists. The nucleotide sequences and the encoded amino acid sequences of anti-Ang-2 monoclonal antibodies are disclosed.

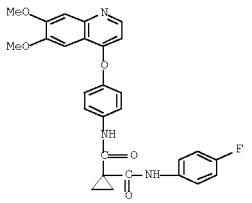
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); BIOL (Biological study)
(combination of anti-angiopoietin 2 human monoclonal antibody and of VEGF-A, KDR and/or FLT1 antagonist for treating cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

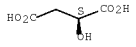
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 382 OF 382 CAPLUS COPYRIGHT 2016 ACS on STN

ACCESSION NUMBER: 2005:300201 CAPLUS Full-text

DOCUMENT NUMBER: 142:373856

TITLE: Preparation of quinolines and quinazolines as inhibitors of c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases

INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-ming; Chen, Jeff; Dalrymple, Lisa Esther; Forsyth, Timothy Patrick; Huynh, Tai Phat; Jammalamadaka, Vasu; Khoury, Richard George; Leahy, James William; Mac, Morrison B.; Mann, Grace; Mann, Larry W.; Nuss, John M.; Parks, Jason Jevious; Takeuchi, Craig Stacy; Wang, Yong; Xu, Wei

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 428 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

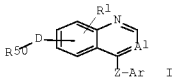
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030140	A2	20050407	WO 2004-US31523	20040924
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US 20090105299	A1	20090423	US 2007-753514	20070524
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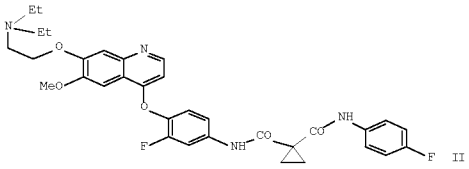
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 142:373856; MARPAT 142:373856

GI



Z-Ar I



II

AB The present invention provides compds. (shown as I; variables defined below; e.g. N-[4-[[7-[[2-(diethylamino)ethyl]oxy]-6-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide (shown as II)) for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. More specifically, the invention provides quinazolines and quinolines which inhibit, regulate and/or modulate kinase receptors, particularly c-Met, KDR, c-Kit, flt-3 and flt-4, signal transduction pathways related to the changes in cellular activities as mentioned above, compns. which contain these compds., and methods of using them to treat kinase-dependent diseases and conditions. The present invention also provides methods for making compds. as mentioned above, and compns. which contain these compds. For I: R1 = H, halogen, OR3, NO2, NH2, NR3R4, and (un)substituted lower alkyl; A1 = :N-, :C(H)-, and :C(CN)-; Z = -S(O)0-2-, -O-, and -NR5-; Ar is aryl or heteroaryl; D = -O-, -S(O)0-2-, and -NR15-; R50 = R3 or bicyclic radical; addnl. details are given in the claims. Methods of preparation are claimed and .apprx.80 example prepns. of I and intermediates are included. For example, II was prepared (34 %) from 2-(diethylamino)ethanol and cyclopropane-1,1-dicarboxylic acid N-[3-fluoro-4-[(7-hydroxy-6-methoxyquinolin-4-yl)oxy]phenyl]amide N-(4-fluorophenyl)amide, which was prepared (89 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-[4-[(7-benzyloxy-6-methoxyquinolin-4-yl)oxy]-3-fluorophenyl]amide N-(4-fluorophenyl)amide, which was prepared (48 %) from trifluoromethanesulfonic acid 7-benzyloxy-6-methoxyquinolin-4-yl ester and cyclopropane-1,1-dicarboxylic acid N-(3-fluoro-4-hydroxyphenyl)amide N-(4-fluorophenyl)amide, which was prepared (85 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-(4-benzyloxy-3-fluorophenyl)amide N-(4-fluorophenyl)amide, which was prepared (98 %) from (4-benzyloxy-3-fluorophenyl)amine and 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid; addnl. details are given in the examples.

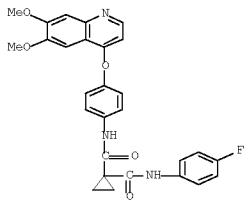
IT 849217-68-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinolines and quinazolines as inhibitors of c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 46 THERE ARE 46 CAPLUS RECORDS THAT CITE THIS RECORD (55 CITINGS)

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(FILE 'HOME' ENTERED AT 12:30:32 ON 28 APR 2016)

FILE 'REGISTRY' ENTERED AT 12:30:36 ON 28 APR 2016
L1 STRUCTURE UPLOADED
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L2 2 SEA FILE=REGISTRY SSS SAM L1
L3 48 SEA FILE=REGISTRY SSS FUL L1

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L8 382 SEA FILE=CAPLUS SPE=ON ABB=ON PLU=ON L7
D IBIB ABS HITSTR -382

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2870.68	6248.02

STN INTERNATIONAL LOGOFF AT 12:35:03 ON 28 APR 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY.DOCKET NO./TITLE	REQUEST ID
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	74767

Acknowledgement of Loss of Entitlement to Entity Status Discount

The entity status change request below filed through Private PAIR on 10/30/2018 has been accepted.

CERTIFICATIONS:

Change of Entity Status:

X Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be notification of loss of entitlement to small or micro entity status, as applicable.

This portion must be completed by the signatory or signatories making the entity status change in accordance with 37 CFR 1.4(d)(4).

Signature:	/Heidi M. Berven/
Name:	Heidi M. Berven
Registration Number:	48951

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	08/01/2017	9717720	224990/10-039C-US/343999	6725

91684 7590 07/12/2017

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Jo Ann Wilson, San Francisco, CA;
Khalid Shah, South San Francisco, CA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 05/26/2017

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	08/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$480	$480	08/28/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address Form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Honigman Miller Schwartz & Cohn LLP
2 Heidi M. Berven, Ph.D.
3 Jonathan P. O'Brien, Ph.D.

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Exelixis, Inc.

(B) RESIDENCE: (CITY and STATE OR COUNTRY): South San Francisco, CA

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

☒ Issue Fee (Please apply issue fee paid in this application 11/10/2016)
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☒ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 503145 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

☒ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

☐ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date June 14, 2017

Typed or printed name Heidi M. Berven, Ph.D. Registration No. 48,951

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Jo Ann Wilson, et al.	Art Unit:	1625
Application No.:	13/984,559	Examiner:	Timothy R. Rozof
Filing Date:	March 20, 2014	Conf. No.:	6725
Atty. Docket No.:	224990/10-039C-US/343999		

Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8(a)

The undersigned hereby certifies that the following documents are being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4) on this 14th day of June, 2017:

1. Cover Letter to the Commissioner for Patents;
2. Part B Fee(s) Transmittal (PTOL-85); and
3. This Certificate of Transmission under 37 C.F.R. § 1.8(a).



Charles Gregg-Geist (for Heidi M. Berven, Ph.D., Reg. No.: 48,951)

Electronic Acknowledgement Receipt

EFS ID:	29498981
Application Number:	13984559
International Application Number:	
Confirmation Number:	6725
Title of Invention:	PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS
First Named Inventor/Applicant Name:	Jo Ann Wilson
Customer Number:	91684
Filer:	Heid Marie Berven/Charles Gregg-Geist
Filer Authorized By:	Heid Marie Berven
Attorney Docket Number:	224990/10-039C-US/343999
Receipt Date:	14-JUN-2017
Filing Date:	20-MAR-2014
Time Stamp:	16:22:58
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		EX10-039C.pdf	1513392 74c8343fd558a1e547d64cbe6cacd485fd0b222a	yes	3

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Miscellaneous Incoming Letter	1	1
	Issue Fee Payment (PTO-85B)	2	2
	Transmittal Letter	3	3
Warnings:			
Information:			
	Total Files Size (in bytes):	1513392	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

HONIGMAN

Honigman Miller Schwartz and Cohn LLP
Attorneys and Counselors

Heidi M. Berven, Ph.D.

(269) 337-7710
Fax: (269) 337-7711
hberven@honigman.com

Via EFS

June 14, 2017

Commissioner for Patents
United States Patent and Trademark Office
P. O. Box 1450
Alexandria, VA 22313

Re: ***Application No.: 13/984,559***
Inventors: Jo Ann Wilson, et al.
Filing Date: March 20, 2014
Title: Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds
Confirmation No.: 6725
Attorney Docket No.: 224990/10-039C-US/343999

Dear Sir or Madam:

Enclosed for filing please find the following documents:

1. This Cover Letter to the Commissioner for Patents;
2. Part B Fee(s) Transmittal (PTOL-85); and
3. Certificate of Transmission under 37 C.F.R. § 1.8(a).

The Applicant requests that the Office reapply the $480.00 Issue Fee previously paid in this application to Issue Fee set forth in the Notice of Allowance and Fee(s) Due mailed May 26, 2017. It is believed that no additional fees are required. However, if there are any other fees due for this submission, or any credits, please apply them to Deposit Account Number 503145, referencing Attorney Docket Number 224990/10-039C-US/343999.

Very truly yours,

HONIGMAN MILLER SCHWARTZ AND COHN LLP

Heidi M. Berven, Ph.D.

HMB/cwg

OPAP AKRMA-14
JUN 14 2017
PATENT & TRADEMARK OFFICE

Best Available Copy

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7596 05/26/2017
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/243999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$420	$480	08/28/2017

06/15/2017 HVUONG2 00000018 503145 13984559
01 FC:2501 480.00 DA

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/(122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 Honigman Miller Schwartz & Cohn LLP
2 Heidi M. Berven, Ph.D.
3 Jonathan P. O'Brien, Ph.D.

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)
PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE	(B) RESIDENCE: (CITY and STATE OR COUNTRY)
Exelixis, Inc.	South San Francisco, CA

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
☒ Issue Fee (Please apply issue fee paid in this application 11/10/2016)
☐ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies .....

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)
☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☒ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 503145 (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)
☐ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
☒ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
☐ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature .....
Date June 14, 2017
Typed or printed name Heidi M. Berven, Ph.D.
Registration No. 48,951

06/15/2017 HVUONG2 00000004 503145 13984559
01 FC:2501 480.00 CR

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

91684 7590 05/26/2017

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 05/26/2017

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$480	$480	08/28/2017

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

91684 7590 05/26/2017
JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

TITLE OF INVENTION: PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$480	$480	08/28/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROZOF, TIMOTHY R	1625	514-312000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
❑ Issue Fee
❑ Publication Fee (No small entity discount permitted)
❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
❑ A check is enclosed.
❑ Payment by credit card. Form PTO-2038 is attached.
❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
❑ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
❑ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
❑ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/984,559	03/20/2014	Jo Ann Wilson	224990/10-039C-US/343999	6725

91684 7590 05/26/2017

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800

EXAMINER	
ROZOF, TIMOTHY R	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 05/26/2017

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 13/984,559	Applicant(s) WILSON ET AL.	
	Examiner TIMOTHY R. ROZOF	Art Unit 1625	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *May 18, 2017, RCE*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *40-51*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/TIMOTHY R ROZOF/
Primary Examiner, Art Unit 1625

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
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BIB DATA SHEET

CONFIRMATION NO. 6725

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/984,559	03/20/2014	514	1625	224990/10-039C-US/343999

APPLICANTS

INVENTORS

Jo Ann Wilson, San Francisco, CA;
Khalid Shah, South San Francisco, CA;

**** CONTINUING DATA ***************************

This application is a 371 of PCT/US12/24591 02/10/2012
which claims benefit of 61/441,520 02/10/2011
and claims benefit of 61/441,527 02/10/2011

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED **** ** SMALL ENTITY **

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☐ No Verified and Acknowledged /TIMOTHY R ROZOF/ Examiner's Signature	☐ Met after Allowance TRR Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		CA	0	25	6

ADDRESS

JONATHAN P. O'BRIEN, PH.D.
HONIGMAN MILLER SCHWARTZ AND COHN LLP
350 EAST MICHIGAN AVENUE, SUITE 300
Kalamazoo, MI 49007-3800
UNITED STATES

TITLE

PROCESSES FOR PREPARING QUINOLINE COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING SUCH COMPOUNDS

FILING FEE RECEIVED		
3890	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13984559	WILSON, JO ANN
	Examiner	Art Unit
	TIMOTHY R ROZOF	1625

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
Class, inventor, and EAST search	5/23/2017	TRR

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
A61K	31/47	5/23/2017	TRR
C07D	215/233	5/23/2017	TRR

	/TIMOTHY R ROZOF/ Primary Examiner.Art Unit 1625

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	7130	A61K31/47.cpc. C07D215/233.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2017/05/23 14:41
L2	4682	L1 and @ad<="20110210"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2017/05/23 14:41
L3	580	L2 and (protein near3 kinase)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2017/05/23 14:41
L4	83	L3 and (compound near3 (IA or IB))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2017/05/23 14:41

EAST Search History (Interference)

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5/ 23/ 2017 2:42:41 PM
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NEWS 14 MAR 29 New Version of Dissertation Abstracts Database Launched on STN
NEWS 15 APR 19 Additional Medline Unique Records Being Added to Embase
NEWS 16 APR 20 Latest Release of New STN Enhances Search History and Expands Database Coverage
NEWS 17 MAY 12 INPADOC/INPAFAM: New Chinese Legal Status Codes

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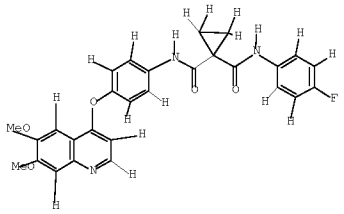
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L1   STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1   STR



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SAMPLE SCREEN SEARCH COMPLETED -   26 TO ITERATE

100.0% PROCESSED   26 ITERATIONS   3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 215 TO   825
PROJECTED ANSWERS: 3 TO   163

L2   3 SEA SSS SAM L1

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100.0% PROCESSED   567 ITERATIONS   41 ANSWERS
SEARCH TIME: 00.00.01

L3   41 SEA SSS FUL L1

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                                                       ENTRY   SESSION
FULL ESTIMATED COST   287.27   287.56

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FILE COVERS 1907 - 23 May 2017 VOL 166 ISS 23
FILE LAST UPDATED: 22 May 2017 (20170522/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

CAplus includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2017.

CAplus now includes the comprehensive Cooperative Patent Classification (CPC). See HELP CPC for details.

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=> s l3
L4   510 L3

=> d ibib abs hitstr -510

L4   ANSWER 1 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:705106 CAPLUS Full-text
DOCUMENT NUMBER: 166:463332
TITLE: Method for the diagnosis, prognosis and treatment of prostate cancer metastasis
INVENTOR(S):   Gomis, Roger; Jean-Mairet, Joel
PATENT ASSIGNEE(S):   Inbiomotion S.L., Spain
SOURCE: U.S. Pat. Appl. Publ., 65pp., Cont.-in-part of U.S. Ser. No. 435,128.
                         CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20170121777	A1	20170504	US 2016-15183419	20160615
WO 2014057357	A2	20140417	WO 2013-IB2866	20131009
WO 2014057357	A3	20140530		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG,

SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

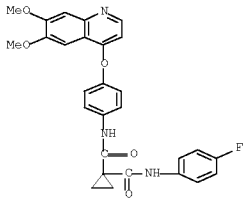
US 20150362495	A1	20151217	US 2015-14435128		20150410
JP 2016105731	A	20160616	JP 2016-48499		20160311
AU 2016213773	A1	20160901	AU 2016-213773		20160810
PRIORITY APPLN. INFO.:			US 2012-61713318	P	20121012
			WO 2013-IB2866	A	20131009
			US 2015-14435128	A2	20150410
			AU 2013-328385	A3	20131009
			JP 2015-536237	A3	20131009

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

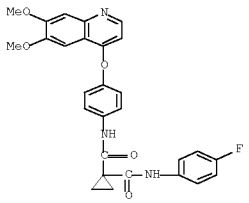
AB The present invention relates to a method for the diagnosis or the prognosis of metastasis, relapse or recurrence in prostate cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for the diagnosis or the prognosis of metastasis, relapse or recurrence in prostate cancer, as well as to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF expression level. Finally, the invention relates to the use of a c-MAF inhibitor as therapeutic target for treating the prostate cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MAF gene expression and therapeutic target for diagnosis or prognosis of metastasis, relapse or recurrence in prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 2 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:698000 CAPLUS Full-text
TITLE: Point mutations Trk inhibitor-resistant cancer and methods relating to the same



L4 ANSWER 3 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:668205 CAPLUS Full-text
DOCUMENT NUMBER: 166:475787
TITLE: Engineered substrates for high-throughput generation of 3d models of tumor dormancy, relapse and micrometastases for phenotype specific drug discovery and development
INVENTOR(S): Rege, Kaushal; Grandhi, Taraka Sai Pavan; Potta, Thrimoorthy
PATENT ASSIGNEE(S): Arizona Board of Regents on behalf of Arizona State University, USA
SOURCE: U.S. Pat. Appl. Publ., 49pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20170115275	A1	20170427	US 2016-15332928	20161024
PRIORITY APPLN. INFO.:			US 2015-62245865 P	20151023

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods to form a novel aminoglycoside based hydrogel for high-throughput generation of 3D dormant, relapsed and micrometastatic tumor microenvironments are disclosed. In addition, methods of screening agents against tumor cells grown in the 3D environments disclosed herein that include, for example, screening of lead drugs and therapies for an effect on dormant, relapsed and/or micrometastatic tumor cells.

IT 849217-68-1, Cabozantinib 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(engineered substrates for high-throughput generation of 3d models of tumor dormancy, relapse and micrometastases for phenotype specific drug discovery and development)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

INVENTOR(S): Nanda, Nisha; Bilenker, Josh H.; Doebele, Robert C.; Blake, James F.; Kolakowski, Gabrielle R.; Brandhuber, Barbara J.; Andrews, Steven W.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 379pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

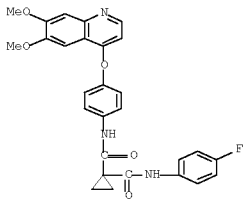
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017075107	A1	20170504	WO 2016-US58951	20161026
PRIORITY APPLN. INFO.:			US 2015-62246580 P	20151026
			US 2016-62287778 P	20160127
			US 2016-62323586 P	20160415

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

AB Provided herein are methods of treating a subject having a cancer, methods of selecting a treatment for a subject having a cancer, methods of selecting a subject having a cancer for a treatment that does not include a Trk inhibitor, methods of determining the likelihood that a subject having a cancer will have a pos. response to a treatment with a Trk inhibitor, methods of predicting the efficacy of a Trk inhibitor in a subject having cancer, methods of determining a subject's risk for developing a Trk inhibitor-resistant cancer, and methods of determining the presence of a Trk inhibitor-resistant cancer in a subject, based on the detection of a cell from a sample from the subject that has at least one of the point mutations in NTRK1 and/or NTRK2 and/or NTRK3.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(point mutations Trk inhibitor-resistant cancer and methods relating to the same)

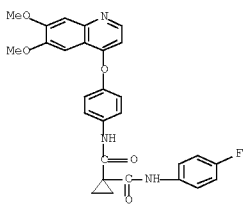
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

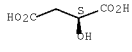
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 4 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:667980 CAPLUS Full-text
DOCUMENT NUMBER: 166:482401
TITLE: Multi-tyrosine kinase inhibitors derivatives and methods of use
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20pp., Cont.-in-part of U.S. Ser. No. 288,820.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20170112821	A1	20170427	US 2017-15402214	20170109
US 20160376239	A1	20161229	US 2016-15194813	20160628
US 20170020856	A1	20170126	US 2016-15288820	20161007

PRIORITY APPLN. INFO.: US 2015-62185785 P 20150629
US 2016-15194813 A2 20160628
US 2016-15288820 A2 20161007

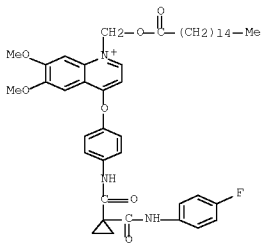
AB The present invention is directed to multi-tyrosine kinase inhibitor compds. The present invention is further directed to compns. comprising those compds. Finally, the present invention is directed to methods of treating eye conditions including, but not limited to, diabetic background retinopathy, diabetic macular edema, diabetic proliferative retinopathy, diabetic macular edema with proliferative retinopathy, proliferative fibrovascular disease, diabetic macular edema with proliferative fibrovascular disease, retinopathy of prematurity, dry macular degeneration, dry macular degeneration with drusen and wet macular degeneration, using compds. and compns. of the invention.

IT 2055907-45-2P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(multi-tyrosine kinase inhibitors derivs. and methods of use)

RN 2055907-45-2 CAPLUS
CN Quinolinium, 4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy-1-[[(1-oxohexadecyl)oxy]methyl]-, tetraphenylborate(1-) (1:1) (CA INDEX NAME)

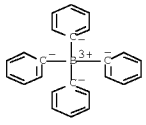
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CRN 2055907-44-1
CMF C45 H57 F N3 O7



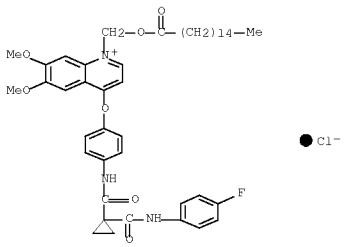
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CRN 4358-26-3
CMF C24 H20 B
CCI CCS



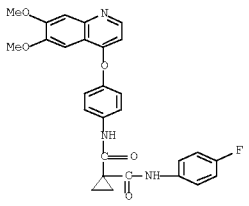
IT 2055907-46-3P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(multi-tyrosine kinase inhibitors derivs. and methods of use)

RN 2055907-46-3 CAPLUS
CN Quinolinium, 4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy-1-[[(1-oxohexadecyl)oxy]methyl]-, chloride (1:1) (CA INDEX NAME)



IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(multi-tyrosine kinase inhibitors derivs. and methods of use)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 5 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:627314 CAPLUS Full-text
TITLE: Patient-reported outcomes labeling for products approved by the office ofhematology and oncology products of the us food and drug administration (2010-2014)
AUTHOR(S): Gnanasakthy, Ari; De Muro, Carla; Clark, Marci; Haydysch, Emily; Ma, Esprit; Bonthapally, Vijayveer
CORPORATE SOURCE: RTI Health Solutions, Research Triangle Park, NC, USA
SOURCE: Journal of Clinical Oncology (2016), 34(16), 1928-1934
CODEN: JCONDN; ISSN: 1527-7755
DIGITAL OBJECT ID: 10.1200/JCO.2015.63.6480
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

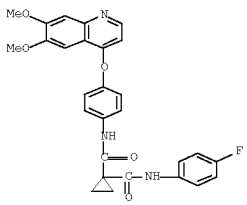
AB Purpose To review the use of patient-reported outcome (PRO) data in medical product labeling granted by the US Food and Drug Administration (FDA) for new mol. entities and biol. license applications by the FDA Office of Hematol. and Oncol. Products (OHOP) between Jan. 2010 and Dec. 2014, to elucidate challenges faced by OHOP for approving PRO labeling, and to understand challenges faced by drug manufacturers to include PRO end points in oncol. clin. trials. Methods FDA Drug Approval Reports by Month were reviewed to obtain the number of new mol. entities and biol. license applications approved from 2010 to 2014. Drugs approved by the FDA OHOP during this period were selected for further review, focusing on brand and generic name; approval date; applicant; indication; PRO labeling describing treatment benefit, measures, end point status, and significant results; FDA reviewer feedback on PRO end points; and study design of registration trials. First in class, priority review, fast track, orphan drug, or accelerated approval status was retrieved for selected oncol. drugs from 2011 to 2014. Descriptive analyses were performed by using Microsoft Excel 2010. Results Of 160 drugs approved by the FDA (2010-2014), 40 were approved by OHOP. Three (7.5%) of the 40 received PRO-related labeling (abiraterone acetate, ruxolitinib phosphate, and crizotinib). Compared with nononcol. drugs (2011-2014), oncol. drugs were more likely to be orphan and first in class. The majority of oncol. drug reviews by FDA were fast track, priority, or accelerated. Conclusion Although symptoms and functional decrements are common among patients with cancer, PRO labeling is rare in the United States, likely because of logistical hurdles and oncol. study design. Recent developments within the FDA OHOP to capture PROs in oncol. studies for the purpose of product labeling are encouraging.

IT INDEXING IN PROGRESS
IT 1140909-48-3, Cabozantinib s-malate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(safety and efficacy evaluation of hematol. and oncol. products approved by food and drug administration by using patient-reported outcome data during medical product labeling in United States)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

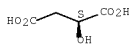
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

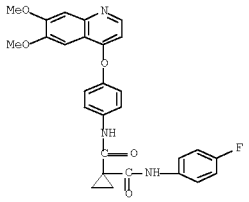
Absolute stereochemistry. Rotation (-).



L4 ANSWER 6 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:593648 CAPLUS Full-text
DOCUMENT NUMBER: 166:435203
TITLE: Stabilized BCL9 peptides for treatment of aberrant Wnt signaling
INVENTOR(S): Zhu, David
PATENT ASSIGNEE(S): Wntrx Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 161pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

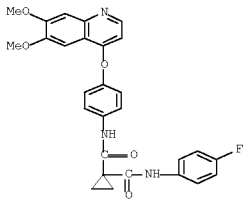
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017062518	A1	20170413	WO 2016-US55589	20161005

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2015-62237489 P 20151005
AB Disclosed here are polypeptides derived from the HD2 domain of human B-cell CLL/lymphoma 9 (BCL9) protein and variants thereof, as well as their use in the diagnosis, prevention, and/or treatment of a disease or disorder; also disclosed are methods of generating such polypeptides and variants thereof. Methods for treating cancer with a stabilized BCL9 peptide are encompassed, wherein the stabilized peptide comprises a portion of the HD2 domain of the BCL9 protein containing a hydrocarbon crosslinker generated using α,α-disubstituted amino acids.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized BCL9 peptides for treatment of aberrant Wnt signaling)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



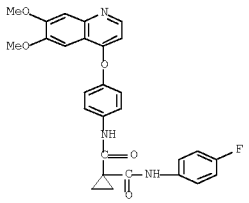
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:520766 CAPLUS Full-text
TITLE: Towards precision oncology in RET-aberrant cancers
AUTHOR(S): Subbiah, Vivek; Roszik, Jason
CORPORATE SOURCE: The University of Texas MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Cell Cycle (2017), 16(9), 813-814
CODEN: CCEYAS; ISSN: 1551-4005
DIGITAL OBJECT ID: 10.1080/15384101.2017.1302235
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review on RET as a druggable target in thyroid and non-small cell lung cancer was discussed.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(towards precision oncol. in RET-aberrant cancers)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:501476 CAPLUS Full-text
TITLE: Effective combinatorial immunotherapy for castration-resistant prostate cancer
AUTHOR(S): Lu, Xin; Horner, James W.; Paul, Erin; Shang, Xiaoying; Troncoso, Patricia; Deng, Pingna; Jiang, Shan; Chang, Qing; Spring, Denise J.; Sharma, Padmanee; Zebala, John A.; Maeda, Dean Y.; Wang, Y. Alan; DePinho, Ronald A.
CORPORATE SOURCE: Department of Cancer Biology, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Nature (London, United Kingdom) (2017), 543(7647), 728-732
CODEN: NATUAS; ISSN: 0028-0836
DIGITAL OBJECT ID: 10.1038/nature21676
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB A significant fraction of patients with advanced prostate cancer treated with androgen deprivation therapy experience relapse with relentless progression to lethal metastatic castration-resistant prostate cancer (mCRPC). Immune checkpoint blockade using antibodies against cytotoxic-T-lymphocyte-associated protein 4 (CTLA4) or programmed cell death 1/programmed cell death 1 ligand 1 (PD1/PD-L1) generates durable therapeutic responses in a significant subset of patients across a variety of cancer types. However, mCRPC showed overwhelming de novo resistance to immune checkpoint blockade, motivating a search for targeted therapies that overcome this resistance. Myeloid-derived suppressor cells (MDSCs) are known to play important roles in tumor immune evasion. The abundance of circulating MDSCs correlates with prostate-specific antigen levels and metastasis in patients with prostate cancer. Mouse models of prostate cancer show that MDSCs (CD11b+Gr1+) promote tumor initiation and progression. These observations prompted the authors to hypothesize that robust immunotherapy responses in mCRPC may be elicited by the combined actions of immune checkpoint blockade agents together with targeted agents that neutralize MDSCs yet preserve T-cell function. Here the authors develop a novel chimeric mouse model of mCRPC to efficiently test combination therapies in an autochthonous setting. Combination of anti-CTLA4 and anti-PD1 engendered only modest efficacy. Targeted therapy against mCRPC-infiltrating MDSCs, using multi-kinase inhibitors such as cabozantinib and BEZ235, also showed minimal anti-tumor activities. Strikingly, primary and metastatic CRPC showed robust synergistic responses when immune checkpoint blockade was combined with MDSC-targeted therapy. Mechanistically, combination therapy efficacy stemmed from the up-regulation of interleukin-1 receptor antagonist and suppression of MDSC-promoting cytokines secreted by prostate cancer cells. These observations illuminate a clin. path hypothesis for combining immune checkpoint blockade with MDSC-targeted therapies in the treatment of mCRPC.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinatorial immunotherapy for castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:471919 CAPLUS Full-text
DOCUMENT NUMBER: 166:366598
TITLE: Modified small molecule cytotoxins and albumin or mimetics for use in treatment of cancer
INVENTOR(S): Callmann, Cassandra E.; Thompson, Matthew P.; Gianneschi, Nathan C.; Leguyader, Clare L. M.; Bertin, Paul A.
PATENT ASSIGNEE(S): University of California, USA; Vybyl, Inc.
SOURCE: U.S. Pat. Appl. Publ., 30pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20170080094	A1	20170323	US 2016-15271822	20160921
WO 2017053391	A1	20170330	WO 2016-US52829	20160921

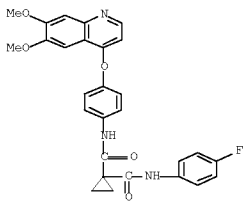
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62222059 P 20150922
OTHER SOURCE(S): MARPAT 166:366598

AB The present disclosure generally provides compds. useful for treating cancer. In some aspects, the disclosure provides small-mol. cytotoxins that are chemical modified to include one or more moieties that include hydrophobic portions. In some embodiments, the disclosure provides small-mol. cytotoxins that are chemical modified with fatty acid-containing moieties. In some aspects, the disclosure provides compns., such as pharmaceutical compns., that include such modified small-mol. cytotoxins and a protein. In some embodiments, the protein is albumin or an albumin mimetic. Further, the disclosure provides various uses of these compds. and compns.

IT 849217-68-1, Carbozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Carbozantinib; modified small mol. cytotoxins and albumin or mimetics for use in treatment of cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



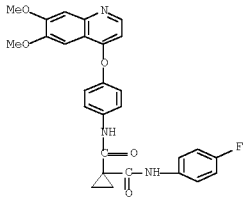
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:428494 CAPLUS Full-text
DOCUMENT NUMBER: 166:345239
TITLE: Methods for developing personalized drug treatment plans and targeted drug development based on proteomic profiles
INVENTOR(S): Gold, Larry; Delisle, Kirk; Sterling, David; Ostroff, Rachel; Zichi, Dom
PATENT ASSIGNEE(S): SomaLogic, Inc., USA
SOURCE: PCT Int. Appl., 120pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017044715	A1	20170316	WO 2016-US50908	20160909

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62215852 P 20150909



L4 ANSWER 10 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:465963 CAPLUS Full-text
TITLE: Brigatinib combined with anti-EGFR antibody overcomes osimertinib resistance in EGFR-mutated non-small-cell lung cancer
AUTHOR(S): Uchibori, Ken; Inase, Naohiko; Araki, Mitsugu; Kamada, Mayumi; Sato, Shigeo; Okuno, Yasushi; Fujita, Naoya; Katayama, Ryohei
CORPORATE SOURCE: Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, 3-8-31, Ariake, Koto-ku, Tokyo, 135-8550, Japan
SOURCE: Nature Communications (2017), 8, 14768
CODEN: NCAOBW; ISSN: 2041-1723
DIGITAL OBJECT ID: 10.1038/ncomms14768
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

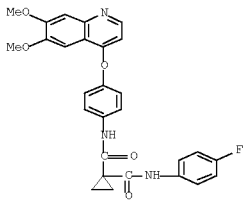
AB Osimertinib has been demonstrated to overcome the epidermal growth factor receptor (EGFR)-T790M, the most relevant acquired resistance to first-generation EGFR-tyrosine kinase inhibitors (EGFR-TKIs). However, the C797S mutation, which impairs the covalent binding between the cysteine residue at position 797 of EGFR and osimertinib, induces resistance to osimertinib. Currently, there are no effective therapeutic strategies to overcome the C797S/T790M/activating-mutation (triple-mutation)-mediated EGFR-TKI resistance. In the present study, we identify brigatinib to be effective against triple-mutation-harbouring cells in vitro and in vivo. Our original computational simulation demonstrates that brigatinib fits into the ATP-binding pocket of triple-mutant EGFR. The structure-activity relationship anal. reveals the key component in brigatinib to inhibit the triple-mutant EGFR. The efficacy of brigatinib is enhanced markedly by combination with anti-EGFR antibody because of the decrease of surface and total EGFR expression. Thus, the combination therapy of brigatinib with anti-EGFR antibody is a powerful candidate to overcome triple-mutant EGFR.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(brigatinib combined with anti-EGFR antibody synergistically suppressed osimertinib resistance in EGFR-mutated non-small-cell lung cancer in human and mouse)

AB The present invention relates to developing customized therapies for a disease or condition in a subject. In particular, the present invention relates to aptamer-based compns. and methods for identifying, modulating and monitoring drug targets in individual with a disease or condition, and further composition and methods for identifying and selecting protein targets for drug development.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for developing personalized drug treatment plans and targeted drug development based on proteomic profiles)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



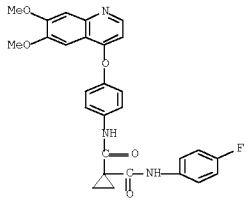
L4 ANSWER 12 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:378169 CAPLUS Full-text
DOCUMENT NUMBER: 166:413680
TITLE: Aldehyde Oxidase Mediated Metabolism in Drug-like Molecules: A Combined Computational and Experimental Study
AUTHOR(S): Xu, Yuan; Li, Liang; Wang, Yulan; Xing, Jing; Zhou, Lei; Zhong, Dafang; Luo, Xiaomin; Jiang, Hualiang; Chen, Kaixian; Zheng, Mingyue; Deng, Pan; Chen, Xiaoyan
CORPORATE SOURCE: Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 201203, Peop. Rep. China
SOURCE: Journal of Medicinal Chemistry (2017), 60(7), 2973-2982
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/acs.jmedchem.7b00019
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Aldehyde oxidase (AOX) is an important drug-metabolizing enzyme. However, the current in vitro models for evaluating AOX metabolism are sometimes misleading, and preclin. animal models generally fail to predict human AOX-mediated metabolism In this study, the authors report a combined

computational and exptl. investigation of drug-like mols. that are potential aldehyde oxidase substrates, of which multiple sites of metabolism (SOMs) mediated by AOX and their preferences for the reaction can be unambiguously identified. In addition, the proposed strategy was used to evaluate the metabolism of newly designed c-Met inhibitors, and a success switch-off of AOX metabolism was observed Overall, this study provide useful information to guide lead optimization and drug discovery based on AOX-mediated metabolism

IT 849217-68-1, Cabozantinib
RL: PKT (Pharmacokinetics); PRP (Properties); BIOL (Biological study)
(aldehyde oxidase mediated metabolism in designed c-Met inhibitors in relation to combined computational and exptl. study)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:363210 CAPLUS Full-text
DOCUMENT NUMBER: 166:280112
TITLE: Anti-cancer agent comprising c-MET inhibitor for synergistic effect of doxorubicin and photodynamic therapy
INVENTOR(S): Kwak, Mi Gyeong; Jung, Gyeong A.; Choi, Bo Hyeon
PATENT ASSIGNEE(S): Catholic University Industry-Academic Cooperation Foundation, S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, 28pp.
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

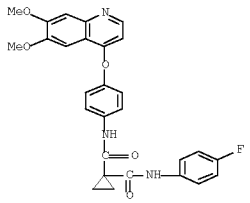
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2017021411	A	20170228	KR 2015-115500	20150817
KR 1723784	B1	20170407		

PRIORITY APPLN. INFO.: KR 2015-115500 20150817

AB The present invention relates to a pharmaceutical compn. comprising c-MET inhibitor as an active ingredient for enhancing doxorubicin and photodynamic cancer therapy. The pharmaceutical composition may further comprise a PI3K inhibitor, wherein the c-MET inhibitor alone or at least one selected from the group consisting of a c-MET inhibitor, a PI3K inhibitor and a mixture thereof is co-treated with doxorubicin in a cancer cell. The intracellular doxorubicin accumulation and ROS levels are increased, and accumulation of intracellular photosensitizer is increased to induce apoptosis. Therefore, it is possible to prevent the resistance of cancer cells to doxorubicin or photodynamic therapy (PDT) treatment and increase the sensitivity to doxorubicin or PDT to improve the efficiency of chemotherapy.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-met inhibitor; anti-cancer agent comprising c-MET inhibitor for enhancing doxorubicin and photodynamic therapy)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

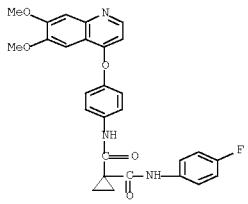


L4 ANSWER 14 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:348683 CAPLUS Full-text
TITLE: Endoscopic ultrasound-guided fine-needle aspirate-derived preclinical pancreatic cancer models reveal panitumumab sensitivity in KRAS wild-type tumors
AUTHOR(S): Berry, William; Algar, Elizabeth; Kumar, Beena; Desmond, Christopher; Swan, Michael; Jenkins, Brendan J.; Croagh, Daniel
CORPORATE SOURCE: Centre for Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research, Clayton, 3168, Australia
SOURCE: International Journal of Cancer (2017), 140(10), 2331-2343
CODEN: IJCNAW; ISSN: 0020-7136
DIGITAL OBJECT ID: 10.1002/ijc.30648
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Pancreatic cancer (PC) is largely refractory to existing therapies used in unselected patient trials, thus emphasizing the pressing need for new approaches for patient selection in personalized medicine. KRAS mutations occur in 90% of PC patients and confer resistance to epidermal growth factor receptor (EGFR) inhibitors (e.g., panitumumab), suggesting that KRAS wild-type PC patients may benefit from targeted panitumumab therapy. Here, we use tumor tissue procured by endoscopic ultrasound-guided fine-needle aspirate (EUS-FNA) to compare the in vivo sensitivity in patient-derived xenografts (PDXs) of KRAS wild-type and mutant PC tumors to panitumumab, and to profile the mol. signature of these tumors in patients with metastatic or localized disease. Specifically, RNASeq of EUS-FNA-derived tumor RNA from localized (n = 20) and metastatic (n = 20) PC cases revealed a comparable transcriptome profile. Screening the KRAS mutation status of tumor genomic DNA obtained from EUS-FNAs stratified PC patients into either KRAS wild-type or mutant cohorts, and the engraftment of representative KRAS wild-type and mutant EUS-FNA tumor samples into NOD/SCID mice revealed that the growth of KRAS wild-type, but not mutant, PDXs was selectively suppressed with panitumumab. Furthermore, in silico transcriptome interrogation of The Cancer Genome Atlas (TCGA)-derived KRAS wild-type (n = 38) and mutant (n = 132) PC tumors revealed 391 differentially expressed genes. Taken together, our study validates EUS-FNA for the application of a novel translational pipeline comprising KRAS mutation screening and PDXs, applicable to all PC patients, to evaluate personalized anti-EGFR therapy in patients with KRAS wild-type tumors.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(application of endoscopic ultrasound-guided fine-needle aspirate was efficient to identify panitumumab sensitivity and KRAS gene mutations in patient derived-pancreatic cancer xenografted mouse models)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

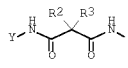


L4 ANSWER 15 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:314322 CAPLUS Full-text
DOCUMENT NUMBER: 166:255210
TITLE: A process for the preparation of malonic acid bisanilide derivatives
INVENTOR(S): Schreiner, Erwin; Nerdinger, Sven; Laus, Gerhard
PATENT ASSIGNEE(S): Sandoz AG, Switz.
SOURCE: PCT Int. Appl., 101pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

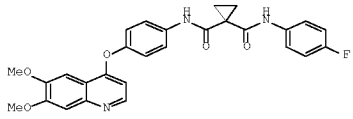
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017029362	A1	20170223	WO 2016-EP69621	20160818

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2015-2462 A 20150819
OTHER SOURCE(S): CASREACT 166:255210; MARPAT 166:255210
GI



I



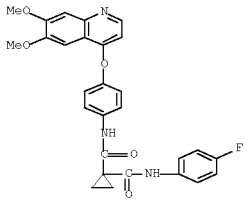
II

AB A process for the prepn. of title compds. I [X = substituted arom. or heteroarom. residue; Y = (un)substituted alkyl, alkenyl, cycloalkyl, etc.; R2 and R3 independently = alkyl, alkoxy, aryl, or heteroaryl; or R2 and R3 are taken together with the C atom to which they are attached form a cycle; with provisions] are disclosed via asym. bisamidation. The process is demonstrated by preparation of cabozantinib (II) by amidation of di-Me cyclopropane-1,1-dicarboxylate with 4-fluoroaniline followed by amidation with 4-((6,7-dimethoxyquinolin-4-yl)oxy)aniline.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(a process for the preparation of malonic acid bisanilide derivs.)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2017:311455 CAPLUS Full-text

DOCUMENT NUMBER: 166:264302

TITLE: Preparation of naphthyridine derivatives for use as mTOR inhibitors

INVENTOR(S): Wagman, Allan S.; Johnson, Russell J.; Cai, Haiying; Hu, Lily W.

PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA

SOURCE: PCT Int. Appl., 195pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017031427	A1	20170223	WO 2016-US47776	20160819

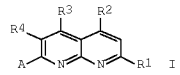
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

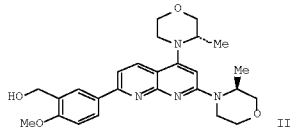
PRIORITY APPLN. INFO.: US 2015-62207039 P 20150819

OTHER SOURCE(S): MARPAT 166:264302

GI



I



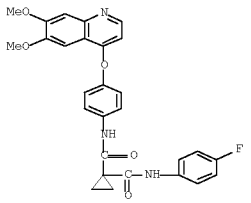
II

AB Title compds. I [A = (un)substituted aryl, or heteroaryl; R1 = (un)substituted alkyl, alkenyl, alkynyl, carbocyclic ring, etc.; R2 = (un)substituted alkyl, alkenyl, alkynyl, aryl, etc.; R3 = H, halo, OH, CN, alkyl, etc.; R4 = H, halo, OH, NH2, CN, alkyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as mTOR inhibitors. Thus, e.g., II was prepared by a multistep procedure (preparation given). I were evaluated in mTOR biochem. assays, e.g., II demonstrated an IC50 value of <0.1 μM.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of naphthyridine derivs. for use as mTOR inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2017:311436 CAPLUS Full-text

DOCUMENT NUMBER: 166:289508

TITLE: Methods for manufacturing phthalocyanine dye conjugates and stable conjugates

INVENTOR(S): Makings, Lewis R.; Heim, Roger; Garcia-Guzman, Miguel; Chin, Eileen Sun; Yadav, Deepak; Fong, Jerry

PATENT ASSIGNEE(S): Aspyrian Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 251pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017031363	A2	20170223	WO 2016-US47636	20160818
WO 2017031363	A3	20170420		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62206774 P 20150818

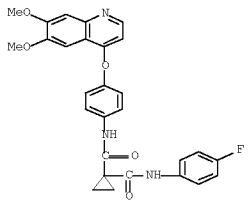
OTHER SOURCE(S): MARPAT 166:289508

AB Provided are methods for manufg. a conjugate contg. a phthalocyanine dye, including methods that include one or more steps of preparing or producing the conjugate, formulating the conjugate and packaging the conjugate. In some aspects, the manufacturing methods result in the generation of a stable conjugate. Also provided are stable phthalocyanine dye conjugates, compns. and articles of manufacture containing the stable conjugates, and methods for their administration to subjects for photoimmunotherapy. In some embodiments, the phthalocyanine dye conjugates are conjugated to a targeting mol., such as an antibody, that targets the conjugate to a cell or pathogen, such as by binding to a cell surface protein.

IT 849217-68-1, Cabozantinib, conjugates with phthalocyanine dyes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photoimmunotherapy with drug-phthalocyanine dye conjugates)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 18 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2017:310367 CAPLUS Full-text

DOCUMENT NUMBER: 166:272435

TITLE: Isothiocyanatostilbenes as a novel method and product for treating cancer

INVENTOR(S): Gray, Alana Lea; Cardelli, James; Coleman, David Thomas; El-Sayed, Khalid; Mohyeldin, Mohamed M.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 72pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

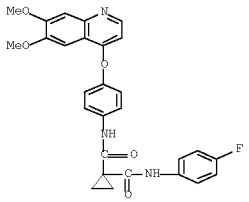
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017031036	A1	20170223	WO 2016-US46989	20160815

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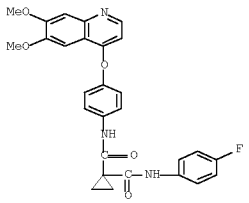
VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2015-62205106 P 20150814
OTHER SOURCE(S): MARPAT 166:272435
AB Products and methods for treating cancer in a human patient comprising administering to the patient therapeutically effective amount of a first pharmaceutically active agent, wherein the first pharmaceutically active agent is one of an isothiocyanatostilbene and a pharmacol. acceptable salt, solvate, ester, amide, clathrate, stereoisomer, enantiomer, prodrug or analog thereof, or a combination thereof.
IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isothiocyanatostilbenes as a novel method and product for treating cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

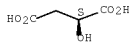
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

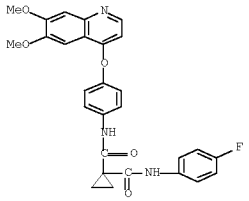
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:290245 CAPLUS Full-text
DOCUMENT NUMBER: 166:336721
TITLE: Identification of selective cytotoxic and synthetic lethal drug responses in triple negative breast cancer cells
AUTHOR(S): Gautam, Prson; Karhinen, Leena; Szwajda, Agnieszka; Kumar, Jha Sawan; Yadav, Bhagwan; Aittokallio, Tero; Wennerberg, Krister
CORPORATE SOURCE: Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland
SOURCE: Molecular Cancer (2016), 15, 34/1-34/16
CODEN: MCOACG; ISSN: 1476-4598
DIGITAL OBJECT ID: 10.1186/s12943-016-0517-3
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Triple neg. breast cancer (TNBC) is a highly heterogeneous and aggressive type of cancer that lacks effective targeted therapy. Despite detailed mol. profiling, no targeted therapy has been established. Hence, with the aim of gaining deeper understanding of the functional differences of TNBC subtypes and how that may relate to potential novel therapeutic strategies, we studied comprehensive anticancer-agent responses among a panel of TNBC cell lines. Method: The responses of 301 approved and investigational oncol. compds. were measured in 16 TNBC cell lines applying a functional profiling approach. To go beyond the standard drug viability effect profiling, which has been used in most chemosensitivity studies, we utilized a multiplexed readout for both cell viability and cytotoxicity, allowing us to differentiate between cytostatic and cytotoxic responses. Results: Our approach revealed that most single-agent anti-cancer compds. that showed activity for the viability readout had no or little cytotoxic effects. Major compound classes that exhibited this type of response included anti-mitotics, mTOR, CDK, and metabolic inhibitors, as well as many agents selectively inhibiting oncogene-activated pathways. However, within the broad viability-acting classes of compds., there were often subsets of cell lines that responded by cell death, suggesting that these cells are particularly vulnerable to the tested substance. In those cases we could identify differential levels of protein markers associated with cytotoxic responses. For example, PAI-1, MAPK phosphatase and Notch-3 levels associated with cytotoxic responses to mitotic and proteasome inhibitors, suggesting that these might serve as markers of response also in clin. settings. Furthermore, the cytotoxicity readout highlighted selective synergistic and synthetic lethal drug combinations that were missed by the cell viability readouts. For instance, the MEK inhibitor trametinib synergized with PARP inhibitors. Similarly, combination of two non-cytotoxic compds., the rapamycin analog everolimus and an ATP-competitive mTOR inhibitor dactolisib, showed synthetic lethality in several mTOR-addicted cell lines. Conclusions: Taken together, by studying the combination of cytotoxic and cytostatic drug responses, we identified a deeper spectrum of cellular responses both to single agents and combinations that may be highly relevant for identifying precision medicine approaches in TNBC as well as in other types of cancers.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of two non-cytotoxic compds., rapamycin analog everolimus and ATP-competitive mTOR inhibitor dactolisib, showed synthetic lethality in human triple neg. breast cancer cell lines)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

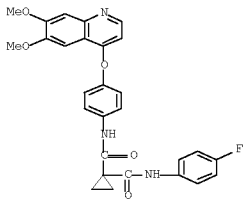


L4 ANSWER 20 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:233954 CAPLUS Full-text
DOCUMENT NUMBER: 166:240656
TITLE: Composition intended to vectorise an anti-cancer agent
INVENTOR(S): Robic, Caroline; Mayer, Jean-Francois
PATENT ASSIGNEE(S): Guerbet, Fr.
SOURCE: Fr. Demande, 50pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 3039767	A1	20170210	FR 2015-57524	20150804
WO 2017021508	A1	20170209	WO 2016-EP68687	20160804

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: FR 2015-57524 A 20150804
AB The invention relates to a stable water-in-oil emulsion compn., comprising: - 20 to 40% (volume/volume) aqueous phase, in the form of droplets, comprising an anti-cancer agent and a bulking agent selected from the non-ionic macrocyclic chelate complexes with a paramagnetic metal, - 60 to 80% (volume/volume) lipid phase comprising an iodized oil and at least one surfactant of formula R2[OCH2[CH(OR3)]sCH2]mOR1 (I) in a proportion, by mass of surfactant with respect to the total volume of the composition, of 0.3 to 5%, the formula I of said surfactant being the following: I in which: - s is 0 or 1, - m represents an integer from 2 to 30, - R1 represents a group of formula -[CO[CH2]n-[CH=CH]r-[CH2]o-CH([CH2]pMe)-O]q-H (II), II in which n represents an integer from 4 to 10, o represents an integer from 1 to 4, p represents an integer from 3 to 7, q represents an integer from 2 to 10 and r is 0 or 1, - R2 represents a hydrogen atom or is identical to R1, - each R3 independently represents a hydrogen atom or is identical to R1. The invention also relates to the method for preparation of same and use of same in the treatment of cancer and the metastases thereof.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition intended to vectorise an anti-cancer agent)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

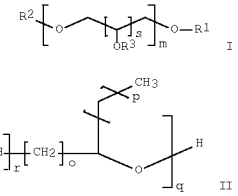


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

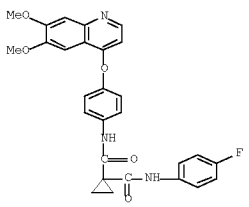
L4 ANSWER 21 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:231763 CAPLUS Full-text
DOCUMENT NUMBER: 166:240653
TITLE: Composition intended to vectorise an anti-cancer agent
INVENTOR(S): Robic, Caroline; Mayer, Jean-Francois
PATENT ASSIGNEE(S): Guerbet, Fr.
SOURCE: PCT Int. Appl., 55pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017021508	A1	20170209	WO 2016-EP68687	20160804
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
FR 3039767	A1	20170210	FR 2015-57524	20150804

PRIORITY APPLN. INFO.: FR 2015-57524 A 20150804
OTHER SOURCE(S): MARPAT 166:240653
GI



AB The invention relates to a stable water-in-oil emulsion compn., comprising: - 20 to 40% (volume/volume) aqueous phase, in the form of droplets, comprising an anti-cancer agent and a bulking agent selected from the non-ionic macrocyclic chelate complexes with a paramagnetic metal, - 60 to 80% (volume/volume) lipid phase comprising an iodized oil and at least one surfactant of formula (I) in a proportion, by mass of surfactant with respect to the total volume of the composition, of 0.3 to 5%, the formula I of said surfactant being the following: I in which: - s is 0 or 1, - m represents an integer from 2 to 30, - R1 represents a group of formula (II), II in which n represents an integer from 4 to 10, o represents an integer from 1 to 4, p represents an integer from 3 to 7, q represents an integer from 2 to 10 and r is 0 or 1, - R2 represents a hydrogen atom or is identical to R1, - each R3 independently represents a hydrogen atom or is identical to R1. The invention also relates to the method for preparation of same and use of same in the treatment of cancer and the metastases thereof.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition intended to vectorise an anti-cancer agent)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

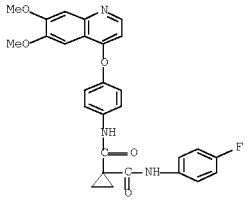
L4 ANSWER 22 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:228693 CAPLUS Full-text
DOCUMENT NUMBER: 166:242580
TITLE: Motile sperm domain contg. protein 2 (MOSPD2) inhibitors for the treatment of cancer
INVENTOR(S): Mendel, Itzhak; Propheta-Meiran, Oshrat; Salem, Yaniv; Shoham, Anat; Yacov, Niva; Breitbart, Eyal
PATENT ASSIGNEE(S): Vascular Biogenics Ltd., Israel
SOURCE: PCT Int. Appl., 149pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017021857	A1	20170209	WO 2016-IB54584	20160729
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2015-62199571 P 20150731
OTHER SOURCE(S): MARPAT 166:242580
AB Disclosed herein are methods of treating, reducing the incidence of, or preventing one or more activities in or of a cancer cell, methods of treating, reducing the incidence of, or preventing migration or metastasis of a cancer cell, methods of treating, reducing the incidence of, or preventing a cancer by reducing tumor associated macrophages (TAMs) or their migration, and methods of treating, reducing the incidence of, or preventing a cancer (including metastatic cancer), for example, with an inhibitor of Motile Sperm Domain containing Protein 2 (MOSPD2). Also disclosed are inhibitors of MOSPD2 (e.g., anti-MOSPD2 antibodies or antigen binding fragments thereof) and pharmaceutical compns. containing MOSPD2 inhibitors. Also disclosed are methods for the prediction, diagnosis, or prognosis of cancer, cancer metastasis, tumor progression, or tumor invasiveness in a subject.
IT 1140909-48-3, Cabozantinib S-malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(motile sperm domain containing protein 2 (MOSPD2) inhibitors for the treatment of inflammation)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

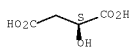
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

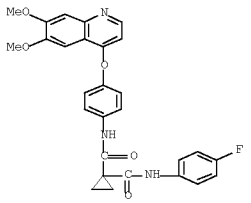


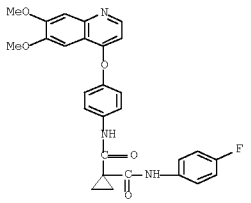
L4 ANSWER 23 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:202491 CAPLUS Full-text
TITLE: High potency VEGFRs/MET/FMS triple blockade by TAS-115 concomitantly suppresses tumor progression and bone destruction in tumor-induced bone disease model with lung carcinoma cells
AUTHOR(S): Fujita, Hidenori; Gomori, Akira; Fujioka, Yayoi; Kataoka, Yuki; Tanaka, Kenji; Hashimoto, Akihiro; Suzuki, Takamasa; Ito, Kenjiro; Haruma, Tomonori; Yamamoto-Yokoi, Hiromi; Harada, Naomoto; Sakuragi, Motomu; Oda, Nobuyuki; Matsuo, Kenichi; Inada, Masaki; Yonekura, Kazuhiko
CORPORATE SOURCE: Discovery and Preclinical Research Division, Taiho Pharmaceutical Co., Ltd., Tsukuba, Ibaraki, Japan
SOURCE: PLoS One (2016), 11(10), e0164830/1-e0164830/21
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0164830
PUBLISHER: Public Library of Science

DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Approx. 25-40% of patients with lung cancer show bone metastasis. Bone modifying agents reduce skeletal-related events (SREs), but they do not significantly improve overall survival. Therefore, novel therapeutic approaches are urgently required. In this study, we investigated the anti-tumor effect of TAS-115, a VEGFRs and HGF receptor (MET)-targeted kinase inhibitor, in a tumor-induced bone disease model. A549-Luc-BM1 cells, an osteo-tropic clone of luciferase-transfected A549 human lung adenocarcinoma cells (A549-Luc), produced aggressive bone destruction associated with tumor progression after intratibial (IT) implantation into mice. TAS-115 significantly reduced IT tumor growth and bone destruction. Histopathol. anal. showed a decrease in tumor vessels after TAS-115 treatment, which might be mediated through VEGFRs inhibition. Furthermore, the number of osteoclasts surrounding the tumor was decreased after TAS-115 treatment. In vitro studies demonstrated that TAS-115 inhibited HGF-, VEGF-, and macrophage-colony stimulating factor (M-CSF)-induced signaling pathways in osteoclasts. Moreover, TAS-115 inhibited Feline McDonough Sarcoma oncogene (FMS) kinase, as well as M-CSF and receptor activator of NF-κB ligand (RANKL)-induced osteoclast differentiation. Thus, VEGFRs/MET/FMS-triple inhibition in osteoclasts might contribute to the potent efficacy of TAS-115. The fact that concomitant dosing of sunitinib (VEGFRs/FMS inhibition) with crizotinib (MET inhibition) exerted comparable inhibitory efficacy for bone destruction to TAS-115 also supports this notion. In conclusion, TAS-115 inhibited tumor growth via VEGFRkinase blockade, and also suppressed bone destruction possibly through VEGFRs/MET/ FMS-kinase inhibition, which resulted in potent efficacy of TAS-115 in an A549-Luc-BM1 bone disease model. Thus, TAS-115 shows promise as a novel therapy for lung cancer patients with bone metastasis.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(high potency TAS-115 treatment blocks VEGFR, MET and FMS signaling pathways which suppresses tumor progression and bone destruction in human lung adenocarcinoma cells implanted xenograft mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:157735 CAPLUS Full-text
DOCUMENT NUMBER: 166:154759
TITLE: Methods, treatment, and compositions for characterizing thyroid nodule
INVENTOR(S): Hahn, Maria A.; Yim, John H.; Fong, Yuman; Li, Arthur X.; Wu, Xiwei
PATENT ASSIGNEE(S): City of Hope, USA
SOURCE: U.S. Pat. Appl. Publ., 305 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20170022570	A1	20170126	US 2016-15217645	20160722
PRIORITY APPLN. INFO.:			US 2015-62196678 P	20150724

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The current disclosure provides, inter alia, method of detg. benign nodules from thyroid cancer in a subject that is found to have a thyroid nodule, method of treating thyroid cancer in a subject detected to have thyroid cancer by the method of the current disclosure, compns. for determining benign nodules from thyroid cancer in a subject, and kits including reagents and composition for determining benign nodules from thyroid cancer in a subject.

IT 1140909-48-3, Cabozantinib-S-Malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biopsy DNA methylation for characterizing thyroid nodule)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1

L4 ANSWER 24 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:196635 CAPLUS Full-text
DOCUMENT NUMBER: 166:215940
TITLE: Methods and compositions comprising epidermal growth factor receptor (EGFR) inhibitors in combination with MEK and MET inhibitors for the treatment of cancer
INVENTOR(S): Klampfer, Lidija
PATENT ASSIGNEE(S): Southern Research Institute, USA
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

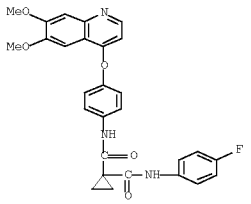
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017019279	A1	20170202	WO 2016-US41569	20160708
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20170027951	A1	20170202	US 2016-15205894	20160708
PRIORITY APPLN. INFO.:			US 2015-62197454 P	20150727

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB In one aspect, the invention relates to pharmaceutical compns. and methods for treating a cancer comprising administration of an EGFR inhibitor (e.g. gefitinib) and a MEK inhibitor (e.g. trametinib) or MET inhibitor (e.g. crizotinib). In various aspects, the methods can comprise determination of increased levels of HGF, e.g., determining if a patient has an increased level of serum HGF. This abstract is intended as a scanning tool for purposes of searching in the particular art and is not intended to be limiting of the present invention.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. comprising epidermal growth factor receptor (EGFR) inhibitors in combination with MEK and MET inhibitors for the treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

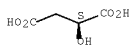
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 26 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:156352 CAPLUS Full-text
DOCUMENT NUMBER: 166:204124
TITLE: N-acylalkyl prodrugs of multi-tyrosine kinase inhibitors and methods of use for treating eye disease
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19pp., Cont.-in-part of U.S. Ser. No. 194,813.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20170020856	A1	20170126	US 2016-15288820	20161007
US 20160376239	A1	20161229	US 2016-15194813	20160628
US 20170112821	A1	20170427	US 2017-15402214	20170109
PRIORITY APPLN. INFO.:			US 2015-62185785 P	20150629
			US 2016-15194813 A2	20160628
			US 2016-15288820 A2	20161007

OTHER SOURCE(S): CASREACT 166:204124; MARPAT 166:204124

AB The present invention is directed to N-acylalkyl prodrugs e.g. cabozantinib N-acyl Me Palmitate as. multi-tyrosine kinase inhibitors. The present invention is further directed to compns. comprising those compds. Finally, the present invention is directed to methods of treating eye conditions including, but not limited to, diabetic background retinopathy, diabetic macular edema, diabetic proliferative retinopathy, diabetic macular edema with proliferative retinopathy, proliferative fibrovascular disease, diabetic macular edema with proliferative fibrovascular disease, retinopathy of prematurity, dry macular degeneration, dry macular degeneration with drusen and wet macular degeneration, using compds. and compns. of the invention.

IT 2055907-45-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(Cabozantinib N-acyl Me palmitate tetraphenylborate; N-acylalkyl prodrugs of multi-tyrosine kinase inhibitors and methods of use for treating eye disease)

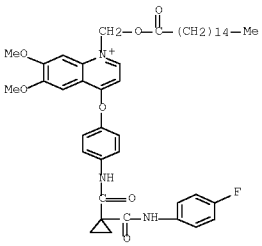
RN 2055907-45-2 CAPLUS

CN Quinolinium, 4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy-1-[[(1-oxohexadecyl)oxy]methyl]-, tetraphenylborate(1-) (1:1) (CA INDEX NAME)

CM 1

CRN 2055907-44-1

CMF C45 H57 F N3 O7

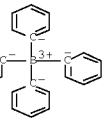


CM 2

CRN 4358-26-3

CMF C24 H20 B

CCI CCS



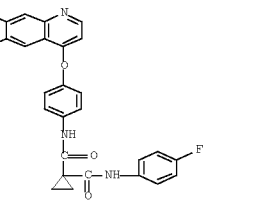
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(N-acylalkyl prodrugs of multi-tyrosine kinase inhibitors and methods of use for treating eye disease)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



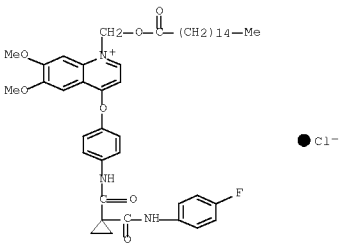
IT 2055907-46-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(N-acylalkyl prodrugs of multi-tyrosine kinase inhibitors and methods of use for treating eye disease)

RN 2055907-46-3 CAPLUS

CN Quinolinium, 4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy-1-[[(1-oxohexadecyl)oxy]methyl]-, chloride (1:1) (CA INDEX NAME)



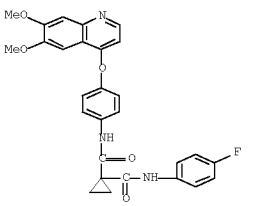
IT 849217-68-1, Cabozantinib, N-acylalkyl prodrugs

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(N-acylalkyl prodrugs of multi-tyrosine kinase inhibitors and methods of use for treating eye disease)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 27 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2017:153494 CAPLUS Full-text

DOCUMENT NUMBER: 166:193176

TITLE: Use of 4-amino-6-(2,6-dichlorophenyl)-8-methyl-2-(phenylamino)-pyrido[2,3-d]pyrimidin-7(8H)-one in formulations for treatment of solid tumors

INVENTOR(S): Molina Vila, Miguel Angel; Garcia Roman, Silvia; Borrell Bilbao, Jose Ignacio; Teixido Closa, Jordi; Estrada Tejedor, Roger; Puig de la Bellacasa Cazorla, Raimon

PATENT ASSIGNEE(S): Pangaea Biotech S.L., Spain; Institut Quimic de Sarria Cets Fundacio Privada

SOURCE: Eur. Pat. Appl., 21pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 3120851	A1	20170125	EP 2015-382375	20150721
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
WO 2017013160	A1	20170126	WO 2016-EP67264	20160720
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: EP 2015-382375 A 20150721

AB The present invention relates to 4-amino-6-(2,6-dichlorophenyl)-8-methyl-2-(phenylamino)-pyrido[2,3-d]pyrimidin-7(8H)-one of formula (1) for use in the treatment and/or prevention of solid tumors, and combinations comprising said compound and a chemotherapeutic drug.

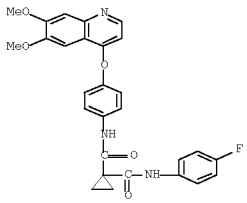
IT 849217-68-1, Cabozantinib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of 4-amino-6-(2,6-dichlorophenyl)-8-methyl-2-(phenylamino)-pyrido[2,3-d]pyrimidin-7(8H)-one in formulations for treatment of solid tumors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

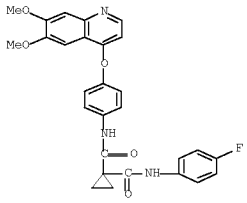


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:153493 CAPLUS Full-text
DOCUMENT NUMBER: 166:193175
TITLE: Use of 4-amino-6-(2,6-dichlorophenyl)-8-methyl-2-(phenylamino)-pyrido[2,3-d]pyrimidin-7(8H)-one in formulations for treatment of solid tumors
INVENTOR(S): Molina Vila, Miguel Angel; Garcia Roman, Silvia; Borrell Bilbao, Jose Ignacio; Teixido Closa, Jordi; Estrada Tejedor, Roger; Puig de la Bellacasa Cazorla, Raimon
PATENT ASSIGNEE(S): Pangaea Biotech, S.L., Spain; Institut Quimic de Sarria, Cets Fundacio Privada
SOURCE: PCT Int. Appl., 51pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

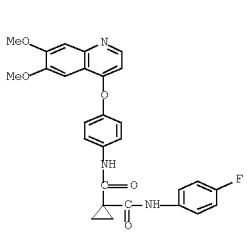
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2017013160	A1	20170126	WO 2016-EP67264	20160720
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 3120851	A1	20170125	EP 2015-382375	20150721
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

PRIORITY APPLN. INFO.: EP 2015-382375 A 20150721
AB The present invention relates to 4-amino-6-(2,6-dichlorophenyl)-8-methyl-2-(phenylamino)-pyrido[2,3-d]pyrimidin-7(8H)-one of formula (1) for use in the treatment and/or prevention of solid tumors, and combinations comprising said compound and a chemotherapeutic drug.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of 4-amino-6-(2,6-dichlorophenyl)-8-methyl-2-(phenylamino)-pyrido[2,3-d]pyrimidin-7(8H)-one in formulations for treatment of solid tumors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

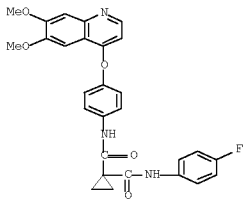
L4 ANSWER 29 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:103210 CAPLUS Full-text
TITLE: Quantification of Pathway Cross-talk Reveals Novel Synergistic Drug Combinations for Breast Cancer
AUTHOR(S): Jaeger, Samira; Igea, Ana; Arroyo, Rodrigo; Alcalde, Victor; Canovas, Begona; Orozco, Modesto; Nebreda, Angel R.; Aloy, Patrick
CORPORATE SOURCE: Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology, Catalonia, Barcelona, Spain
SOURCE: Cancer Research (2017), 77(2), 459-469
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-16-0097
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Combinatorial therapeutic approaches are an imperative to improve cancer treatment, because it is critical to impede compensatory signaling mechanisms that can engender drug resistance to individual targeted drugs. Currently approved drug combinations result largely from empirical clin. experience and cover only a small fraction of a vast therapeutic space. Here we present a computational network biol. approach, based on pathway cross-talk inhibition, to discover new synergistic drug combinations for breast cancer treatment. In silico anal. identified 390 novel anticancer drug pairs belonging to 10 drug classes that are likely to diminish pathway cross-talk and display synergistic antitumor effects. Ten novel drug combinations were validated exptl., and seven of these exhibited synergy in human breast cancer cell lines. In particular, we found that one novel combination, pairing the estrogen response modifier raloxifene with the c-Met/VEGFR2 kinase inhibitor cabozantinib, dramatically potentiated the drugs' individual antitumor effects in a mouse model of breast cancer. When compared with high-throughput combinatorial studies without computational prioritization, our approach offers a significant advance capable of uncovering broad-spectrum utility across many cancer types. Cancer Res; 77(2); 459-69. ©2016 AACR.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(computational network biol. approach based on pathway cross-talk inhibition identified new synergistic drug combinations using raloxifene and cabozantinib for treatment of human breast cancer in xenograft mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 30 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:103199 CAPLUS Full-text
TITLE: Systematic Drug Screening Identifies Tractable Targeted Combination Therapies in Triple-Negative Breast Cancer
AUTHOR(S): Wali, Vikram B.; Langdon, Casey G.; Held, Matthew A.; Platt, James T.; Patwardhan, Gauri A.; Safonov, Anton; Aktas, Bilge; Pusztai, Lajos; Stern, David F.; Hatzis, Christos
CORPORATE SOURCE: Department of Internal Medicine, Section of Medical Oncology, Yale School of Medicine, Yale University, New Haven, CT, USA
SOURCE: Cancer Research (2017), 77(2), 566-578
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-16-1901
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Triple-neg. breast cancer (TNBC) remains an aggressive disease without effective targeted therapies. In this study, we addressed this challenge by testing 128 FDA-approved or investigational drugs as either single agents or in 768 pairwise drug combinations in TNBC cell lines to identify synergistic combinations tractable to clin. translation. Medium-throughput results were scrutinized and extensively analyzed for sensitivity patterns, synergy, anticancer activity, and were validated in low-throughput expts. Principal component anal. revealed that a fraction of all upregulated or downregulated genes of a particular targeted pathway could partly explain cell sensitivity toward agents targeting that pathway. Combination therapies deemed immediately tractable to translation included ABT-263/crizotinib, ABT-263/paclitaxel, paclitaxel/JQ1, ABT-263/XL-184, and paclitaxel/nutlin-3, all of which exhibited synergistic antiproliferative and apoptotic activity in multiple TNBC backgrounds. Mechanistic investigations of the ABT-263/crizotinib combination offering a potentially rapid path to clinic demonstrated RTK blockade, inhibition of mitogenic signaling, and proapoptotic signal induction in basal and mesenchymal stem-like TNBC. Our findings provide preclin. proof of concept for several combination treatments of TNBC, which offer near-term prospects for clin. translation. Cancer Res; 77(2); 566-78. ©2016 AACR.
IT INDEXING IN PROGRESS
IT 1140909-48-3, XL-184
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(investigational drugs as either single agents or in 768 pairwise drug combinations in triple neg. breast cancer cell lines to identify synergistic combinations tractable to clin. translation in human)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

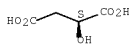
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CM 2

CRN 97-67-6
CMF C4 H6 O5

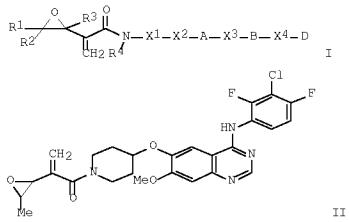
Absolute stereochemistry. Rotation (-).



L4 ANSWER 31 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2017:29259 CAPLUS Full-text
DOCUMENT NUMBER: 166:155901
TITLE: Preparation of ethylene oxide derivatives useful as anticancer agents
INVENTOR(S): Wei, Yonggang; Qiu, Guanpeng; Lei, Bailin; Li, Yao; Wang, Song; Zhu, Guozhi
PATENT ASSIGNEE(S): Sichuan Haisco Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 39pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 106279128	A	20170104	CN 2015-10255885	20150519
PRIORITY APPLN. INFO.:			CN 2015-10255885	20150519

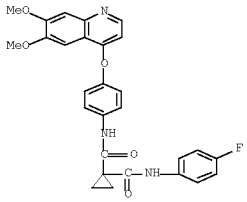
OTHER SOURCE(S): CASREACT 166:155901; MARPAT 166:155901
GI



I

II

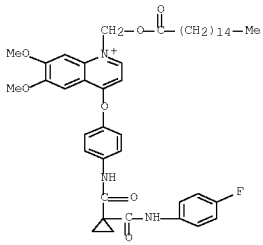
AB The invention relates to ethylene oxide deriatives of formula I, method for their preparation and their use as anticancer agents. Compds. of formula I, wherein, R1-R4 are independently H and C1-6alkyl, which can be substituted with 0-4 of F, Cl, Br and I; X1 is (CX1aX1b)1-6, CO, or absent; X2 is CO, CONH, O, S, etc.; X3 and X4 are independently O, S, NH, etc. X1a, X1b are independently H, F, Br, C1-6alkyl, etc.; ring A and B are independently C6-14 carbon ring or 5- to 15-membered heterocycle; ring C is absent, C6-14 carbon ring and 5- to 15-membered heterocycle, their pharmaceutically acceptable salts, are claimed. Example compound II was prepared via a multistep procedure (procedure given). All the invention compds. were evaluated for their anticancer activity. From the assay, it was determined that example compound II exhibited IC50 value of 0.00147 μM and 0.010 μM towards A431 and NCI-H1975 cell line resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of ethylene oxide derivs. useful as anticancer agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



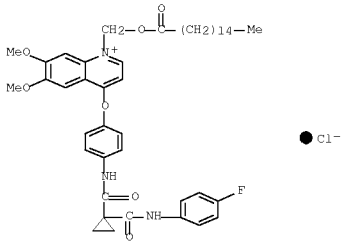
L4 ANSWER 32 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:2171143 CAPLUS Full-text
DOCUMENT NUMBER: 166:106691
TITLE: N-acylalkyl prodrugs of multi-tyrosine kinase inhibitors and methods of use
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160376239	A1	20161229	US 2016-15194813	20160628
WO 2017004005	A1	20170105	WO 2016-US39753	20160628
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20170020856	A1	20170126	US 2016-15288820	20161007
US 20170112821	A1	20170427	US 2017-15402214	20170109
PRIORITY APPLN. INFO.:			US 2015-62185785 P	20150629
			US 2016-15194813 A2	20160628
			US 2016-15288820 A2	20161007

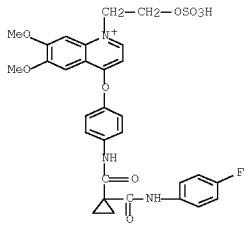
OTHER SOURCE(S): CASREACT 166:106691; MARPAT 166:106691
AB The present invention is directed to N-acylalkyl prodrugs e.g. cabozantinib N-acyl Me Palmitate as. multi-tyrosine kinase inhibitors. The present invention is further directed to compns. comprising compds. of the invention. Finally, the present invention is directed to methods of treating eye conditions including, but not limited to, diabetic background retinopathy, diabetic macular edema, diabetic proliferative retinopathy, diabetic macular edema with proliferative retinopathy, proliferative fibrovascular disease, diabetic macular edema with proliferative fibrovascular disease, retinopathy of prematurity, dry macular degeneration, dry macular degeneration with drusen and wet macular degeneration, using compds. and compns. of the invention.
IT 2055907-44-1P 2055907-46-3P 2055907-47-4P
2055907-48-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-acylalkyl prodrugs as multi-tyrosine kinase inhibitors)
RN 2055907-44-1 CAPLUS
CN Quinolinium, 4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy-1-[[(1-oxohexadecyl)oxy]methyl]- (CA INDEX NAME)



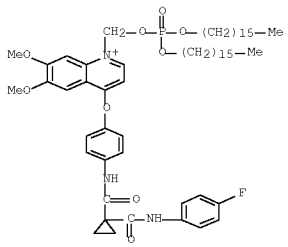
RN 2055907-46-3 CAPLUS
CN Quinolinium, 4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy-1-[[(1-oxohexadecyl)oxy]methyl]-, chloride (1:1) (CA INDEX NAME)



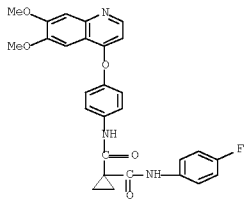
RN 2055907-47-4 CAPLUS
CN Quinolinium, 4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy-1-[2-(sulfooxy)ethyl]- (CA INDEX NAME)



RN 2055907-48-5 CAPLUS
CN Quinolinium, 1-[[[bis(hexadecyloxy)phosphinyl]oxy]methyl]-4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy- (CA INDEX NAME)



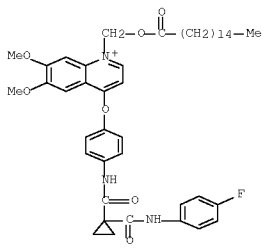
IT 849217-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-acylalkyl prodrugs as multi-tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 2055907-45-2
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-acylalkyl prodrugs as multi-tyrosine kinase inhibitors)
RN 2055907-45-2 CAPLUS
CN Quinolinium, 4-[4-[[[1-[[(4-fluorophenyl)amino]carbonyl]cyclopropyl]carbonyl]amino]phenoxy]-6,7-dimethoxy-1-[[(1-oxohexadecyl)oxy]methyl]-, tetraphenylborate(1-) (1:1) (CA INDEX NAME)

CM 1

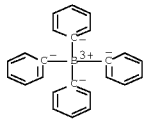
CRN 2055907-44-1
CMF C45 H57 F N3 O7



CM 2

CRN 4358-26-3

CMF C24 H20 B
CCI CCS

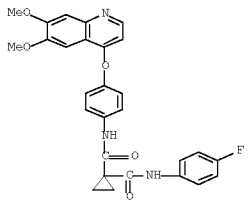


L4 ANSWER 33 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:2167495 CAPLUS Full-text
DOCUMENT NUMBER: 166:120292
TITLE: Biomarker of survival in the treatment of renal cell carcinoma with a vascular endothelial growth factor receptor (VEGFR) inhibitor and an angiopoietin-2 (ANG2) inhibitor
INVENTOR(S): Anderson, Abraham Antonio; Bach, Bruce A.; Pickett-Gies, Cheryl A.; Bass, Michael B.
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 42pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016209972	A1	20161229	WO 2016-US38778	20160622

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62185482 P 20150626
AB The present invention relates to methods, comps., and kits for using placental growth factor (PLGF) as an informative biomarker in determining the clin. benefit to renal cell carcinoma patients by treatment with a VEGFR inhibitor (e.g. trebananib) and an angiopoietin-2 (ANG2) inhibitor e.g. sunitinib.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biomarker of survival in treatment of renal cell carcinoma with a vascular endothelial growth factor receptor (VEGFR) inhibitor and an angiopoietin-2 (ANG2) inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:2129620 CAPLUS Full-text
DOCUMENT NUMBER: 166:92330
TITLE: Methods and compositions for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

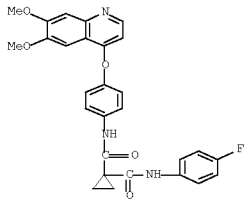
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160367553	A1	20161222	US 2015-14744508	20150619

PRIORITY APPLN. INFO.: US 2015-14744508 20150619
AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 35 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:2100593 CAPLUS Full-text

DOCUMENT NUMBER: 166:300404

TITLE: Changes in plasma biomarkers following treatment with cabozantinib in metastatic castration-resistant prostate cancer: a post hoc analysis of an extension cohort of a phase II trial

AUTHOR(S): Leibowitz-Amit, Raya; Pintilie, Melania; Khoja, Leila; Azad, Arun A.; Berger, Raanan; Laird, A. Douglas; Aftab, Dana T.; Chi, Kim N.; Joshua, Anthony M.

CORPORATE SOURCE: Department of Oncology, Sheba Medical Center, Tel Hashomer, Israel

SOURCE: Journal of Translational Medicine (2016), 14, 12/1-12/8
CODEN: JTMOBV; ISSN: 1479-5876

DIGITAL OBJECT ID: 10.1186/s12967-015-0747-y

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)

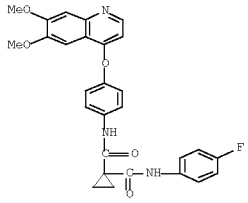
LANGUAGE: English

AB Background: Cabozantinib is an orally available inhibitor of tyrosine kinases including VEGFR2 and c-MET. We performed a post hoc anal. to find assocns. between select plasma biomarkers and treatment response in patients (pts) with metastatic castration resistant prostate cancer (mCRPC) who received cabozantinib 100 mg daily as part of a phase 2 non-randomized expansion cohort (NCT00940225). Methods: Plasma samples were collected at baseline, 6 wk and at time of maximal response from 81 mCRPC pts with bone metastases, of which 33 also had measurable soft-tissue disease. Levels of 27 biomarkers were measured in duplicate using ELISA. Spearman correlation coeffs. were calculated for the association between biomarker levels or their change on treatment and either bone scan response (BSR) or soft tissue response according to RECIST. Results: A BSR and RECIST response were seen in 66/81 pts (81 %) and 6/33 pts (18 %) resp. No significant assocns. were found between any biomarker at any time point and either type of response. Plasma concns. of VEGFA, FLT3L, c-MET, AXL, Gas6A, bone-specific alkaline phosphatase, interleukin-8 and the hypoxia markers CA9 and clusterin significantly increased during treatment with cabozantinib irresp. of response. The plasma concns. of VEGFR2, Trap5b, Angiopoietin-2, TIMP-2 and TIE-2 significantly decreased during treatment with cabozantinib. Conclusions: Our data did not reveal plasma biomarkers associated with response to cabozantinib. The observed alterations in several biomarkers during treatment with cabozantinib may provide insights on the effects of cabozantinib on tumor cells and on tumor micro-environment and may help point to potential co-targeting approaches.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(post hoc anal. of an extension cohort of a phase II trial changes in plasma biomarkers following treatment with cabozantinib in metastatic castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 36 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:2092143 CAPLUS Full-text

TITLE: Preclinical evaluation of dasatinib alone and in combination with cabozantinib for the treatment of diffuse intrinsic pontine glioma

AUTHOR(S): Truffaux, Nathalene; Philippe, Cathy; Paulsson, Janna; Andreiuolo, Felipe; Guerrini-Rousseau, Lea; Cornilleau, Gaetan; Le Dret, Ludivine; Richon, Catherine; Lacroix, Ludovic; Puget, Stephanie; Geoerger, Birgit; Vassal, Gilles; Ostman, Arne; Grill, Jacques

CORPORATE SOURCE: CNRS UMR 8203 Vectorology and Anticancer Therapeutics, Gustave Roussy Cancer Institute, Paris XI University, Villejuif, Fr.

SOURCE: Neuro-Oncology (Cary, NC, United States) (2015), 17(7), 953-964
CODEN: NEURJR; ISSN: 1522-8517

DIGITAL OBJECT ID: 10.1093/neuonc/nou330

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

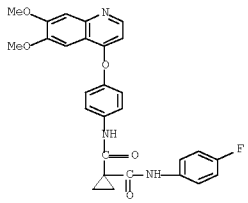
AB Background. Platelet-derived growth factor receptor A is altered by amplification and/or mutation in diffuse intrinsic pontine glioma (DIPG). We explored in vitro on new DIPG models the efficacy of dasatinib, a multi-tyrosine kinase inhibitor targeting this receptor. Gene expression profiles were generated from 41 DIPGs biopsied at diagnosis and compared with the signature associated with sensitivity/resistance to dasatinib. A panel of 12 new DIPG cell lines were established from biopsy at diagnosis, serially passaged, and characterized by gene expression analyses. Effects of dasatinib (1-10 μ M) on proliferation, invasion, and cytotoxicity were determined on 4 of these cell lines using live-cell imaging and flow cytometry assays. Downstream signaling and receptor tyrosine kinases (RTKs) were assessed by western blot and phospho-RTK array. The effect of the combination with the c-Met inhibitor cabozantinib was studied on cellular growth and invasion analyzed by the Chou-Talaly method. DIPG primary tumors and cell lines exhibited the gene expression signature of sensitivity to dasatinib. Dasatinib reduced proliferation (half-maximal inhibitory concentration = 10-100 nM) and invasion (30%-60% reduction) at 100 nM in 4/4 cultures and induced apoptosis in 1 of 4 DIPG cell lines. Activity of downstream effectors of dasatinib targets including activin receptor 1 was strongly reduced. Since multiple RTKs were activated simultaneously in DIPG cell lines, including c-Met, which can be also amplified in DIPG, the benefit of the combination of dasatinib with cabozantinib was explored for its synergistic effects on proliferation and migration/invasion in these cell lines. Conclusion. Dasatinib exhibits antitumor effects in vitro that could be increased by the combination with another RTK inhibitor targeting c-Met.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preclin. evaluation of dasatinib alone and in combination with cabozantinib for treatment of diffuse intrinsic pontine glioma in primary tumor biopsy from patients and human T98G glioblastoma cell line)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 37 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:2077502 CAPLUS Full-text

DOCUMENT NUMBER: 166:77753

TITLE: Compositions and methods for treating pterygium

INVENTOR(S): Ni, Jinsong

PATENT ASSIGNEE(S): Cloudbreak Therapeutics, LLC, USA

SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016200688	A1	20161215	WO 2016-US35726	20160603

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

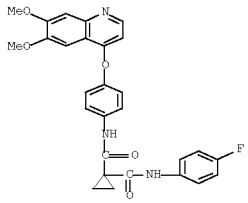
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62172063 P 20150606
US 2015-62186660 P 20150630

AB Compns. and methods for inducing pterygium regression from visual axis/central cornea, stabilizing pterygium, treating hyperemia and symptoms in pterygium patients, and treating pterygium recurrence following pterygiectomy are disclosed. The methods include administration of a multikinase inhibitor, an antimetabolite or a combination thereof to patients in need thereof.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for treating pterygium)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

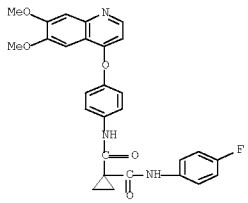
L4 ANSWER 38 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:2017954 CAPLUS Full-text
DOCUMENT NUMBER: 166:61697
TITLE: Screening method for multi-target drug and/or pharmaceutical composition
INVENTOR(S): Zhang, Hongyu; Yang, Qingyong; Quan, Yuan; Luo, Zhihui; Zhu, Lida
PATENT ASSIGNEE(S): Huazhong Agricultural University, Peop. Rep. China
SOURCE: PCT Int. Appl., 37pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016192191	A1	20161208	WO 2015-CN85114	20150724

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CN 104965998	A	20151007	CN 2015-10288863	20150529
PRIORITY APPLN. INFO.:			CN 2015-10288863	A 20150529

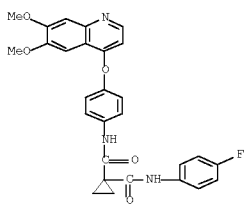
AB The present invention relates to the tech. field of biol. medicine. Disclosed is a screening method for a multi-target drug and/or pharmaceutical composition, comprising the following steps: (1) searching a drug target database, collecting drug targets, targets in research, and drugs corresponding to the targets, and obtaining data of a target-drug corresponding relationship; (2) screening out a target-target combination having relevance through a system genetics method; and (3) screening, according to the data obtained in step (1) and the combination obtained in step (2), the multi-target drug and/or pharmaceutical composition
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(screening method for multi-target drug and/or pharmaceutical composition)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1995172 CAPLUS Full-text
TITLE: Cabozantinib for the treatment of renal cell carcinoma
AUTHOR(S): Escudier, Bernard; Lougheed, Julie C.; Albiges, Laurence
CORPORATE SOURCE: Department of Medical Oncology, Gustave Roussy, Villejuif, Fr.
SOURCE: Expert Opinion on Pharmacotherapy (2016), 17(18), 2499-2504
CODEN: EOPHF7; ISSN: 1465-6566
DIGITAL OBJECT ID: 10.1080/14656566.2016.1258059
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

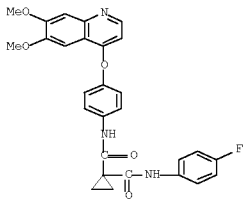
AB : Agents that target the vascular endothelial growth factor (VEGF) or mammalian target of rapamycin (mTOR) pathway as well as the PD-1 checkpoint inhibitor nivolumab are standard therapies for advanced renal cell carcinoma (RCC). Recently, cabozantinib, an inhibitor of MET, VEGF receptors, and AXL, was approved by the FDA and European Commission based on improved progression-free survival (PFS), overall survival (OS), and objective response rate (ORR) compared to standard of care treatment with everolimus in a randomized phase 3 trial in advanced RCC after prior VEGFR-tyrosine kinase inhibitor (TKI) therapy. The preclin. development and scientific rationale, pharmacokinetics, and clin. efficacy and safety of cabozantinib for the treatment of advanced RCC are reviewed. The use of cabozantinib in clin. practice with the growing number of available treatments for advanced RCC is discussed.: Cabozantinib is the only therapy for advanced RCC that has improved PFS, ORR, and OS in a pivotal phase 3 trial after prior antiangiogenic therapy. While no clin. trials have been published comparing cabozantinib with another TKI, available clin. data suggest it could be the most efficacious TKI for second-line therapy. Preliminary encouraging results have also been reported in a phase 2 trial in untreated poor- and intermediate- risk patients with RCC, indicating that treatment with cabozantinib may also be beneficial in the first-line setting.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(study on cabozantinib for treatment of renal cell carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



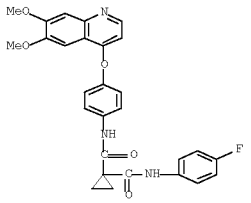
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1984560 CAPLUS Full-text
TITLE: Cabozantinib Is Active against Human Gastrointestinal Stromal Tumor Xenografts Carrying Different KIT Mutations
AUTHOR(S): Gebreyohannes, Yemarshet K.; Schoffski, Patrick; Van Looy, Thomas; Wellens, Jasmien; Vreys, Lise; Cornillie, Jasmien; Vanleeuw, Ulla; Aftab, Dana T.; Debiec-Rychter, Maria; Sciot, Raf; Wozniak, Agnieszka
CORPORATE SOURCE: Laboratory of Experimental Oncology, Department of Oncology, Department of General Medical Oncology, University Hospitals Leuven, KU Leuven, Leuven Cancer Institute, Louvain, Belg.
SOURCE: Molecular Cancer Therapeutics (2016), 15(12), 2845-2852
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-16-0224
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

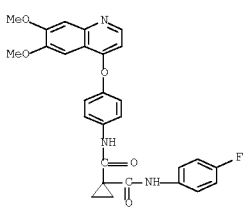
AB In the majority of gastrointestinal stromal tumors (GIST), oncogenic signaling is driven by KIT mutations. Advanced GIST is treated with tyrosine kinase inhibitors (TKI) such as imatinib. Acquired resistance to TKI is mainly caused by secondary KIT mutations, but can also be attributed to a switch of KIT dependency to another receptor tyrosine kinase (RTK). We tested the efficacy of cabozantinib, a novel TKI targeting KIT, MET, AXL, and vascular endothelial growth factor receptors (VEGFR), in patient-derived xenograft (PDX) models of GIST, carrying different KIT mutations. NMRI nu/nu mice (n = 52) were bilaterally transplanted with human GIST: UZLX-GIST4 (KIT exon 11 mutation, imatinib sensitive), UZLX-GIST2 (KIT exon 9, imatinib dose-dependent resistance), or UZLX-GIST9 (KIT exon 11 and 17 mutations, imatinib resistant). Mice were grouped as control (untreated), imatinib (50 mg/kg/bid), and cabozantinib (30 mg/kg/qd) and treated orally for 15 days. Cabozantinib resulted in significant tumor regression in UZLX-GIST4 and -GIST2 and delayed tumor growth in -GIST9. In all three models, cabozantinib inhibited the proliferative activity, which was completely absent in UZLX-GIST4 and significantly reduced in -GIST2 and -GIST9. Increased apoptotic activity was observed only in UZLX-GIST4. Cabozantinib inhibited the KIT signaling pathway in UZLX-GIST4 and -GIST2. In addition, compared with both control and imatinib, cabozantinib significantly reduced microvessel d. in all models. In conclusion, cabozantinib showed antitumor activity in GIST PDX models through inhibition of tumor growth, proliferation, and angiogenesis, in both imatinib-sensitive and imatinib-resistant models. Mol Cancer Ther; 15(12); 2845-52. ©2016 AACR.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vivo efficacy of cabozantinib in gastrointestinal stromal tumor using patient-derived xenograft mouse carrying heterogeneous KIT mutations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 41 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1984548 CAPLUS Full-text
TITLE: CT-707, a Novel FAK Inhibitor, Synergizes with Cabozantinib to Suppress Hepatocellular Carcinoma by Blocking Cabozantinib-Induced FAK Activation
AUTHOR(S): Wang, Dan-Dan; Chen, Ying; Chen, Zi-Bo; Yan, Fang-Jie; Dai, Xiao-Yang; Ying, Mei-Dan; Cao, Ji; Ma, Jian; Luo, Pei-Hua; Han, Yong-Xin; Peng, Yong; Sun, Ying-Hui; Zhang, Hui; He, Qiao-Jun; Yang, Bo; Zhu, Hong
CORPORATE SOURCE: Zhejiang Province Key Laboratory of Anti-Cancer Drug Research, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, Peop. Rep. China
SOURCE: Molecular Cancer Therapeutics (2016), 15(12), 2916-2925
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-16-0282
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hepatocellular carcinoma is among the leading causes of cancer-related deaths worldwide, and the development of new treatment regimens is urgently needed to improve therapeutic approach. In our study, we found that the combination of a Met inhibitor, cabozantinib, and a novel FAK inhibitor, CT-707, exerted synergistic antitumor effects against hepatocellular carcinoma in vitro and in vivo. Interestingly, further studies showed that therapeutic concns. of cabozantinib increased the phosphorylation of FAK, which might attenuate the antitumor activity of cabozantinib. The simultaneous exposure to CT-707 effectively inhibited the activation of FAK that was induced by cabozantinib, which contributes to the synergistic effect of the combination. Furthermore, cabozantinib increased the mRNA and protein levels of integrin α5, which is a canonical upstream of FAK, and the introduction of cilengitide to block integrin function could abrogate FAK activation by cabozantinib, indicating that cabozantinib upregulated the phosphorylation of FAK in an integrin-dependent manner. Similar synergy was also observed on PHA-665752, another selective MET inhibitor, indicating that this observation might be a common characteristic of MET-targeting strategies. Our findings not only favor the development of the novel FAK inhibitor CT-707 as a therapeutic agent against hepatocellular carcinoma but also provide a new strategy of combining MET and FAK inhibitors to potentiate the anticancer activities of these two types of agents for treating hepatocellular carcinoma patients. Mol Cancer Ther; 15(12); 2916-25. ©2016 AACR.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (combination of cabozantinib and CT-707 exerted synergistic antitumor activity against hepatocellular carcinoma in human and mouse models)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

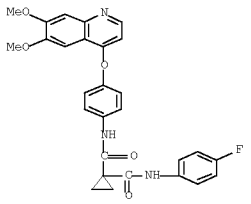


L4 ANSWER 42 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1984513 CAPLUS Full-text
DOCUMENT NUMBER: 166:223268
TITLE: Cell Panel Profiling Reveals Conserved Therapeutic Clusters and Differentiates the Mechanism of Action of Different PI3K/mTOR, Aurora Kinase and EZH2 Inhibitors
AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; Prinsen, Martine B. W.; Willemsen-Seegers, Nicole; de Vetter, Judith R. F.; Dylus, Jelle; van Doornmalen, Antoon M.; Kooijman, Jeffrey; Sawa, Masaaki; van Gerwen, Suzanne J. C.; de Man, Jos; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE: Netherlands Translational Research Center B.V., Kloosterstraat, Neth.
SOURCE: Molecular Cancer Therapeutics (2016), 15(12), 3097-3109
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-16-0403
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cancer cell line panels are important tools to characterize the in vitro activity of new investigational drugs. Here, we present the inhibition profiles of 122 anticancer agents in proliferation assays with 44 or 66 genetically characterized cancer cell lines from diverse tumor tissues (Oncolines). The library includes 29 cytotoxics, 68 kinase inhibitors, and 11 epigenetic modulators. For 38 compds. this is the first comparative profiling in a cell line panel. By strictly maintaining optimized assay protocols, biol. variation was kept to a min. Replicate profiles of 16 agents over three years show a high average Pearson correlation of 0.8 using IC50 values and 0.9 using GI50 values. Good correlations were observed with other panels. Curve fitting appears a large source of variation. Hierarchical clustering revealed 44 basic clusters, of which 26 contain compds. with common mechanisms of action, of which 9 were not reported before, including TTK, BET and two clusters of EZH2 inhibitors. To investigate unexpected clusterings, sets of BTK, Aurora and PI3K inhibitors were profiled in biochem. enzyme activity assays and surface plasmon resonance binding assays. The BTK inhibitor ibrutinib clusters with EGFR inhibitors, because it cross-reacts with EGFR. Aurora kinase inhibitors sep. into two clusters, related to Aurora A or pan-Aurora selectivity. Similarly, 12 inhibitors in the PI3K/AKT/mTOR pathway separated into different clusters, reflecting biochem. selectivity (pan-PI3K, PI3Kβγδ-isoform selective or mTOR-selective). Of these, only allosteric mTOR inhibitors preferentially targeted PTEN-mutated cell lines. This shows that cell line profiling is an excellent tool for the unbiased classification of antiproliferative compds. Mol Cancer Ther; 15(12); 3097-109. ©2016 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell panel profiling reveals conserved therapeutic clusters and differentiates mechanism of action of different PI3K/mTOR, aurora kinase and EZH2 inhibitors exhibits antiproliferative activity against different types of human cancer cells)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 43 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1958744 CAPLUS Full-text
DOCUMENT NUMBER: 166:260134
TITLE: Discovery of 4-Methyl-N-(4-((4-methylpiperazin-1-yl)methyl)-3-(trifluoromethyl)phenyl)-3-((1-nicotinoylpiperidin-4-yl)oxy)benzamide (CHMFL-ABL/KIT-155) as a Novel Highly Potent Type II ABL/KIT Dual Kinase Inhibitor with a Distinct Hinge Binding
AUTHOR(S): Wang, Qiang; Liu, Feiyang; Wang, Beilei; Zou, Fengming; Qi, Ziping; Chen, Cheng; Yu, Kailin; Hu, Chen; Qi, Shuang; Wang, Wenchao; Hu, Zhenquan; Liu, Juan; Wang, Wei; Wang, Li; Liang, Qianmao; Zhang, Shanchun; Ren, Tao; Liu, Qingsong; Liu, Jing
CORPORATE SOURCE: High Magnetic Field Laboratory, Chinese Academy of Sciences, Anhui, 230031, Peop. Rep. China
SOURCE: Journal of Medicinal Chemistry (2017), 60(1), 273-289
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/acs.jmedchem.6b01290
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 166:260134
AB The discovery of a novel potent type II ABL/c-KIT dual kinase inhibitor compound 34 (CHMFL-ABL/KIT-155), which utilized a hydrogen bond formed by NH on the kinase backbone and carbonyl oxygen of 34 as a unique hinge binding, is described. 34 potently inhibited purified ABL (IC50: 46 nM) and c-KIT kinase (IC50: 75 nM) in the biochem. assays and displayed high selectivity (S Score (1) = 0.03) at the concentration of 1 μM among 468 kinases/mutants in KINOMEscan assay. It exhibited strong antiproliferative activities against BCR-ABL/c-KIT driven CML/GISTs cancer cell lines through blockage of the BCR-ABL/c-KIT mediated signaling pathways, arresting cell cycle progression and induction of apoptosis. 34 possessed a good oral PK property and effectively suppressed the tumor progression in the K562 (CML) and GIST-T1 (GISTs) cells mediated xenograft mouse model. The distinct hinge-binding mode of 34 provided a novel pharmacophore for expanding the chemical structure diversity for the type II kinase inhibitors discovery.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel ABL/c-KIT dual kinase inhibitor CHMFL-ABL/KIT-155 preparation)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1941702 CAPLUS Full-text
TITLE: Processes for preparing quinoline compounds and pharmaceutical compositions containing such compounds
INVENTOR(S): Wilson, Jo Ann
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., No pp. given
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140200242	A1	20140717	US 2014-13984559	20140320
WO 2012109510	A1	20120816	WO 2012-US24591	20120210
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
NZ 712808	A	20170331	NZ 2012-712808	20120210
JP 2016188216	A	20161104	JP 2016-94411	20160510
US 20170057921	A1	20170302	US 2016-15348716	20161110

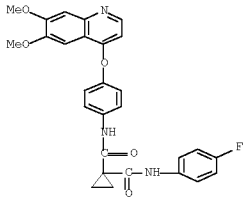
PRIORITY APPLN. INFO.: US 2011-61441520 P 20110210
US 2011-61441527 P 20110210
WO 2012-US24591 W 20120210
JP 2013-553580 A3 20120210
NZ 2012-614130 A3 20120210
US 2014-13984559 A1 20140320

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention is directed to processes for making and compns. containing quinolines such as formula I or pharmaceutically acceptable salts thereof wherein: X1 is H, Br, CI, or X2 is H, Br, CI, or n1 is 1-2; and n2 is 1-2.

IT 849217-68-1P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for preparing quinoline derivs. and pharmaceutical compns. thereof)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

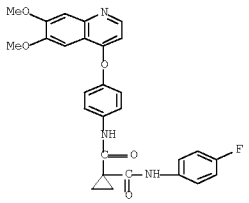


IT 1140909-48-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparing quinoline derivs. and pharmaceutical compns. thereof)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

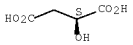
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



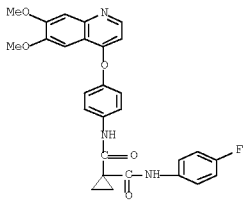
L4 ANSWER 45 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1938450 CAPLUS Full-text
TITLE: Phase III study of cabozantinib in previously treatedmetastatic castration-resistant prostate cancer: COMET-1
AUTHOR(S): Smith, Matthew; De Bono, Johann; Sternberg, Cora; Le Moulec, Sylvestre; Oudard, Stephane; De Giorgi, Ugo; Krainer, Michael; Bergman, Andries; Hoelzer, Wolfgang; De Wit, Ronald; Bogemann, Martin; Saad, Fred; Cruciani, Giorgio; Thiery-Vuillemin, Antoine; Feyerabend, Susan; Miller, Kurt; Houede, Nadine; Hussain, Syed; Lam, Elaine; Polikoff, Jonathan; Stenzl, Arnulf; Mainwaring, Paul; Ramies, David; Hessel, Colin; Weitzman, Aaron; Fizazi, Karim
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Boston, MA, 02114, USA
SOURCE: Journal of Clinical Oncology (2016), 34(25), 3005-3020
CODEN: JCONDN; ISSN: 1527-7755
DIGITAL OBJECT ID: 10.1200/JCO.2015.65.5597
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Purpose Cabozantinib is an inhibitor of kinases, including MET and vascular endothelial growth factor receptors,and has shown activity in men with previously treated metastatic castration-resistant prostate cancer(mCRPC). This blinded phase III trial compared cabozantinib with prednisone in patients with mCRPC. Patients and Methods Men with progressive mCRPC after docetaxel and abiraterone and/or enzalutamide were randomlyassigned at a two-to-one ratio to cabozantinib 60 mg once per day or prednisone 5 mg twice per day.The primary end point was overall survival (OS). Bone scan response (BSR) at week 12 as assessedby independent review committee was the secondary end point; radiog. progression-freesurvival (rPFS) and effects on circulating tumor cells (CTCs), bone biomarkers, serum prostatespecificantigen (PSA), and symptomatic skeletal events (SSEs) were exploratory assessments. Results A total of 1,028 patients were randomly assigned to cabozantinib (n = 682) or prednisone (n = 346).Median OS was 11.0 mo with cabozantinib and 9.8 mo with prednisone (hazard ratio, 0.90;95% CI, 0.76 to 1.06; stratified log-rank P =.213). BSR at week 12 favored cabozantinib (42% v 3%;stratified Cochran-Mantel-Haenszel P <.001). rPFS was improved in the cabozantinib group(median, 5.6 v 2.8 mo; hazard ratio, 0.48; 95% CI, 0.40 to 0.57; stratified log-rank P<.001).Cabozantinib was associated with improvements in CTC conversion, bone biomarkers, andpost-random assignment incidence of SSEs but not PSA outcomes. Grade 3 to 4 adverse eventsand discontinuations because of adverse events were higher with cabozantinib than with prednisone(71% v 56% and 33% v 12%, resp.). Conclusion Cabozantinib did not significantly improve OS compared with prednisone in heavily treated patientswith mCRPC and progressive disease after docetaxel and abiraterone and/or enzalutamide.Cabozantinib had some activity in improving BSR, rPFS, SSEs, CTC conversions, and bone biomarkersbut not PSA outcomes.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib did not significantly improved overall survival in patients with metastatic castration-resistant prostate cancer previously treated with docetaxel and abiraterone and enzalutamide)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

L4 ANSWER 46 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1919613 CAPLUS Full-text
DOCUMENT NUMBER: 166:418102
TITLE: Emp2 regulates angiogenesis in cancer cells through induction of vegf
INVENTOR(S): Wadehra, Madhuri; Braun, Jonathan; Gordon, Lynn K.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S. Pat. Appl. Publ., No pp. given
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150079089	A1	20150319	US 2014-14376724	20140805
WO 2013119693	A1	20130815	WO 2013-US24968	20130206
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK,				

SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

AU 2016204335	A1	20160721	AU 2016-204335	20160624
PRIORITY APPLN. INFO.:			US 2012-61595617 P	20120206
			WO 2013-US24968 W	20130206
			AU 2013-203424 A3	20130206

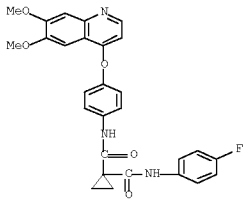
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed herein are methods and compns. for modulating neovascularization. The disclosed compns. find particular use in the treatment of uterine cancers, specifically endometrial cancers.

IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with anti-EMP2 antibodies for treatment of uterine cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 47 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1918425 CAPLUS Full-text
DOCUMENT NUMBER: 166:867
TITLE: Method for predicting the response of melanoma patients to targeted pharmacotherapy with kinase inhibitors by studying phosphorylation levels
INVENTOR(S): Ruijtenbeek, Robbie; Hovestad-Bijl, Liesbeth Coosje
PATENT ASSIGNEE(S): PamGene BV, Neth.
SOURCE: PCT Int. Appl., 39pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016184999	A1	20161124	WO 2016-EP61361	20160520

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

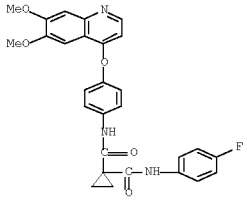
PRIORITY APPLN. INFO.: EP 2015-168371 A 20150520

AB The present invention relates to a method for detg. or predicting the response of a patient diagnosed with melanoma to targeted pharmacotherapy. The present invention also aims to provide methods and devices for predicting the response of patients diagnosed with melanoma to specific medicaments. More specifically, the present invention provides methods which measure kinase activity by studying phosphorylation levels and profiles and inhibitions thereof by drugs in samples of said patients.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for predicting the response of melanoma patients to targeted pharmacotherapy with protein kinase inhibitors by studying phosphorylation levels)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

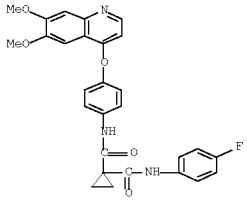


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

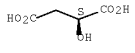
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 48 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1913376 CAPLUS Full-text
DOCUMENT NUMBER: 166:23816
TITLE: Kinase modulation, and indications therefor
INVENTOR(S): Ibrahim, Prabha N.; Zhang, Chao; Spevak, Wayne; Zhang, Jiazhong; Wu, Guoxian; Lin, Jack; Cho, Hanna; Nespi, Marika; Shi, Songyuan; Ewing, Todd; Zhang, Ying; Bollag, Gideon
PATENT ASSIGNEE(S): Plexxikon Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160339025	A1	20161124	US 2016-15160729	20160520
WO 2016191296	A1	20161201	WO 2016-US33587	20160520

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62165813 P 20150522

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

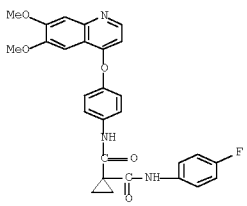
OTHER SOURCE(S): CASREACT 166:23816

AB The present disclosure provides methods of treating a subject suffering from or at risk of a BRAF V600 mutation or BRAF fusion mutation related disease or condition, without activating the MAPK pathway or inducing expression of MAPK pathway genes in cells harboring wild-type BRAF.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kinase modulators)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 49 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1912436 CAPLUS Full-text
DOCUMENT NUMBER: 166:12105
TITLE: Methods for treating tumors in situ including intratumor injection of cytotoxic particles and immune checkpoint blockade therapy
INVENTOR(S): Salem, Aliasger K.; Makkouk, Amani; Joshi, Vijaya B.; Weiner, George
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA

SOURCE: PCT Int. Appl., 100pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016187122	A1	20161124	WO 2016-US32712	20160516

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

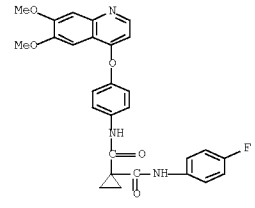
PRIORITY APPLN. INFO.: US 2015-62162397 P 20150515

AB The field of the invention relates to compns., kits, and methods for treating cancer in a subject; in particular, the compns., kits, and methods relate to treating cancer in a subject having a solid tumor via inducing an immune response against the tumor. Disclosed are compns., kits, and methods for treating cancer in a subject in need thereof. The compns., kits, and methods may be used to treat a tumor in a subject in situ. The compns., kits, and methods comprise or utilize cytotoxic particles, immune checkpoint inhibitors, and/or T-cell stimulatory agents.

IT 1140909-68-3, Cabozantinib-S-Malate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treating tumors in situ including intratumor injection of cytotoxic particles and immune checkpoint blockade therapy)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

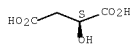
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 50 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1906855 CAPLUS Full-text
DOCUMENT NUMBER: 166:390778
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Institut De Recerca Biomedica (Irb Barcelona), Spain; Institucio Catalana De Recerca I Estudis Avancats
SOURCE: U.S. Pat. Appl. Publ., No pp. given
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160032400	A1	20160204	US 2015-14776412	20150914
WO 2014140933	A2	20140918	WO 2014-IB1253	20140314
WO 2014140933	A3	20141231		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61801718 P 20130315
WO 2014-IB1253 W 20140314

AB The present invention relates to a method for the prognosis of bone metastasis in cancer which comprises using a probe to determine if a gene of interest is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise using a probe to determine the expression level of a gene of interest, or the amplification or translocation of a gene of interest. The invention also relates to a method for predicting early bone metastasis in a subject suffering cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering cancer and for classifying a subject from cancer into a cohort.

IT 849217-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for prognosis and treatment of cancer metastasis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

L4 ANSWER 51 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1906854 CAPLUS Full-text
DOCUMENT NUMBER: 166:393309
TITLE: Method for the prognosis and treatment of renal cell carcinoma metastasis
INVENTOR(S): Gomis, Roger; Lacey, David L.
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: U.S. Pat. Appl. Publ., No pp. given
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

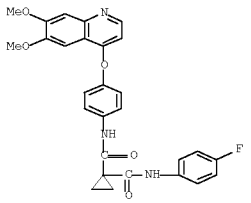
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160032399	A1	20160204	US 2015-14776390	20150914
WO 2014184679	A2	20141120	WO 2014-IB1715	20140313
WO 2014184679	A3	20150319		

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61801642 P 20130315
WO 2014-IB1715 W 20140313

AB The present invention relates to a method for the prognosis of bone metastasis in renal cell carcinoma which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering renal cell carcinoma. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of renal cell carcinoma metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering renal cell carcinoma and for classifying a subject from renal cell carcinoma into a cohort.

IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MAF gene as marker for prognosis and treatment of renal cell carcinoma metastasis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 52 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1877192 CAPLUS Full-text
DOCUMENT NUMBER: 166:345653
TITLE: Retroviral vector with mini-promoter cassette
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Lin, Amy H.; Logg, Christopher R.; Kasahara, Noriyuki
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: U.S. Pat. Appl. Publ., No pp. given
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

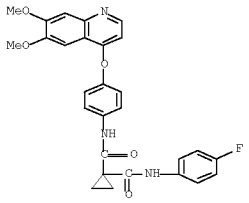
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150273029	A1	20151001	US 2015-14438564	20150424
WO 2014066700	A1	20140501	WO 2013-US66709	20131024

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61718610 P 20121025
WO 2013-US66709 W 20131024
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB This disclosure provides a retroviral replicating vector for gene delivery comprising a therapeutic cassette containing at least one mini-promoter linked to a gene to be expressed.
IT 1140909-48-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in cancer therapy with retroviral gene therapy vectors; retroviral vectors for gene therapy using mini-promoters)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

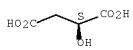
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

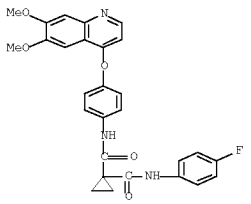


L4 ANSWER 53 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1874511 CAPLUS Full-text
DOCUMENT NUMBER: 166:300776
TITLE: Drug combinations to treat cancer
INVENTOR(S): Sweeney, Christopher J.; Kantoff, Phili W.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., No pp. given
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160082019	A1	20160324	US 2015-14782493	20151005
WO 2014165779	A1	20141009	WO 2014-US33008	20140404

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

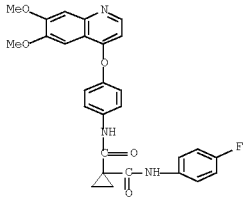
PRIORITY APPLN. INFO.: US 2013-61808516 P 20130404
WO 2014-US33008 W 20140404
AB This invention relates to the combination of cabozantinib and abiraterone to treat cancer, particularly castration resistant prostate cancer.
IT 849217-68-1
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug combinations to treat cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug combinations to treat cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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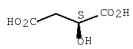
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 54 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1813878 CAPLUS Full-text
DOCUMENT NUMBER: 165:565176
TITLE: Injectable depot formulations for treating macular degeneration and retinal vein occlusion
INVENTOR(S): Ashton, Paul
PATENT ASSIGNEE(S): pSivida US, Inc., USA
SOURCE: PCT Int. Appl., 25pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016179357	A1	20161110	WO 2016-US30912	20160505

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20160324836 A1 20161110 US 2016-15147198 20160505

PRIORITY APPLN. INFO.: US 2015-62157257 P 20150505

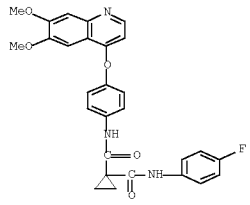
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed are compns. and methods related to the use of kinase inhibitors (e.g. sorafenib) in treating macular degeneration and/or retinal vein occlusion.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(injectable depot formulations for treating macular degeneration and retinal vein occlusion)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 55 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1802438 CAPLUS Full-text

TITLE: Erlotinib, cabozantinib, or erlotinib plus cabozantinib as second-line or third-line treatment of patients with EGFR wild-type advanced non-small-cell lung cancer (ECOG-ACRIN 1512): a randomised, controlled, open-label, multicentre, phase 2 trial

AUTHOR(S): Neal, Joel W.; Dahlberg, Suzanne E.; Wakelee, Heather A.; Aisner, Seena C.; Bowden, Michaela; Huang, Ying; Carbone, David P.; Gerstner, Gregory J.; Lerner, Rachel E.; Rubin, Jerome L.; Owonikoko, Taofeek K.; Stella, Philip J.; Steen, Preston D.; Khalid, Ahmed Ali; Ramalingam, Suresh S.

CORPORATE SOURCE: Stanford Cancer Institute, Stanford, CA, USA

SOURCE: Lancet Oncology (2016), 17(12), 1661-1671
CODEN: LOANBN; ISSN: 1470-2045

DIGITAL OBJECT ID: 10.1016/S1470-2045(16)30561-7

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

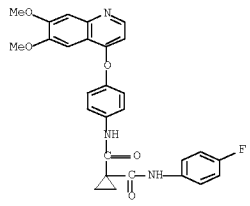
AB Erlotinib is approved for the treatment of all patients with advanced non-small-cell lung cancer (NSCLC), but is most active in the treatment of EGFR mutant NSCLC. Cabozantinib, a small mol. tyrosine kinase inhibitor, targets MET, VEGFR, RET, ROS1, and AXL, which are implicated in lung cancer tumorigenesis. We compared the efficacy of cabozantinib alone or in combination with erlotinib vs. erlotinib alone in patients with EGFR wild-type NSCLC. This three group, randomised, controlled, open-label, multicentre, phase 2 trial was done in 37 academic and community oncol. practices in the USA. Patients were eligible if they had received one or two previous treatments for advanced non-squamous, EGFR wild-type, NSCLC. Patients were stratified by performance status and line of therapy, and randomly assigned using permuted blocks within strata to receive open-label oral daily dosing of erlotinib (150 mg), cabozantinib (60 mg), or erlotinib (150 mg) and cabozantinib (40 mg). Imaging was done every 8 wk. At the time of radiog. progression, there was optional crossover for patients in either single-drug group to receive combination treatment. The primary endpoint was to compare progression-free survival in patients given erlotinib alone vs. cabozantinib alone, and in patients given erlotinib alone vs. the combination of erlotinib plus cabozantinib. We assessed the primary endpoint in the per-protocol population, which was defined as all patients who were eligible, randomly assigned, and received at least one dose of treatment. The safety anal. population included all patients who received study treatment irresp. of eligibility. This trial is registered with ClinicalTrials.gov, number NCT01708954. Between Feb 7, 2013, and July 1, 2014, we enrolled and randomly assigned 42 patients to erlotinib treatment, 40 patients to cabozantinib treatment, and 43 patients to erlotinib plus cabozantinib treatment, of whom 111 (89%) in total were included in the primary anal. (erlotinib [n=38], cabozantinib [n=38], erlotinib plus cabozantinib [n=35]). Compared with erlotinib alone (median 1·8 mo [95% CI 1·7-2·2]), progression-free survival was significantly improved in the cabozantinib group (4·3 mo [3·6-7·4]; hazard ratio [HR] 0·39, 80% CI 0·27-0·55; one-sided p=0·0003) and in the erlotinib plus cabozantinib group (4·7 mo [2·4-7·4]; HR 0·37, 0·25-0·53; one-sided p=0·0003). Among participants included in the safety anal. of the erlotinib (n=40), cabozantinib (n=40), and erlotinib plus cabozantinib (n=39) groups, the most common grade 3 or 4 adverse events were diarrhoea (three [8%] cases in the erlotinib group vs three [8%] in the cabozantinib group vs 11 [28%] in the erlotinib plus cabozantinib group), hypertension (none vs ten [25%] vs one [3%]), fatigue (five [13%] vs six [15%] vs six [15%]), oral mucositis (none vs four [10%] vs one [3%]), and thromboembolic event (none vs three [8%] vs two [5%]). One death due to respiratory failure occurred in the cabozantinib group, deemed possibly related to either drug, and one death due to pneumonitis occurred in the erlotinib plus cabozantinib group, deemed related to either drug or the combination. Despite its small sample size, this trial showed that, in patients with EGFR wild-type NSCLC, cabozantinib alone or combined with erlotinib has clin. meaningful, superior efficacy to that of erlotinib alone, with addnl. toxicity that was generally manageable. Cabozantinib-based regimens are promising for further investigation in this patient population. ECOG-ACRIN Cancer Research Group, National Cancer Institute of the National Institutes of Health.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib alone or combined with erlotinib showed superior efficacy than erlotinib monotherapy and improved progression-free survival in patients with EGFR wild-type advanced non-small-cell lung cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 56 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1802436 CAPLUS Full-text

TITLE: Cabozantinib in patients with advanced RET-rearranged non-small-cell lung cancer: an open-label, single-centre, phase 2, single-arm trial

AUTHOR(S): Drilon, Alexander; Rekhtman, Natasha; Arcila, Maria; Wang, Lu; Ni, Andy; Albano, Melanie; Van Voorthuysen, Martine; Somwar, Romel; Smith, Roger S.; Montecalvo, Joseph; Plodkowski, Andrew; Ginsberg, Michelle S.; Riely, Gregory J.; Rudin, Charles M.; Ladanyi, Marc; Kris, Mark G.

CORPORATE SOURCE: Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, Weill Cornell Medicine, New York, NY, USA

SOURCE: Lancet Oncology (2016), 17(12), 1653-1660
CODEN: LOANBN; ISSN: 1470-2045

DIGITAL OBJECT ID: 10.1016/S1470-2045(16)30562-9

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

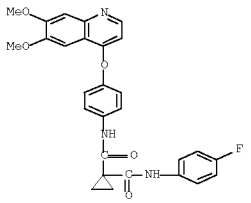
AB RET rearrangements are found in 1-2% of non-small-cell lung cancers. Cabozantinib is a multikinase inhibitor with activity against RET that produced a 10% overall response in unselected patients with lung cancers. To assess the activity of cabozantinib in patients with RET-rearranged lung cancers, we did a prospective phase 2 trial in this mol. subgroup. We enrolled patients in this open-label, Simon two-stage, single-center, phase 2, single-arm trial in the USA if they met the following criteria: metastatic or unresectable lung cancer harbouring a RET rearrangement, Karnofsky performance status higher than 70, and measurable disease. Patients were given 60 mg of cabozantinib orally per day. The primary objective was to determine the overall response (Response Criteria Evaluation in Solid Tumors version 1.1) in assessable patients; those who received at least one dose of cabozantinib, and had been given CT imaging at baseline and at least one protocol-specified follow-up timepoint. We did safety analyses in the modified intention-to-treat population who received at least one dose of cabozantinib. The accrual of patients with RET-rearranged lung cancer to this protocol has been completed but the trial is still ongoing because several patients remain on active treatment. This study was registered with ClinicalTrials.gov, number NCT01639508. Between July 13, 2012, and Apr. 30, 2016, 26 patients with RET-rearranged lung adenocarcinomas were enrolled and given cabozantinib; 25 patients were assessable for a response. KIF5B-RET was the predominant fusion type identified in 16 (62%) patients. The study met its primary endpoint, with confirmed partial responses seen in seven of 25 response-assessable patients (overall response 28%, 95% CI 12-49). Of the 26 patients given cabozantinib, the most common grade 3 treatment-related adverse events were lipase elevation in four (15%) patients, increased alanine aminotransferase in two (8%) patients, increased aspartate aminotransferase in two (8%) patients, decreased platelet count in two (8%) patients, and hypophosphatemia in two (8%) patients. No drug-related deaths were recorded but 16 (62%) patients died during the course of follow-up. 19 (73%) patients required dose redns. due to drug-related adverse events. The reported activity of cabozantinib in patients with RET-rearranged lung cancers defines RET rearrangements as actionable drivers in patients with lung cancers. An improved understanding of tumor biol. and novel therapeutic approaches will be needed to improve outcomes with RET-directed targeted treatment. Exelixis, National Institutes of Health and National Cancer Institute Cancer Center Support Grant P30 CA008748.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(treatment with cabozantinib significantly improved outcomes of patients with advanced RET-rearranged non-small-cell lung cancer)

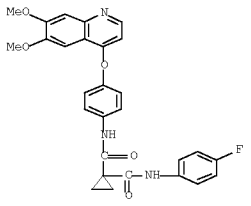
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 57 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1779869 CAPLUS Full-text
TITLE: Activity of erlotinib when dosed below the maximum tolerated dose for EGFR-mutant lung cancer: Implications for targeted therapy development
AUTHOR(S): Lampson, Benjamin L.; Nishino, Mizuki; Dahlberg, Suzanne E.; Paul, Danie; Santos, Abigail A.; Jaenne, Pasi A.; Oxnard, Geoffrey R.
CORPORATE SOURCE: Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE: Cancer (Hoboken, NJ, United States) (2016), 122(22), 3456-3463
CODEN: CANCAR; ISSN: 0008-543X
DIGITAL OBJECT ID: 10.1002/cncr.30270
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB BACKGROUND : Erlotinib is a std. first-line therapy for patients who have metastatic nonsmall cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) mutations. The recommended dose of 150 mg daily is the maximum tolerated dose (MTD). Few clin. data are available regarding its efficacy at doses less than the MTD. METHODS : An institutional database was queried for patients with advanced NSCLC who were pos. for EGFR L858R mutations or exon 19 deletions and had received treatment with erlotinib. The treatment course, including the erlotinib dose at initiation of treatment, at 4 mo into therapy, and at disease progression, was retrospectively studied. Progression-free survival (PFS) was compared between patients who received the MTD (150 mg) and those who received reduced-dose erlotinib (≤100 mg). RESULTS : In total, 198 eligible patients were identified. Thirty-one patients (16%) were initiated on reduced-dose erlotinib; they were older (P = .001) and had lower performance status (P = .01) compared with those who were initiated on erlotinib at the MTD. The response rate to reduced-dose erlotinib was 77%. The median PFS of patients initiated on reduced-dose erlotinib was 9.6 mo vs. 11.4 mo for those initiated at the MTD, a difference that was not statistically significant (hazard ratio, 0.81; 95% confidence interval, 0.54-1.21; P = .30). There was a nonsignificant trend toward higher rates of progression within the central nervous system with reduced-dose erlotinib. CONCLUSIONS : At doses below the MTD, erlotinib treatment results in a high response rate and a prolonged median PFS. Review of the literature indicates that 15 of 30 small-mol. inhibitors that are approved or in late-stage development for cancer therapy have recommended doses below the MTD. When the toxicities of MTD dosing are a concern, an investigation of small-mol. inhibitors at doses below the MTD is warranted. Cancer 2016;122:3456-63. © 2016 American Cancer Society.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activity of erlotinib when dosed below maximum tolerated dose for treatment of non-small cell lung cancer in patients with epidermal growth factor receptor mutation)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 58 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1778137 CAPLUS Full-text
DOCUMENT NUMBER: 165:550894
TITLE: Injectable sustained release intraocular device
INVENTOR(S): Ashton, Paul
PATENT ASSIGNEE(S): pSivida US, Inc., USA
SOURCE: PCT Int. Appl., 31pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

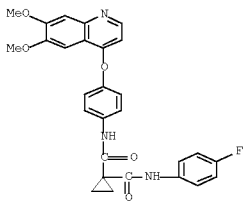
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016176579	A1	20161103	WO 2016-US30125	20160429

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MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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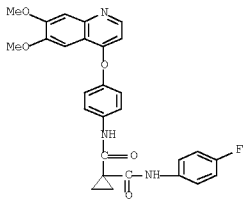
US 20160317438	A1	20161103	US 2016-15142652	20160429
PRIORITY APPLN. INFO.:			US 2015-62154491 P	20150429
			US 2015-62157264 P	20150505

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Disclosed are compns. and methods related to the use of kinase inhibitors in treating macular degeneration and/or retinal vein occlusion. In some aspects, the invention relates to sustained-release drug delivery devices that can deliver effective intraocular concns. of the kinase inhibitor, while delivering low systemic concns. of the kinase inhibitor, e.g., to reduce the risk of toxicity or other undesirable side effects.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(injectable sustained release intraocular device)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

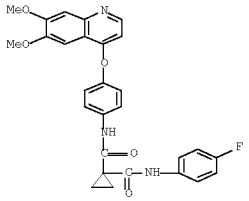
L4 ANSWER 59 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1774443 CAPLUS Full-text
TITLE: Nivolumab versus cabozantinib: comparing overall survival in metastatic renal cell carcinoma
AUTHOR(S): Wiecek, Witold; Karcher, Helene
CORPORATE SOURCE: LASER Analytica, London, EC1N 2JD, UK
SOURCE: PLoS One (2016), 11(6), e0155389/1-e0155389/11
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0155389
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Renal-cell carcinoma (RCC) affects over 330,000 new patients every year, of whom 1/3 present with metastatic RCC (mRCC) at diagnosis. Most mRCC patients treated with a firstline agent relapse within 1 yr and need second-line therapy. The present study aims to compare overall survival (OS) between nivolumab and cabozantinib from two recent pivotal studies comparing, resp., each one of the two emerging treatments against everolimus in patients who relapse following first-line treatment. Comparison is traditionally carried out using the Bucher method, which assumes proportional hazard. Since OS curves intersected in one of the pivotal studies, models not assuming proportional hazards were also considered to refine the comparison. Four Bayesian parametric survival network meta-anal. models were implemented on overall survival (OS) data digitized from the Kaplan- Meier curves reported in the studies. Three models allowing hazard ratios (HR) to vary over time were assessed against a fixed-HR model. The Bucher method favored cabozantinib, with a fixed HR for OS vs. nivolumab of 1.09 (95% confidence interval: [0.77, 1.54]). However, all models with time-varying HR showed better fits than the fixed-HR model. The loglogistic model fitted the data best, exhibiting a HR for OS initially favoring cabozantinib, the trend inverting to favor nivolumab after month 5 (95% credible interval <1 from 10 mo). The initial probability of cabozantinib conferring superior OS was 54%, falling to 41.5% by month 24. Numerical differences in study-adjusted OS ests. between the two treatments remained small. This study evidences that HR for OS of nivolumab vs. cabozantinib varies over time, favoring cabozantinib in the first months of treatment but nivolumab afterwards, a possible indication that patients with poor prognosis benefit more from cabozantinib in terms of survival, nivolumab benefiting patients with better prognosis. More evidence, including real-world observational data, is needed to compare effectiveness between cabozantinib and nivolumab.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nivolumab vs. cabozantinib comparing overall survival in metastatic renal cell carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 60 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1772126 CAPLUS Full-text
TITLE: Thyroid Cancer: Risk-Stratified Management and Individualized Therapy
AUTHOR(S): Raue, Friedhelm; Frank-Raue, Karin
CORPORATE SOURCE: Molecular Laboratory, Endocrine Practice, Heidelberg, Germany
SOURCE: Clinical Cancer Research (2016), 22(20), 5012-5021
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-16-0484
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Thyroid cancer is the most common endocrine malignancy. Differentiated thyroid cancer (DTC) with the two subtypes, papillary thyroid cancer (PTC) and follicular thyroid cancer (FTC), is the most frequent subtype of thyroid cancer; more rare subtypes are medullary thyroid cancer (MTC) and anaplastic thyroid cancer (ATC). The incidence of DTC has increased rapidly in recent years due to the more frequent use of imaging methods such as ultrasound of the neck and fine-needle aspiration (FNA) of thyroid nodules. After total thyroidectomy and radioiodine treatment, DTC remains an indolent and curable disease in most patients, whereas the cure rate in MTC is lower and depends on early diagnosis. Most ATCs are incurable. In recent years, there has been great progress in identifying genetic changes in thyroid cancer, and genetic testing of FNA samples or blood samples provides useful information for clin. decision making. Tumor staging, either postoperatively or by imaging, and measuring the tumor markers thyroglobulin for DTC and calcitonin for MTC, allow for dynamic risk-adapted stratification for follow-up procedures. In advanced metastatic thyroid cancer, mol. targeted therapy using tyrosine kinase receptor inhibitors, including sorafenib, lenvantinib, vandetanib, and cabozantinib, helps control tumor progression and prolongs progression-free survival. Using a dynamic risk-stratified approach to manage thyroid cancer, the outcomes for most thyroid cancer patients are excellent compared with those for other cancers. The major challenge in the future is to identify high-risk patients and to treat and monitor them appropriately. Clin Cancer Res; 22(20); 5012-21.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(risk-stratified management and individualized therapy for thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

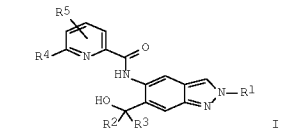


L4 ANSWER 61 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1771773 CAPLUS Full-text
DOCUMENT NUMBER: 165:571275
TITLE: Preparation of indazolecarboxamides as IRAK4 inhibitors useful in combination with BTK-inhibitors
INVENTOR(S): Bothe, Ulrich; Wengner, Antje Margret; Siebeneicher, Holger; Schmidt, Nicole; Nubbemeyer, Reinhard; Boemer, Ulf; Guenther, Judith; Steuber, Holger; Lange, Martin; Stegmann, Christian; Sutter, Andreas; Neuhaus, Roland
PATENT ASSIGNEE(S): Bayer Pharma Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 131pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

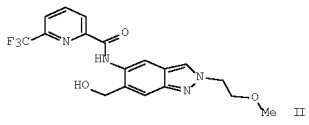
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016174183	A1	20161103	WO 2016-EP59576	20160429

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2015-166016 A 20150430
EP 2016-152499 A 20160125
OTHER SOURCE(S): CASREACT 165:571275; MARPAT 165:571275
GI



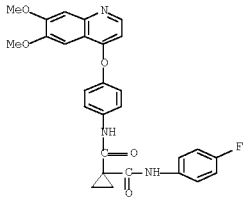
I



II

AB The application relates to novel combinations of at least two components, component A, an interleukin-1 receptor-associated kinase 4 (IRAK4) inhibiting compound of formula I, and component B, a Bruton tyrosine kinase (BTK) inhibiting compound, or a pharmaceutically acceptable salt thereof; and, optionally, one or more components C which are pharmaceutical products; in which one or two of the above-defined compds. A and B are optionally present in pharmaceutical formulations ready for simultaneous, sep. or sequential administration, for treatment and/or prophylaxis of diseases such as endometriosis, lymphoma, macular degeneration, COPD, neoplastic disorders and psoriasis. A pharmaceutical combination comprising a BTK inhibiting compound and I [wherein R1 = (un)substituted C1-6 alkyl, -CH2CH2S(O2)CH3, -CH2CH2CH2CF3, etc.; R2 = R3 = H or C1-6 alkyl; R4 = halo, cyano, (un)substituted C1-6 alkyl, etc.; R5 = H, halo, or (un)substituted C1-6 alkyl] or a diastereomer, enantiomer, metabolite, salt, or solvate thereof, and optionally a third pharmaceutical product is claimed and exemplified. II was prepared via the reduction of the corresponding Me carboxylate intermediate with lithium aluminum hydride. I were evaluate for IRAK-4-inhibitory activity using the TR-FRET anal. (data provided).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of indazolecarboxamides as IRAK4 inhibitors useful in combination with BTk inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 62 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1751341 CAPLUS Full-text
TITLE: Preclinical Modeling of KIF5B-RET Fusion Lung Adenocarcinoma
AUTHOR(S): Huang, Qingling; Schneeberger, Valentina E.; Luetteke, Noreen; Jin, Chengliu; Afzal, Roha; Budzevich, Mikalai M.; Makanji, Rikesh J.; Martinez, Gary V.; Shen, Tao; Zhao, Lichao; Fung, Kar-Ming; Haura, Eric B.; Coppola, Domenico; Wu, Jie
CORPORATE SOURCE: Department of Molecular Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA
SOURCE: Molecular Cancer Therapeutics (2016), 15(10), 2521-2529
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-16-0258
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB RET fusions have been found in lung adenocarcinoma, of which KIF5B-RET is the most prevalent. We established inducible KIF5B-RET transgenic mice and KIF5B-RET-dependent cell lines for preclin. modeling of KIF5B-RET-associated lung adenocarcinoma. Doxycycline-induced CCSP-rtTA/tetO-KIF5B-RET transgenic mice developed invasive lung adenocarcinoma with desmoplastic reaction. Tumors regressed upon suppression of KIF5B-RET expression. By culturing KIF5B-RET-dependent BaF3 (B/KR) cells with increasing concns. of cabozantinib or vandetanib, we identified cabozantinib-resistant RETV804L mutation and vandetanib-resistant-RETG810A mutation. Among cabozantinib, lenvatinib, ponatinib, and vandetanib, ponatinib was identified as the most potent inhibitor against KIF5B-RET and its drug-resistant mutants. Interestingly, the vandetanib-resistant KIF5B-RETG810A mutant displayed gain-of-sensitivity (GOS) to ponatinib and lenvatinib. Treatment of doxycycline-induced CCSP-rtTA/tetO-KIF5B-RET bitransgenic mice with ponatinib effectively induced tumor regression. These results indicate that KIF5B-RET-associated lung tumors are addicted to the fusion oncogene and ponatinib is the most effective inhibitor for targeting KIF5B-RET in lung adenocarcinoma. Moreover, this study finds a novel vandetanib-resistant

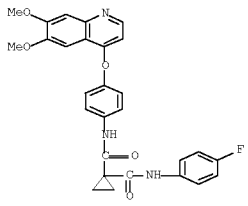
RETG810A mutation and identifies lenvatinib and ponatinib as the secondary drugs to overcome this vandetanib resistance mechanism. Mol Cancer Ther; 15(10); 2521-9.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(KIF5B-RET fusion protein induced development of lung adenocarcinoma with desmoplastic reactions where ponatinib fusion protein inhibitor reduced vandetanib resistance and induced lung tumor regression in RET mutant bitransgenic mouse)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 63 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1693724 CAPLUS Full-text

DOCUMENT NUMBER: 165:503499

TITLE: Nanomicelles for the treatment of cancer

INVENTOR(S): Ozen, Oguz Aslan; Ozgul, Mustafa; Aydin, Muhammed

PATENT ASSIGNEE(S): Turk.

SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016167730	A1	20161020	WO 2015-TR320	20150921

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

TR 2015004504 A2 20150721 TR 2015-4504 20150413

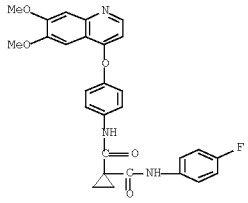
PRIORITY APPLN. INFO.: TR 2015-4504 A 20150413

AB The invention is about a cancer obliterator that contains anticancer drug enriched by H5WYG peptides containing several histidine with a property escaping from endosomes; and solves the problem of the vasoactive intestinal peptides and drug-loaded nanoparticles taken into the cell (which play a role in endocytose process and specifically bind to the receptors on cancer cell membranes) not being released into the cytosol by being held by endosomes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nanomicelles for treatment of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 64 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1677196 CAPLUS Full-text

TITLE: Antiangiogenic tyrosine kinase inhibitors: occurrence and risk factors of hemoptysis in refractory thyroid cancer

AUTHOR(S): Lamartina, Livia; Ippolito, S.; Danis, M.; Bidault, F.; Borget, I.; Berdelou, A.; Al Ghuzlan, A.; Hartl, D.; Blanchard, P.; Terroir, M.; Deandreis, D.; Schlumberger, M.; Baudin, E.; Leboulleux, S.

CORPORATE SOURCE: Departments of Nuclear Medicine and Endocrine Oncology, Gustave Roussy and University Paris Saclay, Villejuif, 94805, Fr.

SOURCE: Journal of Clinical Endocrinology & Metabolism (2016), 101(7), 2733-2741
CODEN: JCEMAZ; ISSN: 1945-7197

DIGITAL OBJECT ID: 10.1210/jc.2015-4391

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

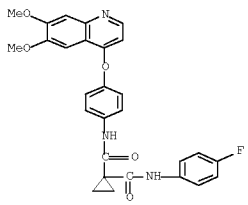
AB Background: Antiangiogenic tyrosine kinase inhibitors (TKIs) are the mainstay of advanced thyroid cancer (TC) treatment. Concern is rising about TKI-related toxicity. Objective: To determine the incidence and to investigate the risk factors of hemoptysis in TC patients during TKI treatment. Methods: We analyzed consecutive TC patients treated with TKI in our center between 2005 and 2013 and performed an independent review of computed tomog. scan images for airway invasion assessment. Occurrence of grade 1-2 or grade 3-5 hemoptysis according to Common Terminol. Criteria for Adverse Events version 4.03 and risk factors for hemoptysis were investigated. Results: A total of 140 patients (89 males; median age, 52 y) with medullary (56%), differentiated (33%), and poorly differentiated (11%) TC were enrolled. Thyroidectomy±neck dissection was performed in 123 patients and neck/mediastinum external-beam radiotherapy in 41 (32% with therapeutic purpose and 68% with adjuvant purpose). Patients received from 1 to 4 lines of TKI (median 1). Median follow-up was 24 mo. Airway invasion was found in 65 (46%) cases. Hemoptysis occurred in 9 patients: grade 1-2 in 7 cases (5%) and grade 3-5 in 2 (1.4%) cases (fatal in 1). Hemoptysis was associated with presence of airway invasion (P = .04), poorly differentiated pathol. (P = .03), history of therapeutic external-beam radiotherapy (P = .003), and thyroidectomy without neck dissection (P = .02). Conclusion: Airway invasion, poorly differentiated pathol., therapeutic external-beam radiotherapy, and thyroidectomy without neck dissection are associated with and increased risk of hemoptysis in TC patients during antiangiogenic TKI treatment. Further research is needed to confirm this data and to sort out interactions between these risk factors. A careful assessment of airway invasion is mandatory before TKI introduction.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antiangiogenic tyrosine kinase inhibitors occurrence and risk factors of hemoptysis in refractory thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 65 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1646170 CAPLUS Full-text

TITLE: Cabozantinib for metastatic breast carcinoma: results of a phase II placebo-controlled randomized discontinuation study

AUTHOR(S): Tolaney, Sara M.; Nechushtan, Hovav; Ron, Ilan-Gil; Schoffski, Patrick; Awada, Ahmad; Yasenchak, Chris A.; Laird, A. Douglas; O'Keeffe, Bridget; Shapiro, Geoffrey I.; Winer, Eric P.

CORPORATE SOURCE: Department of Medical Oncology, Breast Oncology Center, Dana-Farber Cancer Institute, Boston, MA, 02215, USA

SOURCE: Breast Cancer Research and Treatment (2016), 160(2), 305-312
CODEN: BCTRD6; ISSN: 0167-6806

DIGITAL OBJECT ID: 10.1007/s10549-016-4001-y

PUBLISHER: Springer

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

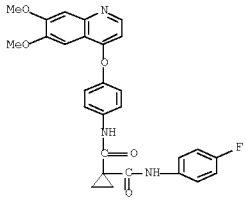
AB Purpose: Cabozantinib (XL184), a multi-targeted oral tyrosine kinase inhibitor with activity against MET, VEGFR2, AXL, and other tyrosine kinases, was assessed in a cohort of metastatic breast cancer (MBC) patients in a phase II randomized discontinuation trial (RDT). Methods: Patients received 100 mg cabozantinib daily during a 12-wk lead-in stage. Those with stable disease per modified Response Evaluation Criteria in Solid Tumors version 1.0 at 12 wk were randomized to either continue cabozantinib or receive placebo. Primary endpoints were objective response rate (ORR) during the 12-wk lead-in stage and progression-free survival (PFS) after randomization. Patients were also followed for overall survival (OS). Results: Forty-five patients with MBC and a median of three prior lines of chemotherapy for metastatic disease were enrolled. The ORR during the lead-in stage was 13.6 % (95 % confidence interval [CI] 6-25.7 %), and the disease control rate at week 12 was 46.7 % (95 % CI 31.7-61.6 %). Per the initial RDT study design, patients with stable disease at week 12 were randomized to cabozantinib or placebo. Following a Study Oversight Committee recommendation, randomization was suspended. Patients in the lead-in stage continued on open-label cabozantinib. Patients in the randomization stage were subsequently unblinded. The overall median PFS for all MBC patients was 4.3 mo. Median OS was 11.4 mo (95 % CI 10.5-16.5 mo). The most common grade 3/4 adverse events in the lead-in stage were palmar-plantar erythrodysesthesia (13 %) and fatigue (11 %). One death from respiratory failure was reported as drug-related during the lead-in stage. Conclusions: In heavily pretreated MBC patients, cabozantinib monotherapy demonstrated clin. activity including objective response and disease control.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib for metastatic breast carcinoma: results of a phase II placebo-controlled randomized discontinuation study)

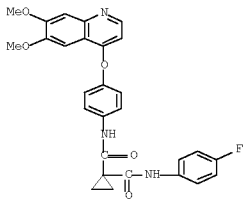
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 66 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1633250 CAPLUS Full-text
TITLE: Phase IB study of cabozantinib in patients with relapsed and/or refractory multiple myeloma
AUTHOR(S): Lendvai, Nikoletta; Yee, Andrew J.; Tsakos, Ioanna; Alexander, Aeri; Devlin, Sean M.; Hassoun, Hani; Korde, Neha; Lesokhin, Alexander M.; Landau, Heather; Mailankody, Sham; Koehne, Guenther; Chung, David J.; Landgren, Ola; Raje, Noopur S.; Giralt, Sergio
CORPORATE SOURCE: Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Blood (2016), 127(19), 2355-2356
CODEN: BLOOAW; ISSN: 1528-0020
DIGITAL OBJECT ID: 10.1182/blood-2016-01-694786
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB This article discusses about cabozantinib may have activity in myeloma patients with higher levels of HGF or where disease is driven by HGF.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (discussion on phase IB study of cabozantinib in patients with relapsed and/or refractory multiple myeloma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



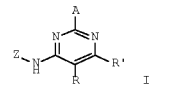
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 67 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1616504 CAPLUS Full-text
DOCUMENT NUMBER: 165:487681
TITLE: Preparation of pyrazole derivatives as GDF-8 and TGF-β inhibitors for the treatment of diseases
INVENTOR(S): Gelman, Marina; Ding, Pingyu; Kinsella, Todd; Singh, Rajinder; Bhamidipati, Somasekhar; Clough, Jeffrey
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 98pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

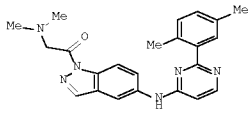
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016160833	A1	20161006	WO 2016-US24755	20160329

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62141441 P 20150401
OTHER SOURCE(S): CASREACT 165:487681; MARPAT 165:487681
GI

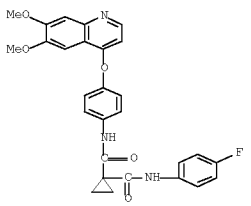


I



II

AB The invention relates to prepn. of aryl pyrimidine compds. of formula I wherein all the variables are as defined in the disclosure, as well as pharmaceutical compns. and methods of use thereof. The example compound II was prepared according to the procedure shown and was tested for GDF-8 and TGF-β inhibitory activity (data disclosed). In certain embodiments, a compound disclosed herein inhibits the activity of one or more members of the TGF-β superfamily, and can be used to treat disease by blocking such activity.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of aryl pyrimidine derivs. as GDF-8 and TGF-β inhibitors for mono- and combination therapy of diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

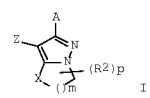
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 68 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1616478 CAPLUS Full-text
DOCUMENT NUMBER: 165:487643
TITLE: Preparation of pyrazole derivatives as GDF-8 and TGF-β inhibitors for the treatment of diseases
INVENTOR(S): Gelman, Marina; Kinsella, Todd; Bhamidipati, Somasekhar; Darwish, Ihab; Singh, Rajinder; Yu, Jiaxin
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 128pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

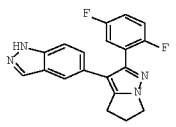
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016160881	A1	20161006	WO 2016-US24840	20160330

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62141511 P 20150401
OTHER SOURCE(S): CASREACT 165:487643; MARPAT 165:487643
GI



I

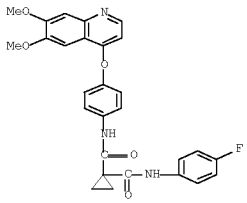


II

AB The invention relates to prepn. of pyrazole compds. of formula I wherein all the variables are as defined in the disclosure, as well as pharmaceutical compns. and methods of use thereof. The example compound II was prepared according to the procedure shown and was tested for GDF-8 and TGF-β inhibitory activity (data disclosed). In certain embodiments, a compound disclosed herein inhibits the activity of one or more members of the TGF-β superfamily, and can be used to treat disease by blocking such activity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pyrazole derivs. as GDF-8 and TGF-β inhibitors for mono- and combination therapy of diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



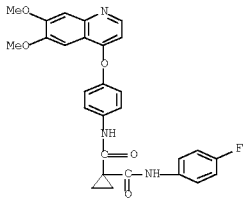
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 69 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1605657 CAPLUS Full-text
TITLE: Evaluation of Alternative In Vivo Drug Screening Methodology: A Single Mouse Analysis
AUTHOR(S): Murphy, Brendan; Yin, Han; Maris, John M.; Kolb, E. Anders; Gorlick, Richard; Reynolds, C. Patrick; Kang, Min H.; Keir, Stephen T.; Kurmasheva, Raushan T.; Dvorchik, Igor; Wu, Jianrong; Billups, Catherine A.; Boateng, Nana; Smith, Malcolm A.; Lock, Richard B.; Houghton, Peter J.
CORPORATE SOURCE: Center for Childhood Cancer and Blood Diseases, The Research Institute, Nationwide Children's Hospital, Columbus, OH, USA
SOURCE: Cancer Research (2016), 76(19), 5798-5809
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-16-0122
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Traditional approaches to evaluating antitumor agents using human tumor xenograft models have generally used cohorts of 8 to 10 mice against a limited panel of tumor models. An alternative approach is to use fewer animals per tumor line, allowing a greater number of models that capture greater mol./genetic heterogeneity of the cancer type. We retrospectively analyzed 67 agents evaluated by the Pediatric Preclin. Testing Program to determine whether a single mouse, chosen randomly from each group of a study, predicted the median response for groups of mice using 83 xenograft models. The individual tumor response from a randomly chosen mouse was compared with the group median response using established response criteria. A total of 2,134 comparisons were made. The single tumor response accurately predicted the group median response in 1,604 comparisons (75.16%). The mean tumor response correct prediction rate for 1,000 single mouse random samples was 78.09%. Models had a range for correct prediction (60%-87.5%). Allowing for misprediction of ± one response category, the overall mean correct single mouse prediction rate was 95.28%, and predicted overall objective response rates for group data in 66 of 67 drug studies. For molecularly targeted agents, occasional exceptional responder models were identified and the activity of that agent confirmed in addnl. models with the same genotype. Assuming that large treatment effects are targeted, this alternate exptl. design has similar predictive value as traditional approaches, allowing for far greater nos. of models to be used that more fully encompass the heterogeneity of disease types. Cancer Res; 76(19); 5798-809. ©2016 AACR.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(single mouse anal. on evaluation of alternative in vivo drug screening methodol.)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 70 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1580775 CAPLUS Full-text
DOCUMENT NUMBER: 165:458312
TITLE: Combination therapy using enantiopure, oxy-substituted, deuterium-enriched 5-(benzyl)-5-deutero-thiazolidine-2, 4-diones for treatment of medical disorders
INVENTOR(S): Dewitt, Sheila; Jacques, Vincent; Van der Ploeg, Leonardus H. T.
PATENT ASSIGNEE(S): DeuteRx LLC, USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016153948	A1	20160929	WO 2016-US23007	20160318

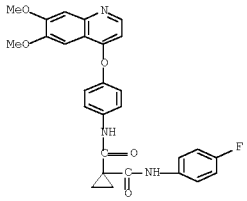
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62135988 P 20150320
OTHER SOURCE(S): CASREACT 165:458312; MARPAT 165:458312

AB The invention provides combination therapy using enantiopure deuterium-enriched pioglitazone, pharmaceutical compns., and methods of treating nonalcoholic steatohepatitis, diabetes, fibrotic disorders, and other disorders using the combination therapy.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy using enantiopure, oxy-substituted, deuterium-enriched benzyldeutero-thiazolidinediones for treatment of medical disorders)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 71 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1577100 CAPLUS Full-text
DOCUMENT NUMBER: 165:468731
TITLE: Crystalline forms of cabozantinib phosphate and cabozantinib hydrochloride
INVENTOR(S): Stefinovic, Marijan; Schreiner, Erwin Paul
PATENT ASSIGNEE(S): Sandoz AG, Switz.
SOURCE: PCT Int. Appl., 51pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016150966	A1	20160929	WO 2016-EP56267	20160322

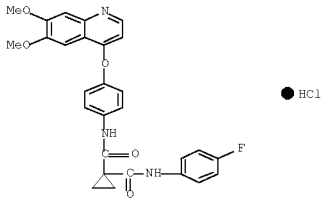
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2015-160869 A 20150325

AB The present invention relates to cryst. forms of cabozantinib phosphoric acid salt and cabozantinib hydrochloric acid salt and to a method for their preparation Furthermore, the invention relates to pharmaceutical compns. comprising said crystalline forms and their use as anti-cancer medicaments.

IT 1817763-82-4P, Cabozantinib hydrochloride (1:1)
2551238-89-2P, Cabozantinib phosphate salt
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

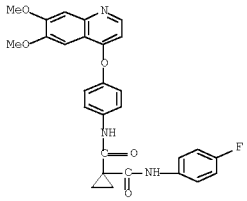
BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline forms of cabozantinib phosphate and cabozantinib hydrochloride)
RN 1817759-42-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrochloride (1:1) (CA INDEX NAME)



RN 2015216-89-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 7664-38-2
CMF H3 O4 P



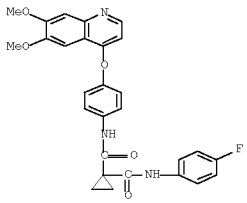
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 72 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1576981 CAPLUS Full-text
DOCUMENT NUMBER: 165:452131
TITLE: Cabozantinib salts and their use as anti-cancer agents
INVENTOR(S): Stefinovic, Marijan; Schreiner, Erwin Paul
PATENT ASSIGNEE(S): Sandoz AG, Switz.
SOURCE: PCT Int. Appl., 43pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016150963	A1	20160929	WO 2016-EP56262	20160322

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

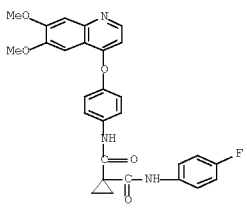
PRIORITY APPLN. INFO.: EP 2015-160877 A 20150325
AB The present invention relates to cryst. forms of cabozantinib succinate (Form A) and cabozantinib acetate (Form A-1) and to pharmaceutical compns. comprising said crystalline forms and their use as anti-cancer medicaments.
IT 849217-68-1, Cabozantinib 2014399-87-0 2014399-88-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib salts and their use as anti-cancer agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 2014399-87-0 CAPLUS
CN Butanedioic acid, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



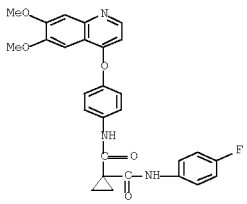
CM 2

CRN 110-15-6
CMF C4 H6 O4

RN 2014399-88-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, acetate (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 73 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1542135 CAPLUS Full-text
DOCUMENT NUMBER: 165:425258
TITLE: Heterocyclic modulators of lipid synthesis
INVENTOR(S): Oslob, Johan D.; McDowell, Robert S.; Johnson, Russell; Yang, Hanbiao; Evanchik, Marc; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.; Duke, Gregory; Ohol, Yamini; Heuer, Timothy Sean; O'Farrell, Marie
PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 164pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

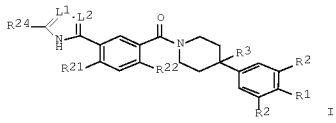
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016149271	A1	20160922	WO 2016-US22471	20160315

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62135631 P 20150319
OTHER SOURCE(S): MARPAT 165:425258
GI

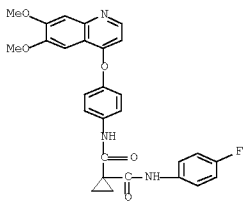


I

AB Provided are heterocyclic compds. that are fatty acid synthesis modulators such as formula I (wherein R1 is H, -CN, halogen, C1-C4 straight or branched alkyl, -O-(C3-C5 cycloalkyl), etc.; each R2 is independently hydrogen, halogen or C1-C4 straight or branched alkyl; R3 is H, -OH, or halogen; R21 is H, halogen, C1-C4 straight or branched alkyl, C3-C5 cycloalkyl wherein the C3-C1 cycloalkyl optionally includes an oxygen or nitrogen heteroatom; R22 is H, halogen, or C1-C2 alkyl; R24 is H, C1-C4 straight or branched alkyl, -(C1-C4 alkyl)t-OH, etc. and t is 0 or 1; L1 is CR23 or N; L2 is CH or N; and R23 is H or C1-C4 straight or branched alkyl). The compds. may be used to treat disorders characterized by dysregulation of the fatty acid synthase function by modulating the function and/or the fatty acid synthase pathway. Methods are provided for treating such disorders including viral infections, such as hepatitis C infection, cancer and metabolic disorders.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic modulators of lipid synthesis for disease treatment and combination with other agents)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



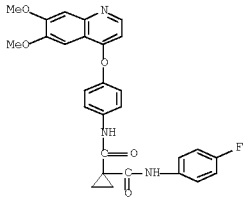
L4 ANSWER 75 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1479914 CAPLUS Full-text
TITLE: Avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma: a multicentre, single-group, open-label, phase 2 trial
AUTHOR(S): Kaufman, Howard L.; Russell, Jeffery; Hamid, Omid; Bhatia, Shailender; Terheyden, Patrick; D'Angelo, Sandra P.; Shih, Kent C.; Lebbe, Celeste; Linette, Gerald P.; Milella, Michele; Brownell, Isaac; Lewis, Karl D.; Lorch, Jochen H.; Chin, Kevin; Mahnke, Lisa; von Heydebreck, Anja; Cuillerot, Jean-Marie; Nghiem, Paul
CORPORATE SOURCE: Rutgers Cancer Institute of New Jersey, Rutgers, The State University of New Jersey, New Brunswick, NJ, USA
SOURCE: Lancet Oncology (2016), 17(10), 1374-1385
CODEN: LOANBN; ISSN: 1470-2045
DIGITAL OBJECT ID: 10.1016/S1470-2045(16)30364-3
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Merkel cell carcinoma is a rare, aggressive skin cancer with poor prognosis in patients with advanced disease. Current standard care uses various cytotoxic chemotherapy regimens, but responses are seldom durable. Tumor oncogenesis is linked to Merkel cell polyomavirus integration and UV-radiation-induced mutations, providing rationale for treatment with immunotherapy antibodies that target the PD-L1/PD-1 pathway. We assessed treatment with avelumab, an anti-PD-L1 monoclonal antibody, in patients with stage IV Merkel cell carcinoma that had progressed after cytotoxic chemotherapy. In this multicentre, international, prospective, single-group, open-label, phase 2 trial, patients with stage IV chemotherapy-refractory, histol. confirmed Merkel cell carcinoma (aged ≥18 years) were enrolled from 35 cancer treatment centers and academic hospitals in North America, Europe, Australia, and Asia. Key eligibility criteria were an ECOG performance status of 0 or 1, measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, adequate haematol., hepatic, and renal function, and immune-competent status (patients with HIV, immunosuppression, haematol. malignancies, and previous organ transplantation were excluded). Patient selection was not based on PD-L1 expression or Merkel cell polyomavirus status. Collection of biopsy material or use of archival tissue for these assessments was mandatory. Avelumab was given i.v. at a dose of 10 mg/kg every 2 wk. The primary endpoint was confirmed objective response (complete response or partial response) assessed according to RECIST version 1.1 by an independent review committee. Safety and clin. activity were assessed in all patients who received at least one dose of study drug (the modified intention-to-treat population). This trial is registered with ClinicalTrials.gov as NCT02155647. Between July 25, 2014, and Sept 3, 2015, 88 patients were enrolled and received at least one dose of avelumab. Patients were followed up for a median of 10·4 mo (IQR 8·6-13·1). The proportion of patients who achieved an objective response was 28 (31·8% [95·9% CI 21·9-43·1]) of 88 patients, including eight complete responses and 20 partial responses. Responses were ongoing in 23 (82%) of 28 patients at the time of anal. Five grade 3 treatment-related adverse events occurred in four (5%) patients: lymphopenia in two patients, blood creatine phosphokinase increase in one patient, aminotransferase increase in one patient, and blood cholesterol increase in one patient; there were no treatment-related grade 4 adverse events or treatment-related deaths. Serious treatment-related adverse events were reported in five patients (6%): enterocolitis, infusion-related reaction, aminotransferases increased, chondrocalcinosis, synovitis, and interstitial nephritis (n=1 each). Avelumab was associated with durable responses, most of which are still ongoing, and was well tolerated; hence, avelumab represents a new therapeutic option for advanced Merkel cell carcinoma.Merck KGaA, Darmstadt, Germany.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 74 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

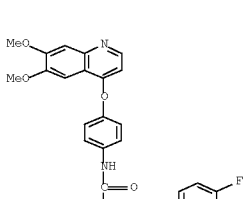
ACCESSION NUMBER: 2016:1483145 CAPLUS Full-text
TITLE: Anti-angiogenic agents and osteonecrosis of jaw
AUTHOR(S): Chouksey, Gunjan; Bhargava, Sudip; Raipure, Amrusha; Bhargava, Sumit
CORPORATE SOURCE: Department of Dental and Maxillofacial Prosthetic Clinic, Asian Institute of Oncology, Mumbai, India
SOURCE: European Journal of Biomedical and Pharmaceutical Sciences (2016), 3(5), 73-79
CODEN: EJBPBO; ISSN: 2349-8870
URL: http://www.ejbps.com/ejbps/archive_show/2016/Volume%203,%20May%20Issue%205

PUBLISHER: European Journal of Biomedical and Pharmaceutical Sciences
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Anti angiogenic agents is a highly promising therapeutic approach for the management of cancer. However one of the serious side effects associated with these drugs is Osteonecrosis of the Jaw. This review aims at understanding the association of anti angiogenic agents with occurrence, prevention and management of osteonecrosis of the jaw (ONJ). A PubMed search of the literature for relevant articles using the Medical Subject Heading (MeSH) terms "Anti-angiogenic agents", "Bevacizumab", "Sunitinib", "Trastuzumab", "Everolimus", "Cabozantinib", "Sorafenib", "Tyrosine Kinase Inhibitors", "Mammalian Target Of Rapamycin (Mtor) Inhibitors", "Osteonecrosis of jaw", was performed in various combinations. Addnl. articles were assessed in the reference lists of the retrieved articles.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-angiogenic agents and osteonecrosis of jaw)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

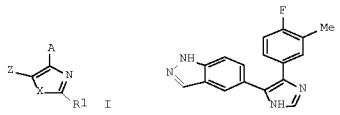


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 76 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1473431 CAPLUS Full-text
DOCUMENT NUMBER: 165:392751
TITLE: Preparation of imidazole and thiazole compounds as TGF-β inhibitors
INVENTOR(S): Kinsella, Todd; Gelman, Marina; Hong, Hui; Darwish, Ihab S.; Singh, Rajinder; Yu, Jiaxin; Borzilleri, Robert M.; Velaparthi, Upender; Liu, Peiying; Darne, Chetan; Rahaman, Hasibur; Warrier, Jayakumar Sankara
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA; Bristol-Myers Squibb Company
SOURCE: PCT Int. Appl., 378pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016140884	A1	20160909	WO 2016-US19830	20160226
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20160257690	A1	20160908	US 2016-15054895	20160226

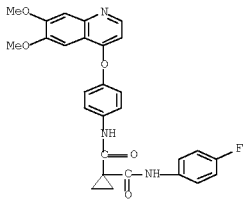
PRIORITY APPLN. INFO.: US 2015-62127109 P 20150302
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 165:392751; MARPAT 165:392751
GI



AB The invention relates to imidazole and thiazole compds. of formula I, and their use as inhibiting TGF-β and treating disease by blocking TGF-β signaling. Compds. of formula I wherein A is (un)substituted phenyl; R1 is H, (un)substituted C1-6 alkyl, (un)substituted C1-6 haloalkyl, (un)substituted C1-6 alkyloxy, etc.; X is S, NH and derivs.; Z is (un)substituted fused bicyclic ring; and pharmaceutically acceptable salts, prodrugs, N-oxides, solvates and hydrates thereof, are claimed. Compound II was prepared by cross coupling reaction of 4-bromo-1H-imidazole with (4-fluoro-3-methylphenyl)boronic acid followed bromination; the resulting 5-bromo-4-(4-fluoro-3-methylphenyl)-1H-imidazole underwent cross coupling reaction with indazole-5-boronic acid pinacol ester to give compound II. The invention compds. were evaluated for GDF8 and TGF-β inhibitory activity (data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of imidazole and thiazole compds. as TGF-β inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 77 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1435485 CAPLUS Full-text
DOCUMENT NUMBER: 165:350913
TITLE: Anti-tumor effect enhancer containing coumarin derivative, and antitumor composition
INVENTOR(S): Matsumoto, Shigeji
PATENT ASSIGNEE(S): Hyogo College of Medicine, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 76pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

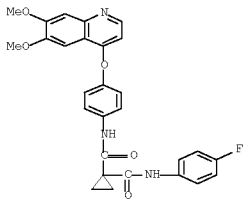
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2016155776	A	20160901	JP 2015-34544	20150224

PRIORITY APPLN. INFO.: JP 2015-34544 20150224
OTHER SOURCE(S): MARPAT 165:350913

AB The present invention relates to an agent for enhancing antitumor effect of MEK inhibitor and/or c-Met inhibitor. The antitumor effect enhancer contains a coumarin derivative, or its pharmaceutically acceptable salt as an active ingredient. An example of the antitumor effect enhancer is 4-Me umbelliferone. Also disclosed is an antitumor agent containing a MEK inhibitor and/or c-Met inhibitor, and the antitumor effect enhancer.

IT 849217-68-1, Cabozantinib 1140909-48-3, Cabozantinib-s-malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-tumor effect enhancer containing coumarin derivative, and antitumor composition)

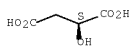
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

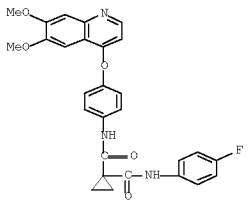


CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).





RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

L4 ANSWER 78 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1352723 CAPLUS Full-text
DOCUMENT NUMBER: 165:323067
TITLE: Dye-stabilized nanoparticles and methods of their manufacture and therapeutic use
INVENTOR(S): Heller, Daniel A.; Shamay, Yosef
PATENT ASSIGNEE(S): Memorial Sloan Kettering Cancer Center, USA
SOURCE: PCT Int. Appl., 188pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016130546	A1	20160818	WO 2016-US17153	20160209
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR,				

HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

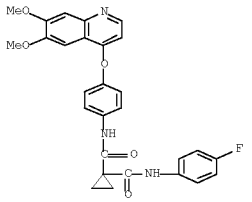
PRIORITY APPLN. INFO.: US 2015-62114507 P 20150210

AB Described herein are nanoparticles which are largely made of (e.g., 90 wt%) hydrophobic drugs and are stabilized by water soluble dyes. The nanoparticles can range in size from 30 nm to 150 nm and have highly neg. surface charge (e.g., -55 mV). These nanoparticles are highly soluble in water, stable for days in PBS buffer and can be easily lyophilized and reconstituted in water. Using quant. self-assembly prediction calcns., topochem. mol. descriptors were identified and validated as highly predictive indicators of nano-assembly, nanoparticle size, and drug loading. The resulting nanoparticles selectively targeted kinase inhibitors to caveolin-1-expressing human colon cancer and autochthonous liver cancer models to yield striking therapeutic effects while avoiding pERK inhibition in healthy skin. The nanoparticles exhibited remarkable anti-tumor efficacy in vitro and in vivo in models of hepatocellular carcinoma. Thus, dye-encapsulated sorafenib nanoparticles (IR783-SFB) were synthesized using the nanopptn. method; 0.1 mL of sorafenib dissolved in DMSO (10 mg/mL) was added dropwise (20 μL per 15 s) to a 0.4 aqueous IR783 solution (1 mg/mL) containing 0.05 mM sodium bicarbonate; the solution was centrifuged twice and resuspension in 1 mL of sterile PBS; the suspension of nanoparticles was sonicated for 10 s with a probe sonicator at 40 % intensity; the resulted IR783-SFB nanoparticles had zeta potential of -52 mV and a size of 95 nm with a PDI of 0.1; by suspending the nanoparticles in lower vols. they were able to solubilize sorafenib up to 16 mg/mL in saline solution which is 2000 times better than free drug; the nanoparticles were easily lyophilized with a saline/sucrose 5 % solution and reconstituted in water at this concentration

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dye-stabilized nanoparticles and methods of their manufacture and therapeutic use)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 79 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1338975 CAPLUS Full-text

DOCUMENT NUMBER: 166:452875

TITLE: A Pilot Study of Clinical Targeted Next Generation Sequencing for Prostate Cancer: Consequences for Treatment and Genetic Counseling

AUTHOR(S): Cheng, Heather H.; Klemfuss, Nola; Montgomery, Bruce; Higano, Celestia S.; Schweizer, Michael T.; Mostaghel, Elahe A.; McFerrin, Lisa G.; Yu, Evan Y.; Nelson, Peter S.; Pritchard, Colin C.

CORPORATE SOURCE: Division of Oncology, Department of Medicine, University of Washington, Seattle, WA, USA

SOURCE: Prostate (Hoboken, NJ, United States) (2016), 76(14), 1303-1311
CODEN: PRSTDS; ISSN: 0270-4137

DIGITAL OBJECT ID: 10.1002/pros.23219

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; (online computer file)

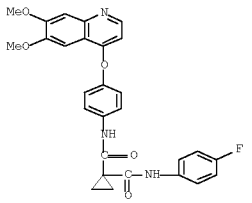
LANGUAGE: English

AB BACKGROUND : Targeted next generation sequencing (tNGS) is increasingly used in oncol. for therapeutic decision-making, but is not yet widely used for prostate cancer. The objective of this study was to determine current clin. utility of tNGS for prostate cancer management. METHODS : Seven academic genitourinary medical oncologists recruited and consented patients with prostate cancer, largely with unusual clin. and/or pathol. features, from 2013 to 2015. UW-OncoPlex was performed on formalin-fixed, paraffin-embedded (FFPE) primary tumors and/or metastatic biopsies. Results were discussed at a multidisciplinary precision tumor board prior to communicating to patients. FFPE tumor DNA was extracted for tNGS anal. of 194 cancer-associated genes. Results, multidisciplinary discussion, and treatment changes were recorded. RESULTS : Forty-five patients consented and 42 had reportable results. Findings included mutations in genes frequently observed in prostate cancer. We also found alterations in genes where targeted treatments were available and/or in clin. trials. 4/42 (10%) cases, change in treatment directly resulted from tNGS and multidisciplinary discussion. In 30/42 (71%) cases addnl. options were available but not pursued and/or were pending. Notably, 10/42 (24%) of patients harbored suspected germline mutations in moderate or high-penetrance cancer risk genes, including BRCA2, TP53, ATM, and CHEK2. One patient's tumor had bi-allelic MSH6 mutation and microsatellite instability. In total, 34/42 (81%) cases resulted in some measure of treatment actionability. Limitations include small size and limited clin. outcomes. CONCLUSIONS : Targeted NGS tumor sequencing may help guide immediate and future treatment options for men with prostate cancer. A substantial subset had germline mutations in cancer predisposition genes with potential clin. management implications for men and their relatives.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pilot study of clin. targeted next generation sequencing for prostate cancer, consequences for treatment and genetic counseling)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 80 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1327927 CAPLUS Full-text

TITLE: The Emerging Role of Tyrosine Kinase Inhibitors in Ovarian Cancer Treatment: A Systematic Review

AUTHOR(S): Ntanasis-Stathopoulos, Ioannis; Fotopoulos, George; Tzanninis, Ioannis-Georgios; Kotteas, Elias A.

CORPORATE SOURCE: Oncology Unit, Sotiria General Hospital, Athens School of Medicine, Athens, Greece

SOURCE: Cancer Investigation (2016), 34(7), 313-339
CODEN: CINVD7; ISSN: 0735-7907

DIGITAL OBJECT ID: 10.1080/07357907.2016.1206117

PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

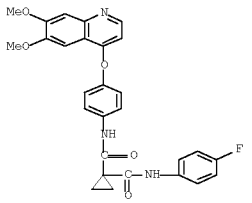
AB The present systematic review summarizes current evidence regarding the mechanisms of action, the efficacy, and the adverse effects of tyrosine kinase inhibitors (TKIs) in ovarian cancer patients. Phase II and III clin. trials were sought in the PubMed database and in the Clin. Trials.gov registry through Sept. 30, 2015. Seventy-five clin. trials regarding TKIs targeting mainly vascular endothelial growth factor receptor, epidermal growth factor receptor, platelet-derived growth factor receptor, and sarcoma tyrosine kinase (Src) were yielded. The most promising results were noted with cediranib, nintedanib, and pazopanib. However, drawing universal conclusions about the potential integration of TKIs in ovarian cancer therapy remains elusive. Furthermore, emerging challenges and directions for the future research are critically discussed.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(emerging role of tyrosine kinase inhibitors in ovarian cancer treatment)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 81 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1320889 CAPLUS Full-text

TITLE: Effect of Renal and Hepatic Impairment on the Pharmacokinetics of Cabozantinib

AUTHOR(S): Nguyen, Linh; Holland, Jaymes; Ramies, David; Mamelok, Richard; Benrimoh, Natacha; Ciric, Sabrina; Marbury, Thomas; Preston, Richard A.; Heuman, Douglas M.; Gavis, Edith; Lacy, Steven

CORPORATE SOURCE: Exelixis, South San Francisco, CA, USA

SOURCE: Journal of Clinical Pharmacology (2016), 56(9), 1130-1140
CODEN: JCPCBR; ISSN: 0091-2700

DIGITAL OBJECT ID: 10.1002/jcph.714

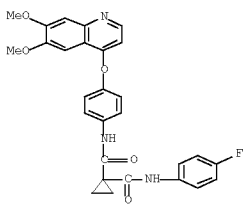
PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Cabozantinib is a tyrosine kinase inhibitor approved for the treatment of patients with progressive, metastatic medullary thyroid cancer. Two clin. pharmacol. studies were conducted to characterize single-dose pharmacokinetics (PK) of cabozantinib in renally or hepatically impaired subjects. Study 1 enrolled 10 subjects, each with mild or moderate impairment of renal function; 12 healthy subjects were matched to the moderate group for age, sex, and body mass index (BMI). Study 2 enrolled 8 males each with mild or moderate hepatic impairment; 10 healthy males were matched to the moderate group for age, BMI, and ethnicity. All subjects received one 60 mg cabozantinib oral capsule dose followed by PK sampling over 21 days. Plasma concentration and protein binding were determined by liquid chromatog. tandem mass spectrometry and equilibrium dialysis, resp. PK parameters were computed using noncompartmental methods. Geometric least squared mean (LSM) ratios for plasma cabozantinib AUC0-∞ for impaired to normal organ function cohorts were (1) approx. 30% and 6% higher in subjects with mild and moderate renal impairment, resp., and (2) approx. 81% and 63% higher in subjects with mild and moderate hepatic impairment, resp. The percentage of unbound drug was slightly higher in both moderately impaired cohorts. No deaths or discontinuations due to adverse events occurred in either study. Cabozantinib should be used with caution in subjects with mild or moderate renal impairment. Subjects with mild or

moderate hepatic impairment administered cabozantinib should be monitored closely for potential treatment-emergent drug toxicity that may necessitate a dose hold or reduction
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (effect of renal and hepatic impairment on pharmacokinetics of cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



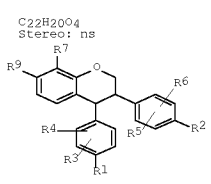
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 82 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1315151 CAPLUS Full-text
DOCUMENT NUMBER: 165:280723
TITLE: Complexes of abiraterone acetate, process for the preparation thereof and pharmaceutical compositions containing them
INVENTOR(S): Angi, Reka; Jordan, Tamas; Basa-Denes, Orsolya; Solymosi, Tamas; Oetvoes, Zsolt; Glavinas, Hristos; Filipcsei, Genoveva
PATENT ASSIGNEE(S): Druggability Technologies Holdings Ltd., Ire.
SOURCE: U.S. Pat. Appl. Publ., 33pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160228455	A1	20160811	US 2016-15019037	20160209
US 9623034	B2	20170418		
HU 2015000055	A2	20160829	HU 2015-55	20150209
WO 2016128891	A1	20160818	WO 2016-IB50672	20160209

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-62111030 P 20150202
OTHER SOURCE(S): MARPAT 165:284020
GI

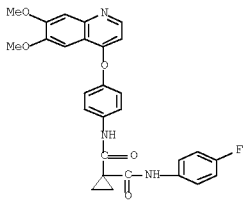


I

AB Provided herein are methods of treating and sensitizing cancer comprising administering a glycolytic inhibitor and an oxidative phosphorylation inhibitor of general Formula I (wherein, R1 = hydroxy, alkoxy, haloalkyl, halo; R2 = hydroxy, alkoxy; R3, R4, R5, R6 = independently, H, hydroxy, alkoxy, halo, haloalkyl, alkyl; R7 = H, alkyl; R9 = hydroxy, alkoxy).
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cometriq; combination therapies)
RN 849217-68-1 CAPLUS

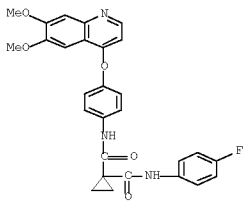
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20160331763 A1 20161117 US 2016-15222301 20160728
US 9592244 B2 20170314
PRIORITY APPLN. INFO.: HU 2015-55 A 20150209
US 2016-15019037 A3 20160209
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present disclosure relates to pharmaceutically acceptable complex formulas comprising complexes of Abiraterone acetate and pharmaceutically acceptable excipients, process for the preparation thereof and pharmaceutical compns. containing them. The complex formulas of the present disclosure have improved physicochem. properties which results in reduced food effect which allows significant dose reduction and the abandoning of the requirement of taking the drug on an empty stomach.
IT 849217-68-1, Cabo-zantinib
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(complexes of abiraterone acetate, process for the preparation thereof and
pharmaceutical compns. containing them)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 83 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1311663 CAPLUS Full-text
DOCUMENT NUMBER: 165:284020
TITLE: Combination therapies for Cancer
INVENTOR(S): Gold, Daniel P.; Quintela-Fandino, Miguel

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 84 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1276478 CAPLUS Full-text
DOCUMENT NUMBER: 165:265439
TITLE: Compositions and methods of using tyrosine kinase inhibitors
INVENTOR(S): Bennett, Anton; Yi, Jae-Sung
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 113pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016123086	A1	20160804	WO 2016-US14882	20160126

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

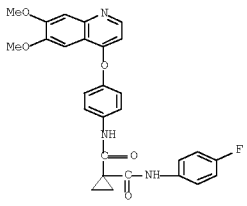
PRIORITY APPLN. INFO.: US 2015-62107553 P 20150126
US 2015-62250052 P 20151103
AB The present invention provides compns. and methods of inhibiting tyrosine phosphorylation. In one aspect, a composition includes comprising a

low-dosage tyrosine kinase inhibitor, where the low-dosage tyrosine kinase inhibitor decreases tyrosine phosphorylation. In another aspect, a method is described for treating cardiovascular disease or condition associated with a RASopathy having aberrant protein tyrosine phosphorylation. Methods for treating congenital heart disease associated with Noonan or Noonan syndrome with multiple lentigines and decreasing aberrant levels of Protein Zero-Related (PZR) tyrosyl phosphorylation are also described.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods of using tyrosine kinase inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 85 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1276023 CAPLUS Full-text

DOCUMENT NUMBER: 165:256806

TITLE: Kinase drug combinations and methods of use thereof for inhibiting cancer cell growth

INVENTOR(S): Johnson, Gary L.; Graves, Lee M.; Jin, Jian

PATENT ASSIGNEE(S): The University of North Carolina At Chapel Hill, USA

SOURCE: PCT Int. Appl., 78pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016123054	A2	20160804	WO 2016-US14831	20160126
WO 2016123054	A3	20161020		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA,

PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

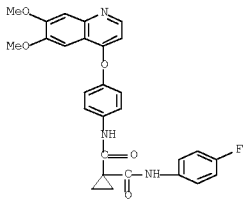
PRIORITY APPLN. INFO.: US 2015-62107788 P 20150126
US 2015-62144457 P 20150408
US 2015-62195435 P 20150722

AB The present disclosure relates to method for inhibiting cancer cell growth or inducing apoptosis in cancer cells by inhibiting kinome reprogramming in a combination therapy involving kinase inhibitors. A kinase inhibitor in combination with a P-TEFb inhibitor and/or p300/CBP inhibitor provides a stable growth suppression of the cancer cells, blocking kinome reprogramming response to kinase inhibitors.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kinase inhibitor drug combinations and methods of use thereof for inhibiting cancer cell growth)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 86 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1240142 CAPLUS Full-text

TITLE: A phase I trial of cabozantinib and gemcitabine in advanced pancreatic cancer

AUTHOR(S): Zhen, David B.; Griffith, Kent A.; Ruch, Joshua M.; Camphausen, Kevin; Savage, Jason E.; Kim, Edward J.; Sahai, Vaibhav; Simeone, Diane M.; Zalupski, Mark M.

CORPORATE SOURCE: Division of Hematology/Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, 48109-5934, USA

SOURCE: Investigational New Drugs (2016), 34(6), 733-739
CODEN: INNDDK; ISSN: 0167-6997

DIGITAL OBJECT ID: 10.1007/s10637-016-0376-1

PUBLISHER: Springer

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

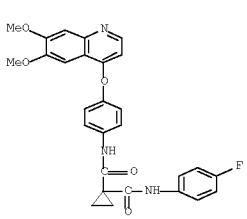
AB Background Cabozantinib and gemcitabine improve tumor control in pancreatic ductal adenocarcinoma (PDAC) in preclin. models through c-Met inhibition. We sought to determine the maximum tolerated dose (MTD) of this combination in patients with advanced PDAC. Methods Patients with ≤1 prior treatment and adequate performance status were eligible. Cabozantinib was given orally once daily, beginning day (-)7 and continued with gemcitabine given i.v. on days 1, 8, and 15 every 28 days. Dose level was assigned using Time to Event Continual Reassessment Method (TITE-CRM). Primary endpoint was MTD, defined as the highest dose level at which ≤25 % of patients incurred a dose-limiting toxicity (DLT). Secondary endpoints included response rate, progression-free survival (PFS), overall survival (OS) and urinary biomarker assessment. Results Twelve patients were enrolled and treated with 10 patients evaluable for DLT. The probability of DLT was >25 % for all dose levels tested, and thus an MTD was not determined DLTs included grade 3 ALT/AST elevations and thrombocytopenia. Three patients had partial responses, but each discontinued therapy due to toxicity. Median PFS and OS were 4.7 (95 % CI: 1.4-9.7) and 10.1 mo (95 % CI: 3.6-20.6). Exploratory biomarker anal. showed correlation of c-Met and VEGF levels with response. Conclusions An MTD for the combination was not established. Cabozantinib and gemcitabine appear impractical for further development due to DLT at low doses and continuing toxicities with ongoing therapy. Acknowledging the small sample size, responses were seen suggesting further investigation of c-Met inhibition in PDAC may be warranted.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phase I trial of cabozantinib and gemcitabine in advanced pancreatic cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 87 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1189164 CAPLUS Full-text

DOCUMENT NUMBER: 165:209245

TITLE: Methods for targeting host vascular mechanism for therapeutic protection against hemorrhagic fever

INVENTOR(S): Shresta, Sujan

PATENT ASSIGNEE(S): La Jolla Institute for Allergy and Immunology, USA

SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016115092	A1	20160721	WO 2016-US12985	20160112

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

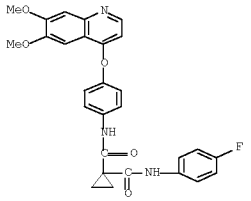
PRIORITY APPLN. INFO.: US 2015-62102490 P 20150112
US 2015-62157464 P 20150506

AB Presented herein are compns. and methods for preventing and treating hemorrhagic fever, viral infections and symptoms thereof. Also presented herein are compns. and methods for treating viral infection caused by a virus selected from the family of Arenaviridae, Filoviridae, Bunyaviridae, Flaviviridae, and Rhabdoviridae. The methods presented herein are based, in part, on modulating the vascular endothelial growth factor (VEGF) pathway, the angiopoietin (Ang-1 and Ang-2 in particular) pathway, as well as tight junction proteins and adherens junction proteins, which are involved in the pathogenesis of viral hemorrhagic fever.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for targeting host vascular mechanism for therapeutic protection against hemorrhagic fever)

RN 849217-68-1 CAPLUS

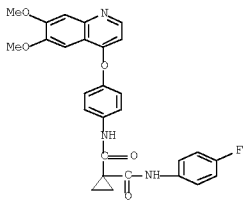
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



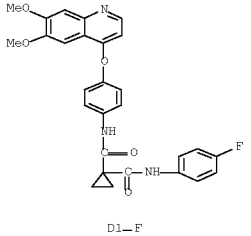
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 88 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1092828 CAPLUS Full-text
TITLE: Mechanism and clinical progress of molecular targeted cancer therapy
AUTHOR(S): Hu, Hong-xiang; Wang, Xue-qing; Zhang, Hua; Zhang, Qiang
CORPORATE SOURCE: School of Pharmacy, Peking University, Beijing, 100191, Peop. Rep. China
SOURCE: Yaoxue Xuebao (2015), 50(10), 1232-1239
CODEN: YHHPAL; ISSN: 0513-4870
PUBLISHER: Yaoxue Xuebao Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 34 ref. is given on mechanism and clin. progress of mol. targeted cancer therapy. Mol. target-based cancer therapy is playing a more and more important role in cancer therapy because of its high specificity, good tolerance and so on. There are different kinds of mol. targeted drugs such as monoclonal antibodies and small mol. kinase inhibitors, and more than 50 drugs have been approved since 1997. When the first monoclonal antibody, rituximab, was on the market. The development of mol. target-based cancer therapeutics has become the main approach. Based on this, we summarized the drugs approved by FDA and introduced their mechanism of actions and clin. applications. In order to incorporate most mol. targeted drugs and describe clearly various characteristics, we divided them into four categories: drugs related to EGFR, drugs related to antiangiogenesis, drugs related to specific antigen and other targeted drugs. The purpose of this review is to provide a current status of this field and discover the main problems in the mol. targeted therapy.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism and clin. progress of mol. targeted cancer therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(method of discovering fluoro-containing compds.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

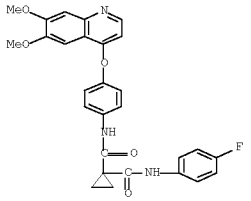


IT 1961203-44-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of discovering fluoro-containing compds.)
RN 1961203-44-0 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, monofluoro deriv. (CA INDEX NAME)



D1—F

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 89 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1073135 CAPLUS Full-text
DOCUMENT NUMBER: 165:171684
TITLE: Method of discovering fluoro-containing compounds
INVENTOR(S): Ma, Yao; Liang, Qing; Li, Weilin; Tang, Yu; Wen, Weidong
PATENT ASSIGNEE(S): Shanxi Chemical Research Institute Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 76pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016106161	A1	20160630	WO 2015-US66957	20151220

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62095055 P 20141221
OTHER SOURCE(S): CASREACT 165:171684
AB The present teachings relate to a methods for drug discovery. In one particular example, the method includes providing a substrate, modifying the substrate by using an electrochem. fluorination, screening a reaction mixture of the electrochem. fluorination, and identifying a fluorinated compound in the reaction mixture

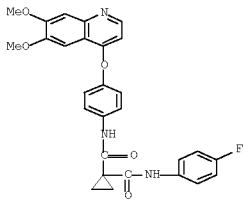
L4 ANSWER 90 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1073026 CAPLUS Full-text
DOCUMENT NUMBER: 165:145231
TITLE: High frequency auxiliary agent, medical system, and method for the selective treatment of cancer tissue
INVENTOR(S): Noack, Andreas
PATENT ASSIGNEE(S): Olympus Winter & Ibe GmbH, Germany
SOURCE: PCT Int. Appl., 45pp.; Chemical Indexing Equivalent to 165:119507 (DE)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016102179	A1	20160630	WO 2015-EP78768	20151207

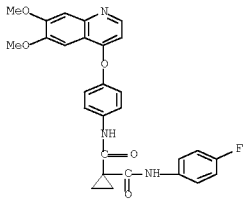
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

DE 102014226903	A1	20160623	DE 2014-102014226903	20141223

PRIORITY APPLN. INFO.: DE 2014-102014226903 A 20141223
AB The invention relates to an high frequency (HF) auxiliary agent as well as to a medical system and a method for selectively treating cancer tissue. A mol. of the HF auxiliary agent comprises a first group that specifically interacts with a surface feature of a cancer cell as well as a polar second group that is coupled to said first group.
IT 849217-68-1, CABOZANTINIB
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high frequency auxiliary agent, medical system, and method for selective treatment of cancer tissue)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 91 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1071388 CAPLUS Full-text
TITLE: Identification of clinically achievable combination therapies in childhood rhabdomyosarcoma
AUTHOR(S): Kahen, Elliot; Yu, Diana; Harrison, Douglas J.; Clark, Justine; Hingorani, Pooja; Cubitt, Christopher L.; Reed, Damon R.
CORPORATE SOURCE: Sunshine Project Translational Research Lab, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA
SOURCE: Cancer Chemotherapy and Pharmacology (2016), 78(2), 313-323
CODEN: CCPHDZ; ISSN: 0344-5704
DIGITAL OBJECT ID: 10.1007/s00280-016-3077-8
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Purpose: Systemic therapy has improved rhabdomyosarcoma event-free and overall survival; however, approx. 40 % of patients will have progressive or recurrent disease which is difficult to cure and remains a considerable challenge. Minimal progress has been made in improving outcomes for metastatic or relapsed RMS due to a lack of effective therapeutic agents. Targeted therapies are likely to be incorporated into regimens which rely on conventional cytotoxic chemotherapy. A system to evaluate novel combinations of interest is needed. Methods: In this study, we explored 8 agents, 5 that are routinely used or similar to agents used in the clin. management of RMS and 3 biol. targeted agents with novel mechanisms of action, the Wee1 inhibitor AZD1775, the tyrosine kinase inhibitor cabozantinib, and the proteasome inhibitor bortezomib. All were tested individually at clin. achievable concns. for activity in 4 RMS cell lines and then for potential synergy in two-drug combinations. Results: We found single-agent activity in five of the agents (or their active metabolites) that constitute the standard of care in RMS and for AZD1775 with mean IC50 values of 207 ng/mL, well below clin. achievable levels. In addition, the combination of individual cytotoxic chemotherapeutics currently used for RMS demonstrated largely synergistic activity with higher, but clin. achievable concns. of AZD1775 in our assays. Conclusions: Prioritization of chemotherapeutics in RMS is possible using an in vitro system that can define novel drug combinations worthy of future investigation. AZD1775 exhibits single-agent activity, as well as synergy with conventional cytotoxic chemotherapy, and is a novel targeted agent that warrants further study in RMS.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identification of clin. achievable combination therapies in childhood rhabdomyosarcoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



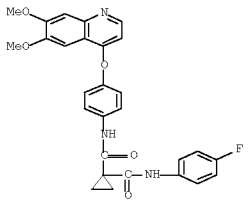
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 92 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1036670 CAPLUS Full-text
DOCUMENT NUMBER: 165:122253
TITLE: Antifibrotic activity of growth arrest-specific 6 (GAS6) inhibitors
INVENTOR(S): Miao, Yu Rebecca; Tabibiazar, Raymond; Giaccia, Amato J.; Kariolis, Mihalis
PATENT ASSIGNEE(S): Ruga Corporation, USA
SOURCE: PCT Int. Appl., 51pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016100738	A2	20160623	WO 2015-US66498	20151217
WO 2016100738	A3	20160909		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

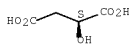
PRIORITY APPLN. INFO.: US 2014-62093937 P 20141218
AB Compns. and methods are provided for treating fibrosis in a mammal by administering a therapeutic dose of a pharmaceutical composition that inhibits AXL, MER or Tyro3 protein activity, for example by inhibition of the binding interaction between AXL, MER or Tyro3 and its ligand GAS6.
IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antifibrotic activity of growth arrest-specific 6 (GAS6) inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

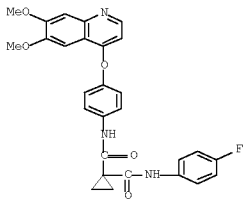


CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).





RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

L4 ANSWER 93 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:1036074 CAPLUS Full-text
DOCUMENT NUMBER: 165:65584
TITLE: Genomic classifier that predicts response to multi-kinase inhibitor treatment introduction
INVENTOR(S): Blay, Jean-Yves; Jiang, Xiaojun; Tredan, Olivier; Ray Coquard, Isabelle
PATENT ASSIGNEE(S): Centre Leon-Berard, Fr.
SOURCE: PCT Int. Appl., 49pp.; Chemical Indexing Equivalent to 165:50011 (EP)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016097285	A1	20160623	WO 2015-EP80475	20151218

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,

VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 3034622 A1 20160622 EP 2014-307115 20141219

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

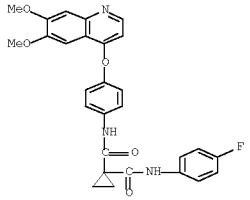
PRIORITY APPLN. INFO.: EP 2014-307115 A 20141219

AB The method for predicting the anti-tumor response in a human or animal having a tumor to multiple kinase inhibitors, using any multiple kinase inhibitor, comprises selection of genes encoding for protein kinases targeted by the said tyrosine kinase inhibitor, for each one of these genes, providing at least one nucleic acid probe which hybridizes to said gene under stringent conditions, thus providing an array of nucleic acid probes, having a biol. sample containing cancer cells from said human or animal, extracting DNA from the sample, fragmenting into DNA fragments, optionally labeling the DNA fragments, submitting the optionally labeled DNA fragments to hybridization with the array of nucleic acid probes, recovering and quantifying for all the genes the gains or losses in gene copy nos., wherein gains and losses of gene copy nos. of each selected gene are used to determine whether the tumor is sensitive or not to said kinase inhibitor.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genomic classifier that predicts response to multi-kinase inhibitor treatment introduction)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 94 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1025744 CAPLUS Full-text

DOCUMENT NUMBER: 165:119516

TITLE: Adoptive immunotherapy methods for producing tumor-infiltrating lymphocytes for treating cancer

INVENTOR(S): Doucey, Marie-Agnes; Xenarios, Ioannis; Guex, Nicolas; Crespo, Isaac

PATENT ASSIGNEE(S): Universite de Lausanne, Switz.

SOURCE: Eur. Pat. Appl., 21pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 3034092	A1	20160622	EP 2014-198399	20141217

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

WO 2016096903 A1 20160623 WO 2015-EP79867 20151215

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

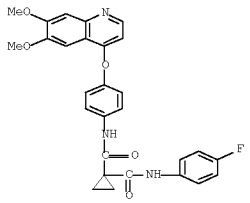
PRIORITY APPLN. INFO.: EP 2014-198399 A 20141217

AB The present invention provides methods for producing and/or expanding tumor-infiltrating lymphocytes (TIL) that can be used in adoptive immunotherapy in cancer treatment. Thus, it was found that TIE-2 and VEGFR pathways synergistically control TEM proangiogenic activity; TIL can expand from breast tumor fragments treated with TIE-2 and VEGFR kinase inhibitors; treatment of breast tumor tissue fragments with TIE-2 and VEGFR kinase inhibitors allows TIL expansion.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adoptive immunotherapy methods for producing tumor-infiltrating lymphocytes for treating cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 95 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1025737 CAPLUS Full-text

DOCUMENT NUMBER: 165:119515

TITLE: Adoptive immunotherapy methods for producing tumor-infiltrating lymphocytes for treating cancer

INVENTOR(S): Doucey, Marie-Agnes; Guex, Nicolas; Crespo, Isaac; Xenarios, Ioannis

PATENT ASSIGNEE(S): Universite de Lausanne, Switz.

SOURCE: PCT Int. Appl., 59pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016096903	A1	20160623	WO 2015-EP79867	20151215

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 3034092 A1 20160622 EP 2014-198399 20141217

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

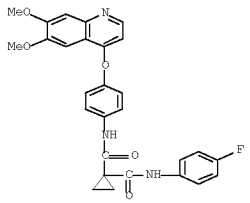
PRIORITY APPLN. INFO.: EP 2014-198399 A 20141217

AB The present invention provides methods for producing and/or expanding tumor-infiltrating lymphocytes (TIL) that can be used in adoptive immunotherapy in cancer treatment. Thus, it was found that TIE-2 and VEGFR pathways synergistically control TEM proangiogenic activity; TIL can expand from breast tumor fragments treated with TIE-2 and VEGFR kinase inhibitors; treatment of breast tumor tissue fragments with TIE-2 and VEGFR kinase inhibitors allows TIL expansion.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adoptive immunotherapy methods for producing tumor-infiltrating lymphocytes for treating cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 96 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1024796 CAPLUS Full-text

DOCUMENT NUMBER: 165:50011

TITLE: Genomic classifier that predicts response to multi-kinase inhibitor treatment introduction

INVENTOR(S): Blay, Jean-Yves; Jiang, Xiaojun; Tredan, Olivier; Ray Coquard, Isabelle

PATENT ASSIGNEE(S): Centre Leon Berard, Fr.

SOURCE: Eur. Pat. Appl., 35pp.; Chemical Indexing Equivalent to 165:65584 (WO)
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 3034622	A1	20160622	EP 2014-307115	20141219

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

WO 2016097285 A1 20160623 WO 2015-EP80475 20151218

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

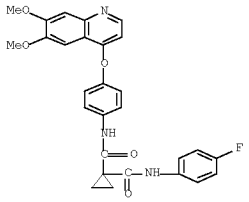
PRIORITY APPLN. INFO.: EP 2014-307115 A 20141219

AB The method for predicting the anti-tumor response in a human or animal having a tumor to multiple kinase inhibitors, using any multiple kinase inhibitor, comprises selection of genes encoding for protein kinases targeted by the said tyrosine kinase inhibitor, for each one of these genes, providing at least one nucleic acid probe which hybridizes to said gene under stringent conditions, thus providing an array of nucleic acid probes, having a biol. sample containing cancer cells from said human or animal, extracting DNA from the sample, fragmenting into DNA fragments, optionally labeling the DNA fragments, submitting the optionally labeled DNA fragments to hybridization with the array of nucleic acid probes, recovering and quantifying for all the genes the gains or losses in gene copy nos., wherein gains and losses of gene copy nos. of each selected gene are used to determine whether the tumor is sensitive or not to said kinase inhibitor.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genomic classifier that predicts response to multi-kinase inhibitor treatment introduction)

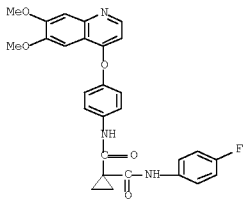
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 97 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 98 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:1007974 CAPLUS Full-text

TITLE: Pharmacokinetics of cabozantinib tablet and capsule formulations in healthy adults

AUTHOR(S): Nguyen, Linh; Benrimoh, Natacha; Xie, Yuli; Offman, Elliot; Lacy, Steven

CORPORATE SOURCE: Exelixis Inc., San Francisco, CA, USA

SOURCE: Anti-Cancer Drugs (2016), 27(7), 669-678
CODEN: ANTDEV; ISSN: 0959-4973

DIGITAL OBJECT ID: 10.1097/CAD.0000000000000366

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Cabozantinib capsules (COMETRIQ) are approved for the treatment of patients with progressive metastatic medullary thyroid cancer. Cabozantinib tablets are investigational drug products considered to be potentially preferred pharmaceutical dosing forms. Two phase I open-label single-dose studies in healthy individuals were carried out to characterize the plasma pharmacokinetics of cabozantinib capsule and tablet formulations: a two-way crossover bioequivalence study (n=77) comparing the tablet formulation and the marketed capsule formulation at the approved 140 mg dose and a dose-proportionality study (n=21 per treatment arm) evaluating the 20, 40, and 60 mg tablet strengths. In the bioequivalence study, plasma exposure [area under the plasma concentration-time curve (AUC0-t and AUC0-inf)] values were similar (<10% difference) for both formulations and the 90% confidence intervals (CIs) around the ratio of geometric least-squares means (GLSM) were within the accepted bioequivalence limits of 80-125%. However, the GLSM for Cmax was 19% higher for the tablet formulation and the upper 90% CI for the ratio of GLSM (131.65%) was beyond the 80-125% range. Thus, the tablet and capsule formulations failed to fulfill the bioequivalence study acceptance criteria. In the dose-proportionality study, single doses of the 20, 40, and 60 mg cabozantinib tablet strengths showed dose-proportional increases where the 95% CIs for the slopes of the ln-transformed Cmax, AUC0-t, and AUC0-inf values vs. ln-transformed cabozantinib dose included the value of 1. These findings indicate that cabozantinib plasma exposures increased proportionally with increasing cabozantinib dose over the 20-60 mg tablet strength dose range.

ACCESSION NUMBER: 2016:1021197 CAPLUS Full-text

DOCUMENT NUMBER: 165:119507

TITLE: High frequency auxiliary agent, medical system, and method for the selective treatment of cancer tissue

INVENTOR(S): Noack, Andreas

PATENT ASSIGNEE(S): Olympus Winter & Ibe GmbH, Germany

SOURCE: Ger. Offen., 11pp.; Chemical Indexing Equivalent to 165:145231 (WO)
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102014226903	A1	20160623	DE 2014-102014226903	20141223
WO 2016102179	A1	20160630	WO 2015-EP78768	20151207

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: DE 2014-102014226903 A 20141223

AB The invention relates to an high frequency (HF) auxiliary agent as well as to a medical system and a method for selectively treating cancer tissue. A mol. of the HF auxiliary agent comprises a first group that specifically interacts with a surface feature of a cancer cell as well as a polar second group that is coupled to said first group.

IT 849217-68-1, CABOZANTINIB
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high frequency auxiliary agent, medical system, and method for selective treatment of cancer tissue)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

IT INDEXING IN PROGRESS

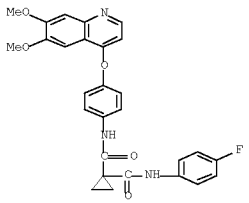
IT 1140909-48-3, COMETRIQ
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetics of cabozantinib tablet and capsule formulations in healthy adults)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

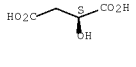
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 99 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

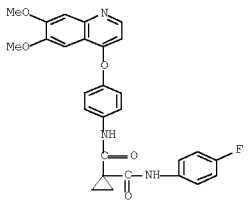
ACCESSION NUMBER: 2016:978010 CAPLUS Full-text

TITLE: Cabozantinib versus everolimus in advanced renal cell carcinoma (METEOR): final results from a randomised, open-label, phase 3 trial

AUTHOR(S): Choueiri, Toni K.; Escudier, Bernard; Powles, Thomas; Tannir, Nizar M.; Mainwaring, Paul N.; Rini, Brian I.; Hammers, Hans J.; Donskov, Frede; Roth, Bruce J.; Peltola, Katriina; Lee, Jae Lyun; Heng, Daniel Y. C.; Schmidinger, Manuela; Agarwal, Neeraj; Sternberg, Cora N.; McDermott, David F.; Aftab, Dana T.; Hessel, Colin; Scheffold, Christian; Schwab, Gisela; Hutson, Thomas E.; Pal, Sumanta; Motzer, Robert J.
CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE: Lancet Oncology (2016), 17(7), 917-927
CODEN: LOANBN; ISSN: 1470-2045
DIGITAL OBJECT ID: 10.1016/S1470-2045(16)30107-3
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Cabozantinib is an oral inhibitor of tyrosine kinases including MET, VEGFR, and AXL. The randomised phase 3 METEOR trial compared the efficacy and safety of cabozantinib vs. the mTOR inhibitor everolimus in patients with advanced renal cell carcinoma who progressed after previous VEGFR tyrosine-kinase inhibitor treatment. Here, we report the final overall survival results from this study based on an unplanned second interim anal. In this open-label, randomised phase 3 trial, we randomly assigned (1:1) patients aged 18 years and older with advanced or metastatic clear-cell renal cell carcinoma, measurable disease, and previous treatment with one or more VEGFR tyrosine-kinase inhibitors to receive 60 mg cabozantinib once a day or 10 mg everolimus once a day. Randomisation was done with an interactive voice and web response system. Stratification factors were Memorial Sloan Kettering Cancer Center risk group and the number of previous treatments with VEGFR tyrosine-kinase inhibitors. The primary endpoint was progression-free survival as assessed by an independent radiol. review committee in the first 375 randomly assigned patients and has been previously reported. Secondary endpoints were overall survival and objective response in all randomly assigned patients assessed by intention-to-treat. Safety was assessed per protocol in all patients who received at least one dose of study drug. The study is closed for enrolment but treatment and follow-up of patients is ongoing for long-term safety evaluation. This trial is registered with ClinicalTrials.gov, number NCT01865747. Between Aug 8, 2013, and Nov 24, 2014, 658 patients were randomly assigned to receive cabozantinib (n=330) or everolimus (n=328). The median duration of follow-up for overall survival and safety was 18·7 mo (IQR 16·1-21·1) in the cabozantinib group and 18·8 mo (16·0-21·2) in the everolimus group. Median overall survival was 21·4 mo (95% CI 18·7-not estimable) with cabozantinib and 16·5 mo (14·7-18·8) with everolimus (hazard ratio [HR] 0·66 [95% CI 0·53-0·83]; p=0·00026). Cabozantinib treatment also resulted in improved progression-free survival (HR 0·51 [95% CI 0·41-0·62]; p<0·0001) and objective response (17% [13-22] with cabozantinib vs 3% [2-6] with everolimus; p<0·0001) per independent radiol. review among all randomised patients. The most common grade 3 or 4 adverse events were hypertension (49 [15%] in the cabozantinib group vs 12 [4%] in the everolimus group), diarrhoea (43 [13%] vs 7 [2%]), fatigue (36 [11%] vs 24 [7%]), palmar-plantar erythrodysaesthesia syndrome (27 [8%] vs 3 [1%]), anemia (19 [6%] vs 53 [17%]), hyperglycemia (3 [1%] vs 16 [5%]), and hypomagnesemia (16 [5%] vs none). Serious adverse events grade 3 or worse occurred in 130 (39%) patients in the cabozantinib group and in 129 (40%) in the everolimus group. One treatment-related death occurred in the cabozantinib group (death; not otherwise specified) and two occurred in the everolimus group (one aspergillus infection and one pneumonia aspiration). Treatment with cabozantinib increased overall survival, delayed disease progression, and improved the objective response compared with everolimus. Based on these results, cabozantinib should be considered as a new standard-of-care treatment option for previously treated patients with advanced renal cell carcinoma. Patients should be monitored for adverse events that might require dose modifications.Exelixis Inc.

IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cabozantinib vs. everolimus in advanced renal cell carcinoma (METEOR))
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

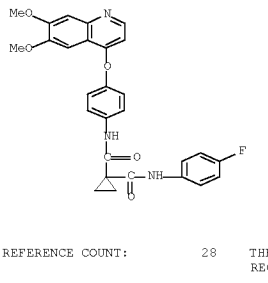


OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 100 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:959887 CAPLUS Full-text
DOCUMENT NUMBER: 166:154348
TITLE: Impact of IDH1 mutation status on outcome in clinical trials for recurrent glioblastoma
AUTHOR(S): Mandel, Jacob J.; Cachia, David; Liu, Diane; Wilson, Charmaine; Aldape, Ken; Fuller, Greg; de Groot, John F.
CORPORATE SOURCE: Department of Neurology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Journal of Neuro-Oncology (2016), 129(1), 147-154
CODEN: JNODD2; ISSN: 0167-594X
DIGITAL OBJECT ID: 10.1007/s11060-016-2157-2
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB IDH1 mutated glioblastoma (GB) has a better prognosis than IDH1 wildtype GB. However, it remains unknown whether patients (pts) with IDH1 mutated GB have a higher 6-mo progression free survival (PFS6) or radiog. response (RR) rate on clin. trials for recurrence. Retrospective review of GB pts at MDACC between 2006 and 2012 identified 330 patients in recurrent GB trials. 93 patients (28 %) had either PFS6 or a complete/partial RR per RANO criteria. 49/93 (53 %) patients with PFS6 or a complete/partial RR had tumor tissue for IDH1 testing. A matched cohort of 49 patients on recurrent GB clin. trials that failed to achieve PFS6 or RR (also with tissue for IDH1 testing) was identified for comparison. IDH1 status was obtained in 92/98 (94 %) patients of which 17 (18 %) had an IDH1 mutation. PFS6 was seen in 26/49 (53 %) patients. IDH status was unknown in two of these patients. 5/24 (21 %) were IDH1 mutated compared to 5/24 (21 %) of their matched cohort without PFS6. RR was found in 47/49 (94 %) patients. IDH status was unknown in four of these patients. IDH1 mutation was present in 7/43 (16 %) patients with RR compared to 10/43 (23 %) in the matched cohort without RR (p = 0.48). Median OS for trials at first recurrence was 9.8 mo for IDH1 wildtype GB vs. 19.32 mo for IDH1 mutated GB (p = 0.14). IDH1 mutation status was not predictive of PFS6 or RR in recurrent GB trials for this data set. However, further examination in larger randomized prospective studies is needed.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(impact of IDH1 mutation status on outcome in clin. trials for recurrent glioblastoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

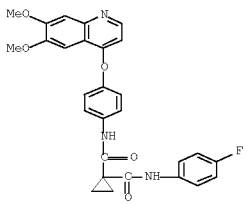
L4 ANSWER 101 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:937400 CAPLUS Full-text
DOCUMENT NUMBER: 165:77360
TITLE: Glycogen Synthase Kinase 3β Promotes the Endocytosis of Transferrin in the African Trypanosome
AUTHOR(S): Guyett, Paul J.; Xia, Shuangluo; Swinney, David C.; Pollastri, Michael P.; Mensa-Wilmot, Kojo
CORPORATE SOURCE: Department of Cellular Biology, The Center for Tropical and Emerging Global Diseases, University of Georgia, Athens, GA, 30605, USA
SOURCE: ACS Infectious Diseases (2016), 2(7), 518-528
CODEN: AIDCBC; ISSN: 2373-8227
DIGITAL OBJECT ID: 10.1021/acsinfecdis.6b00077
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Human parasite Trypanosoma brucei proliferates in the blood of its host, where it takes up iron via receptor-mediated endocytosis of transferrin (Tf). Mechanisms of Tf endocytosis in the trypanosome are not fully understood. Small mol. lapatinib inhibits Tf endocytosis in T. brucei and assocs. with protein kinase GSK3β (TbGSK3β). Therefore, we hypothesized that Tf endocytosis may be regulated by TbGSK3β, and we used three approaches (both genetic and small mol.) to test this possibility. First, the RNAi knock-down of TbGSK3β reduced Tf endocytosis selectively, without affecting the uptake of haptaglobin-Hb (Hp-Hb) or bovine serum albumin (BSA). Second, the overexpression of TbGSK3β increased the Tf uptake. Third, small-mol. inhibitors of TbGSK3β, TWS119 (IC50 = 600 nM), and GW8510 (IC50 = 8 nM) reduced Tf endocytosis. Furthermore, TWS119, but not GW8510, selectively blocked Tf uptake. Thus, TWS119 phenocopies the selective endocytosis effects of a TbGSK3β knockdown. Two new inhibitors of TbGSK3β, LY2784544 (IC50 = 0.6 μM) and sorafenib (IC50 = 1.7 μM), were discovered in a focused screen: at low micromolar concns., they prevented Tf endocytosis as well as trypanosome proliferation (GI50's were 1.0 and 3.1 μM, resp.). These studies show that (a) TbGSK3β regulates Tf endocytosis, (b) TWS119 is a small-mol. tool for investigating the endocytosis of Tf, (c) endocytosis of GPI-anchored TfR and HpHbR are differentially regulated, and (d) the imidazopyridazine aminopyrazole scaffold of LY2784544 is attractive for a hit-to-lead optimization program in antitrypanosome drug discovery.

IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycogen synthase kinase 3β promotes endocytosis of transferrin in african trypanosome and drug screening of transferrin endocytosis inhibitors)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

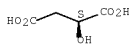
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

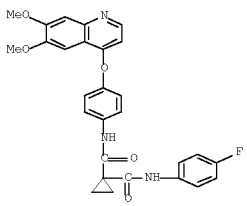


REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 102 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:932798 CAPLUS Full-text
DOCUMENT NUMBER: 165:37653
TITLE: CD44v6-derived cyclic peptides for treating cancers and angiogenesis related diseases
INVENTOR(S): Matzke-Ogi, Alexandra; Orian-Rousseau, Veronique; Haberkorn, Uwe; Lindner, Thomas; Mier, Walter
PATENT ASSIGNEE(S): amcure GmbH, Germany; Ruprecht-Karls-Universitaet; Karlsruher Institut fuer Technologie
SOURCE: PCT Int. Appl., 107pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

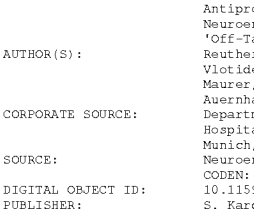
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016087680	A1	20160609	WO 2015-EP78892	20151207

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: GB 2014-21647 A 20141205
OTHER SOURCE(S): MARPAT 165:37653
AB The present invention relates to compds., pharmaceutical compns. and methods for treating different forms of cancer and angiogenesis related diseases using cyclic peptides.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD44v6-derived cyclic peptides for treating cancers and angiogenesis related diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



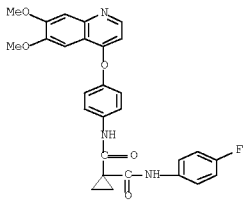
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 104 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:891116 CAPLUS Full-text
TITLE: Cabozantinib and Tivantinib, but Not INC280, Induce Antiproliferative and Antimigratory Effects in Human Neuroendocrine Tumor Cells in vitro: Evidence for 'Off-Target' Effects Not Mediated by c-Met Inhibition
AUTHOR(S): Reuther, Clemens; Heinzle, Vera; Spampatti, Matilde; Vlotides, George; de Toni, Enrico; Spoettl, Gerald; Maurer, Julian; Noelting, Svenja; Goeke, Burkhard; Auernhammer, Christoph J.
CORPORATE SOURCE: Department of Internal Medicine II, University Hospital, Ludwig Maximilian University of Munich, Munich, Germany
SOURCE: Neuroendocrinology (2016), 103(3-4), 383-401
CODEN: NUNDAJ; ISSN: 0028-3835
DIGITAL OBJECT ID: 10.1159/000439431
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background/Aims: The hepatocyte growth factor/transmembrane tyrosine kinase receptor c-Met has been defined as a potential target in antitumoral treatment of various carcinomas. We aimed to investigate the direct effect of c-Met inhibition on neuroendocrine tumor cells in vitro. Methods: The effects of the multi-tyrosine kinase inhibitors cabozantinib and tivantinib and of the highly specific c-Met inhibitor INC280 were investigated in human pancreatic neuroendocrine BON1, bronchopulmonary NCI-H727 and midgut GOT1 cells in vitro. Results: INC280, cabozantinib and tivantinib inhibited c-Met phosphorylation, resp. However, while equimolar concns. (10 μM) of cabozantinib and tivantinib inhibited cell viability and cell migration, INC280 had no inhibitory effect. Knockdown expts. with c-Met siRNA also did not demonstrate effects on cell viability. Cabozantinib and tivantinib caused a G2 arrest in neuroendocrine tumor cells. Conclusions: Our in vitro data suggest that c-Met inhibition alone is not sufficient to exert direct antitumoral or antimigratory effects in neuroendocrine tumor cells. The multi-tyrosine kinase inhibitors cabozantinib and tivantinib show promising antitumoral and antimigratory effects in neuroendocrine tumor cells, which are most probably 'off-target' effects, not mediated by c-Met.
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antiproliferative and antimigratory effects of cabozantinib and tivantinib in human neuroendocrine tumor cells)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



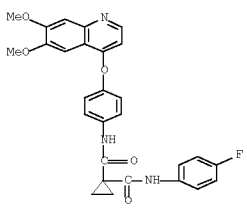
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 105 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:885616 CAPLUS Full-text
DOCUMENT NUMBER: 165:62415
TITLE: Preparation method of -tinib drug albumin nano-formulation for injection



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 103 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:903743 CAPLUS Full-text
TITLE: Lessons Learned: Dose Selection of Small Molecule-Targeted Oncology Drugs
AUTHOR(S): Bullock, Julie M.; Rahman, Atiqur; Liu, Qi
CORPORATE SOURCE: d3 Medicine LLC, Parsippany, NJ, USA
SOURCE: Clinical Cancer Research (2016), 22(11), 2630-2638
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-2646
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Evaluation of dose plays a crit. role in a successful oncol. development program. Typically for oncol. agents, the first-in-man phase I dose-escalation trials are conducted to determine a maximum tolerated dose (MTD). This MTD is taken forward into subsequent trials to establish the safety and efficacy of the drug product. Although this approach was appropriate historically for cytotoxics, the application of MTD as the recommend phase II dose has been problematic for the newer small mol.-targeted oncol. agents. Promising alternative approaches using dose and exposure exploration, including lessons learned from recent targeted oncol. agent development and approvals, are summarized and discussed. Clin Cancer Res; 22(11); 2630-8. ©2016 AACR. See all articles in this CCR Focus section, "New Approaches for Optimizing Dosing of Anticancer Agents".
IT INDEXING IN PROGRESS
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(study on dose selection of small mol.-targeted oncol. drugs)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



INVENTOR(S): Zhang, Qizhi; Wan, Xu; Pang, Xiaoying; Gao, Huiyue; Jiang, Xinguo
PATENT ASSIGNEE(S): Fudan University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 18pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

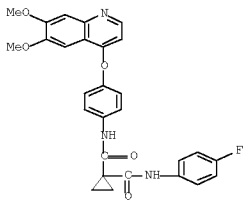
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105616361	A	20160601	CN 2014-10605531	20141030

PRIORITY APPLN. INFO.: CN 2014-10605531 20141030

AB The invention belongs to the field of pharmaceutical prepns., relating to a preparation method of -tinib drug albumin nano-formulation for injection. This method comprises: placing a mixture of oil phase dissolved with -tinib drugs and aqueous phase of human serum albumin in a high-pressure homogenizer, processing under high shear conditions to obtain nano-formulation, removing organic solvent by film evaporation, and freeze-drying to obtain the finished product. The method adds solubilizer, oil stabilizer and pH regulating agent to ensure the stability of the nanoparticles and smaller particle size and distribution. The method of the present invention has good reproducibility, which can significantly improve tinib drugs content in nanoparticles. The technol. used has corresponding laboratory scale to ancillary equipment for large-scale production, showing good prospects for industrial production

IT 849217-68-1, Cabozantinib
RL: NANO (Nanomaterial); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation method of -tinib drug albumin nano-formulation for injection)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 106 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:851904 CAPLUS Full-text
DOCUMENT NUMBER: 165:792
TITLE: Combination cancer therapy with c-Met inhibitors and synthetic oligonucleotides
INVENTOR(S): Bader, Andreas; Zhao, Jane; Guerrero, Adriana
PATENT ASSIGNEE(S): Mirna Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 85pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

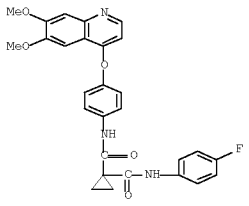
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016081773	A2	20160526	WO 2015-US61687	20151119
WO 2016081773	A3	20160714		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20160151406	A1	20160602	US 2015-14946456	20151119

PRIORITY APPLN. INFO.: US 2014-62081882 P 20141119
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods of inhibiting, and preventing the proliferation of, cancer cells, as well as treating cancer in an individual (e.g., a liver cancer, for example hepatocellular carcinoma) can include providing both a synthetic miR-34 family mol. and a c-Met inhibitor (e.g., tivantinib) to an individual in need thereof. The combination of the synthetic miRNA mol. and c-Met inhibitor can provide a desirable or superior effect, for example a more efficacious treatment than an alternative therapy, or the synthetic miRNA mol. or c-Met inhibitor alone. In some embodiments, the combinations provide a synergistic or greater than additive effect, or reduce toxicity and/or other side effects.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy with c-Met inhibitors and synthetic oligonucleotides)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 107 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:848837 CAPLUS Full-text
DOCUMENT NUMBER: 165:13215
TITLE: Combination therapy of c-met-associated cancers using c-met inhibitors and IGF-1 receptor inhibitors
INVENTOR(S): Shim, Seon Hui; Lee, Ji Min; Jung, Soo Yeon; Kwon, Woo Sun; Kim, Kyung Ah; Kim, Jeong Min; Rha, Sun Young; Lee, Won Suk
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea; Yonsei University, University-Industry Foundation (UIF)
SOURCE: U.S. Pat. Appl. Publ., 88pp. CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

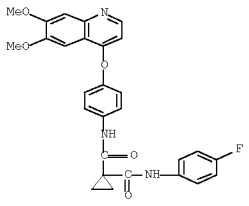
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160144027	A1	20160526	US 2015-14949041	20151123
KR 2016061200	A	20160531	KR 2014-163792	20141121

PRIORITY APPLN. INFO.: KR 2014-163792 A 20141121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A method of preventing or treating a c-met-dependent cancer by coadministration of dual inhibitor of c-Met and an IGF-1 receptor (IGF-1R) inhibitor to avoid the problem of c-met inhibitor resistance is described. IGF-1R as a marker for resistance to a c-Met inhibitor. Very high IGF-1R levels are associated with c-met inhibitor resistance, and so they can be used in detecting the development of the resistance.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in cancer therapy with anti-c-met antibodies; combination therapy of c-met-associated cancers using c-met inhibitors and IGF-1 receptor inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 108 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:847879 CAPLUS Full-text
DOCUMENT NUMBER: 165:20051
TITLE: Lipophilic bisphosphonates and methods of use
INVENTOR(S): Verma, Inder M.; Zhang, Yonghui; Oldfield, Eric; Xia, Yifeng
PATENT ASSIGNEE(S): Salk Institute for Biological Studies, USA; University of Illinois
SOURCE: PCT Int. Appl., 146pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016081281	A1	20160526	WO 2015-US60451	20151112
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2014-62080801 P 20141117
OTHER SOURCE(S): CASREACT 165:20051; MARPAT 165:20051

AB Disclosed herein are lipophilic bisphosphonate compds., ArCH2CX[P(O)[O(M)q]2]2 (M = Li+, Na+, K+, Ca2+, Mg2+, organoammonium, etc.; Ar = imidazole, pyrazole, pyrrole, furan, thiophene, oxazole, isoxazole, thiazole, isothiazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole; X = H, OH, halo, etc.), and embodiments of a method for

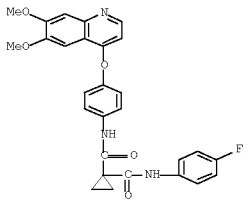
making the same. The compds. may inhibit FPPS and/or GGPPS enzymes. The compds. are useful for treating a disease, such as cancer, such as those with a KRAS mutation. In some embodiments, the compds. are used to prevent or treat a cancer, such as a lung cancer that has a KRAS mutation.

IT 1140909-48-3, Cabozantinib-S-Malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of lipophilic bisphosphonates for treatment and prevention of cancer, such as lung cancer that has KRAS mutation)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

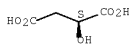
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



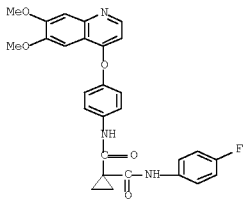
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 109 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:846635 CAPLUS Full-text
DOCUMENT NUMBER: 165:6482
TITLE: Preparation of imidazole derivatives for use as TGF-β inhibitors
INVENTOR(S): Singh, Rajinder; Kinsella, Todd; Yu, Jiaxin; Gelman, Marina; Darwish, Ihab S.
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 259pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016081364	A1	20160526	WO 2015-US60872	20151116

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62082959 P 20141121
US 2015-62141509 P 20150401
OTHER SOURCE(S): CASREACT 165:6482; MARPAT 165:6482
GI



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [each R1 independently = H, halo, alkyl, alkoxy, etc.; A = (un)substituted Ph or pyridyl; X = CH2, NH, O, etc.; Z = (un)substituted fused heterobicyclic ring; m = 1 or 2; p = 0 to 6: with provisions], and their pharmaceutically acceptable salts, are prepared and disclosed as TGF-β inhibitors. Thus, e.g., II was prepared by a multistep procedure (preparation given). I were evaluated in GDF8 and TGF-β activity assays, e.g., II demonstrated inhibition signaling of <0.05 μM and 0.1-<1.0 μM (date = pSMAD (MPC11)), resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; Preparation of imidazole derivs. for use as TGF-β inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 110 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:807583 CAPLUS Full-text
DOCUMENT NUMBER: 165:16514
TITLE: Inhibition of proline catabolism for the treatment of cancer and other therapeutic applications
INVENTOR(S): Scott, Gary K.; Benz, Christopher C.
PATENT ASSIGNEE(S): Buck Institute for Research On Aging, USA
SOURCE: PCT Int. Appl., 145pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

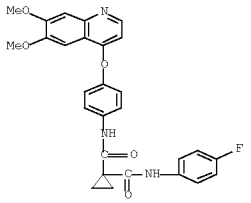
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016077632	A2	20160519	WO 2015-US60458	20151112
WO 2016077632	A3	20160825		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2014-62079382 P 20141113
OTHER SOURCE(S): MARPAT 165:16514
AB In various embodiments a cancer treatment method is provided based on inhibition of proline catabolism. When combined with p53 protein restoration therapy and/or inhibition of glutaminase, the inhibition of proline catabolism results in a "synthetic lethal" and synergistic anticancer response. Novel suicide inhibitors that induce the degradation of proline dehydrogenase (PRODH) are also provided. Also provided is a method of assaying PRODH to identify responders/non-responders to inhibition of proline catabolism and/or glutaminase.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of proline catabolism for treatment of cancer and other therapeutic applications)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 111 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:805607 CAPLUS Full-text
DOCUMENT NUMBER: 164:576584
TITLE: Enhancement of tumor response to chemotherapy by activation of the asmase/ceramide pathway through timed administration of a short-acting anti-angiogenic agent
INVENTOR(S): Kolesnick, Richard; Haimovitz-Friedman, Adriana; Sala, Evis; Fuks, Zvi
PATENT ASSIGNEE(S): Memorial Sloan-Kettering Cancer Center, USA
SOURCE: PCT Int. Appl., 90pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016077652	A2	20160519	WO 2015-US60486	20151112

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA,

PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

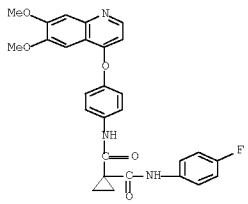
PRIORITY APPLN. INFO.: US 2014-62078280 P 20141111

AB Disclosed is a method for enhancing the tumor response to chemotherapy comprising: (a) administering a short-acting anti-angiogenic agent (AAA) to a subject afflicted with a solid tumor, thereby creating a time interval of increased susceptibility of said tumor to at least one chemotherapeutic agent; (b) administering said at least one chemotherapeutic agent that has the property of activating the ASMase/ceramide signaling pathway to said subject at a time point within said interval; hereby enhancing the effect of the at least one chemotherapeutic agent against said tumor. Enhancement can be assessed by comparison to the chemotherapeutic agent being used (i) without the anti-angiogenic agent or (ii) at a time point outside the interval of increased susceptibility.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of tumor response to chemotherapy by activation of asmase/ceramide pathway through timed administration of short-acting anti-angiogenic agent)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 112 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:794768 CAPLUS Full-text

DOCUMENT NUMBER: 165:147400

TITLE: Cabozantinib versus everolimus in advanced renal-cell carcinoma

AUTHOR(S): Choueiri, T. K.; Escudier, B.; Powles, T.; Mainwaring, P. N.; Rini, B. I.; Donskov, F.; Hammers, H.; Hutson, T. E.; Lee, J.-L.; Peltola, K.; Roth, B. J.; Bjarnason, G. A.; Geczi, L.; Keam, B.; Maroto, P.; Heng, D. Y. C.; Schmidinger, M.; Kantoff, P. W.; Borgman-Hagey, A.; Hessel, C.; Scheffold, C.; Schwab, G. M.; Tannir, N. M.; Motzer, R. J.

CORPORATE SOURCE: METEOR Investigators, Dana-Farber Cancer Institute, Boston, MA, 02215, USA

SOURCE: New England Journal of Medicine (2015), 373(19), 1814-1823
CODEN: NEJMAG; ISSN: 1533-4406

DIGITAL OBJECT ID: 10.1056/NEJMoa1510016

PUBLISHER: Massachusetts Medical Society

DOCUMENT TYPE: Journal; (online computer file)

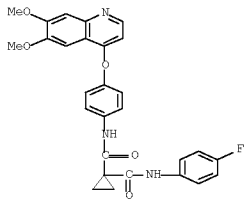
LANGUAGE: English

AB Cabozantinib is an oral, small-mol. tyrosine kinase inhibitor that targets vascular endothelial growth factor receptor (VEGFR) as well as MET and AXL, each of which has been implicated in the pathobiol. of metastatic renal-cell carcinoma or in the development of resistance to antiangiogenic drugs. This randomized, open-label, phase 3 trial evaluated the efficacy of cabozantinib, as compared with everolimus, in patients with renal-cell carcinoma that had progressed after VEGFR-targeted therapy. We randomly assigned 658 patients to receive cabozantinib at a dose of 60 mg daily or everolimus at a dose of 10 mg daily. The primary end point was progression-free survival. Secondary efficacy end points were overall survival and objective response rate. Median progression-free survival was 7.4 mo with cabozantinib and 3.8 mo with everolimus. The rate of progression or death was 42% lower with cabozantinib than with everolimus (hazard ratio, 0.58; 95% confidence interval [CI] 0.45 to 0.75; P<0.001). The objective response rate was 21% with cabozantinib and 5% with everolimus (P<0.001). A planned interim anal. showed that overall survival was longer with cabozantinib than with everolimus (hazard ratio for death, 0.67; 95% CI, 0.51 to 0.89; P = 0.005) but did not cross the significance boundary for the interim anal. Adverse events were managed with dose redns.; doses were reduced in 60% of the patients who received cabozantinib and in 25% of those who received everolimus. Discontinuation of study treatment owing to adverse events occurred in 9% of the patients who received cabozantinib and in 10% of those who received everolimus. Progression-free survival was longer with cabozantinib than with everolimus among patients with renal-cell carcinoma that had progressed after VEGFR-targeted therapy.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progression-free survival was longer with cabozantinib than with everolimus among patients with renal-cell carcinoma that had progressed after VEGFR-targeted therapy)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 55 THERE ARE 55 CAPLUS RECORDS THAT CITE THIS RECORD (55 CITINGS)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 113 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:775132 CAPLUS Full-text

TITLE: A Novel Crizotinib-Resistant Solvent-Front Mutation Responsive to Cabozantinib Therapy in a Patient with ROS1-Rearranged Lung Cancer

AUTHOR(S): Drilon, Alexander; Somwar, Romel; Wagner, Jacob P.; Vellore, Nadeem A.; Eide, Christopher A.; Zabriskie, Matthew S.; Arcila, Maria E.; Hechtman, Jaclyn F.; Wang, Lu; Smith, Roger S.; Kris, Mark G.; Riely, Gregory J.; Druker, Brian J.; O'Hare, Thomas; Ladanyi, Marc; Davare, Monika A.

CORPORATE SOURCE: Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

SOURCE: Clinical Cancer Research (2016), 22(10), 2351-2358
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-2013

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

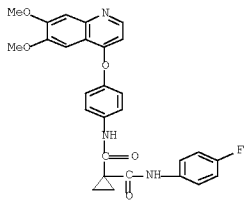
AB Purpose: Rearranged ROS1 is a crizotinib-sensitive oncogenic driver in lung cancer. The development of acquired resistance, however, poses a serious clin. challenge. Consequently, exptl. and clin. validation of resistance mechanisms and potential second-line therapies is essential. Exptl. Design: We report the discovery of a novel, solvent-front ROS1D2033N mutation in a patient with CD74-ROS1-rearranged lung adenocarcinoma and acquired resistance to crizotinib. Crizotinib resistance of CD74-ROS1D2033N was functionally evaluated using cell-based assays and structural modeling. Results: In biochem. and cell-based assays, the CD74-ROS1D2033N mutant demonstrated significantly decreased sensitivity to crizotinib. Mol. dynamics simulation revealed compromised crizotinib binding due to drastic changes in the electrostatic interaction between the D2033 residue and crizotinib and reorientation of neighboring residues. In contrast, cabozantinib binding was unaffected by the D2033N substitution, and inhibitory potency against the mutant was retained. Notably, cabozantinib treatment resulted in a rapid clin. and near-complete radiog. response in this patient. Conclusions: These results provide the first example of successful therapeutic intervention with targeted therapy to overcome crizotinib resistance in a ROS1-rearranged cancer. Clin Cancer Res; 22(10); 2351-8. ©2015 AACR.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel crizotinib-resistant solvent-front mutation responsive to cabozantinib therapy in patient with ROS1-rearranged lung cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 114 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:765273 CAPLUS Full-text

DOCUMENT NUMBER: 165:256316

TITLE: ISMP adverse drug reactions

AUTHOR(S): Mancano, Michael A.

CORPORATE SOURCE: Department of Pharmacy Practice, Temple University School of Pharmacy, Philadelphia, PA, USA

SOURCE: Hospital Pharmacy (2015), 50(8), 662-666
CODEN: HOPHAZ; ISSN: 0018-5787

DIGITAL OBJECT ID: 10.1310/hpj5008-662

PUBLISHER: Thomas Land Publishers, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

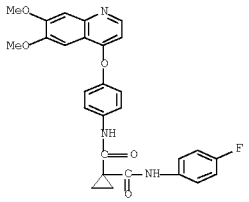
AB The purpose of this feature is to heighten awareness of specific adverse drug reactions (ADRs), discuss methods of prevention, and promote reporting of ADRs to the US Food and Drug Administration's (FDA's) MedWatch program (800-FDA-1088). If you have reported an interesting, preventable ADR to MedWatch, please consider sharing the account with our readers. Write to Dr. Mancano at ISMP, 200 Lakeside Drive, Suite 200, Horsham, PA 19044 (phone: 215-707-4936; e-mail: mmancano@temple.edu). Your report will be published anonymously unless otherwise requested. This feature is provided by the Institute for Safe Medication Practices (ISMP) in cooperation with the FDA's

MedWatch program and Temple University School of Pharmacy. ISMP is an FDA MedWatch partner.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ISMP adverse drug reactions)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 115 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:732674 CAPLUS Full-text

DOCUMENT NUMBER: 164:591127

TITLE: Combination pharmaceutical composition containing Bcr-Abl tyrosine kinase inhibitor composition and Met tyrosine kinase inhibitor composition or Met/MEK/ERK signal-related kinase inhibitor against CML

INVENTOR(S): Nishida, Shozo; Tsubaki, Masahiro; Takeda, Tomoya; Nishio, Kazuto; Nakayama, Takashi; Sakai, Kazuko; Komai, Makiko; Ono, Yuri; Fukamatsu, Mai

PATENT ASSIGNEE(S): Kinki University, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 30pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2016069348	A	20160509	JP 2014-202529	20140930

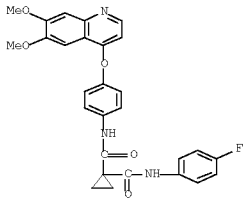
PRIORITY APPLN. INFO.: JP 2014-202529 20140930

AB A therapeutic compn. for CML (chronic myeloid leukemia) resistant to Bcr-Abl tyrosine kinase inhibitors comprises a 1st composition that inhibits Bcr-Abl tyrosine kinase and a 2nd composition that inhibits Met tyrosine kinase or a 3rd composition that inhibits any one of kinases in Met/MEK/ERK signaling pathway. Thus, treatment of imatinib-resistant strain of K562 leukemia cell with imatinib and PHA-665752 (Met inhibitor) decreased cell survival rate in a dose-dependent manner.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination chemotherapy against chronic myeloid leukemia with Bcr-Abl tyrosine kinase inhibitor and Met tyrosine kinase inhibitor or Met/MEK/ERK signaling pathway-related kinase inhibitor)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 116 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:718319 CAPLUS Full-text

TITLE: Discovery of a new series of imidazo[1,2-a]pyridine compounds as selective c-Met inhibitors

AUTHOR(S): Liu, Tong-chao; Peng, Xia; Ma, Yu-chi; Ji, Yin-chun; Chen, Dan-qi; Zheng, Ming-yue; Zhao, Dong-mei; Cheng, Mao-sheng; Geng, Mei-yu; Shen, Jing-kang; Ai, Jing; Xiong, Bing

CORPORATE SOURCE: Key Laboratory of Structure-Based Drug Design & Discovery of Ministry of Education, Shenyang Pharmaceutical University, Shenyang, Peop. Rep. China

SOURCE: Acta Pharmacologica Sinica (2016), 37(5), 698-707
CODEN: APSCG5; ISSN: 1671-4083

DIGITAL OBJECT ID: 10.1038/aps.2016.11

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

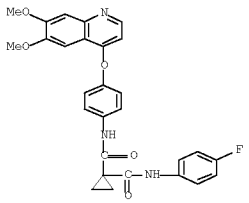
AB Aim: Aberrant c-Met activation plays a crit. role in cancer formation, progression and dissemination, as well as in development of resistance to anticancer drugs. Therefore, c-Met has emerged as an attractive target for cancer therapy. The aim of this study was to develop new c-Met inhibitors and elaborate the structure-activity relationships of identified inhibitors. Methods: Based on the predicted binding modes of Compds. 5 and 14 in docking studies, a new series of c-Met inhibitor-harboring 3-((1H-pyrrolo[3,2-c]pyridin-1-yl)sulfonyl)imidazo[1,2- a]pyridine scaffolds was discovered. Potent inhibitors were identified through extensive optimizations combined with enzymic and cellular assays. A promising compound was further investigated in regard to its selectivity, its effects on c-Met signaling, cell proliferation and cell scattering in vitro. Results: The most potent Compound 31 inhibited c-Met kinase activity with an IC50 value of 12.8 nmol/L, which was >78-fold higher than those of a panel of 16 different tyrosine kinases. Compound 31 (8, 40, 200 nmol/L) dose-dependently inhibited the phosphorylation of c-Met and its key downstream Akt and ERK signaling cascades in c-Met aberrant human EBC-1 cancer cells. In 12 human cancer cell lines harboring different background levels of c-Met expression/activation, Compound 31 potently inhibited c-Met-driven cell proliferation. Furthermore, Compound 31 dose-dependently impaired c-Met-mediated cell scattering of MDCK cells. Conclusion: This series of c-Met inhibitors is a promising lead for development of novel anticancer drugs.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(discovery of new series of imidazo[1,2-a]pyridine compds. as selective c-Met inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 117 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:689059 CAPLUS Full-text

DOCUMENT NUMBER: 165:16208

TITLE: Selective targeting of CTNNB1-, KRAS- or MYC-driven cell growth by combinations of existing drugs [Erratum to document cited in CA164:550339]

AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; Spijkers-Hagelstein, Jill A. P.; de Vetter, Judith R. F.; de Man, Jos; Buijsman, Rogier C.; Zaman, Guido J. R.

CORPORATE SOURCE: Netherlands Translational Research Center B.V., Oss, Neth.

SOURCE: PLoS One (2015), 10(6), e0132230/1
CODEN: POLNCL; ISSN: 1932-6203

DIGITAL OBJECT ID: 10.1371/journal.pone.0132230

PUBLISHER: Public Library of Science

DOCUMENT TYPE: Journal; (online computer file)

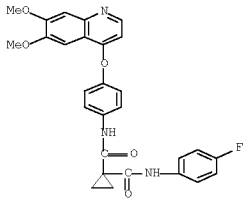
LANGUAGE: English

AB This article was republished to correct an error in the title.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective targeting of CTNNB1-, KRAS-or MYC-driven human cancer cell growth by combinations of existing drugs (Erratum))

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 118 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:676774 CAPLUS Full-text

DOCUMENT NUMBER: 166:93

TITLE: Management of advanced medullary thyroid cancer

AUTHOR(S): Hadoux, Julien; Pacini, Furio; Tuttle, R. Michael; Schlumberger, Martin

CORPORATE SOURCE: Department of Nuclear Medicine and Endocrine Oncology, Gustave Roussy and University Paris Sud, Villejuif, Fr.

SOURCE: Lancet Diabetes & Endocrinology (2016), 4(1), 64-71
CODEN: LDEAAS; ISSN: 2213-8587

DIGITAL OBJECT ID: 10.1016/S2213-8587(15)00337-X

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

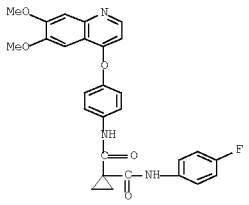
AB Medullary thyroid cancer arises from calcitonin-producing C-cells and accounts for 3-5% of all thyroid cancers. The discovery of a locally advanced medullary thyroid cancer that is not amenable to surgery or of distant metastases needs careful work-up, including measurement of serum calcitonin and carcinoembryonic antigen (and their doubling times), in addition to comprehensive imaging to determine the extent of the disease, its aggressiveness, and the need for any treatment. In the past, cytotoxic

chemotherapy was used for treatment but produced little benefit. For the past 10 years, tyrosine kinase inhibitors targeting vascular endothelial growth factor receptors and RET (rearranged during transfection) have been used when a systemic therapy is indicated for large tumor burden and documented disease progression. Vandetanib and cabozantinib have shown benefits on progression-free survival compared with placebo in this setting, but their toxic effect profiles need thorough clin. management in specialised centers. This review describes the management and treatment of patients with advanced medullary thyroid cancer with emphasis on current targeted therapies and perspectives to improve patient care. Most treatment responses are transient, emphasizing that mechanisms of resistance need to be better understood and that the efficacy of treatment approaches should be improved with combination therapies or other drugs that might be more potent or target other pathways, including immunotherapy.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(management of advanced medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 119 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:672202 CAPLUS Full-text

DOCUMENT NUMBER: 166:45575

TITLE: Simultaneous determination of lapatinib, cabozantinib, imatinib, dasatinib, sorafenib, crizotinib, erlotinib and SAHA in rat plasma by UPLC-MS/MS

AUTHOR(S): Wang, Jiazhi; Zhou, Yunfang; Wang, Cheng; Chen, Jianmiao

CORPORATE SOURCE: The Affiliated Hospital, Hangzhou Normal University, Hangzhou, 310000, Peop. Rep. China

SOURCE: Latin American Journal of Pharmacy (2015), 34(8), 1576-1584
CODEN: LAJPA9; ISSN: 0326-2383

PUBLISHER: Colegio de Farmaceuticos de la Provincia de Buenos Aires

DOCUMENT TYPE: Journal

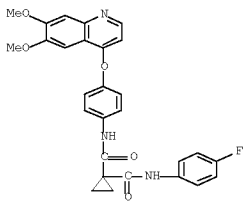
LANGUAGE: English

AB An ultra-performance liq. chromatog. tandem mass spectrometry (UPLC-MS/MS) method has been developed for the specific and simultaneous determination of receptor tyrosine kinases (RTKs) inhibitors (lapatinib, cabozantinib, imatinib, dasatinib, sorafenib, crizotinib, erlotinib) and histone deacetylase (HDAC) inhibitor SAHA in rat plasma with midazolam as internal standard The plasma samples can be extracted with minimal effort by utilizing a simple protein precipitation with acetonitrile. The chromatog. separation was achieved using a C18 column (2.1 × 100 mm, 1.7 μm). The mobile phase consisted of acetonitrile and water (containing 0.1% formic acid) with gradient elution. The triple quadrupole mass spectrometric detection was performed by using multiple reactions monitoring in pos. electrospray ionization. The intra-day and inter-day RSD value were < 14%, and the accuracy ranged from 85.4 to 112.2%. The recoveries were > 64.1% and the matrix effects ranged from 92.4 to 108.2%. The calibration curves in plasma were linear in the range of 2-2000 ng/mL for all analytes with correlation coefficient > 0.993. Effectiveness of this method was validated with pharmacokinetic studies of the dasatinib and sorafenib in rat plasma.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simultaneous determination of lapatinib, cabozantinib, imatinib, dasatinib, sorafenib, crizotinib, erlotinib and SAHA in rat plasma by UPLC-MS/MS)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 120 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:645289 CAPLUS full-text

DOCUMENT NUMBER: 166:475537

TITLE: Sustained inhibition of cMET-VEGFR2 signaling using liposome-mediated delivery increases efficacy and reduces toxicity in kidney cancer

AUTHOR(S): Kulkarni, Ashish A.; Vijaykumar, Vijay Elakkya; Natarajan, Siva Kumar; Sengupta, Shiladitya; Sabbisetti, Venkata S.

CORPORATE SOURCE: Harvard Medical School, Division of Biomedical Engineering, Brigham and Women's Hospital, Boston, MA, USA

SOURCE: Nanomedicine (New York, NY, United States) (2016), 12(7), 1853-1861
CODEN: NANOBF; ISSN: 1549-9634

DIGITAL OBJECT ID: 10.1016/j.nano.2016.04.002

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB C-Met pathway is implicated in the resistance to anti-VEGF therapy in renal cell carcinoma (RCC). However, clin. translation of therapies targeting these pathways has been limited due to dose-limiting toxicities, feedback signaling, and low intratumoral drug accumulation. Here, we developed liposomes encapsulating a multi-receptor tyrosine kinase inhibitor (XL184) to explore the possibility of improving intratumoral concentration, enhancing antitumor efficacy and reducing toxicities. The liposomes showed increased cytotoxicity than XL184, and resulted in a sustained inhibition of phosphorylation of Met, AKT and MAPK pathways in RCC cells. In a RCC tumor xenograft model, the liposomes induced sustained inhibition of tumor growth as compared to XL184, consistent with higher inhibition of kinase signaling pathways. Biodistribution studies revealed higher accumulation of the liposomes in tumor, which translated into lower toxicities. This study shows the use of liposomes for effective inhibition of multi-kinase pathways, which can potentially emerge as a new treatment for RCC.

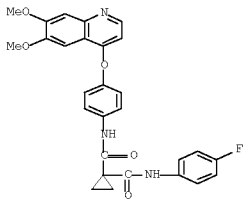
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained inhibition of cMET-VEGFR2 signaling using liposome-mediated delivery of XL184 increases efficacy and reduces toxicity in human renal cell carcinoma xenograft mouse model)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

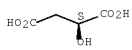
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 121 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:640334 CAPLUS Full-text

DOCUMENT NUMBER: 164:531226

TITLE: Preparation of specific conjugation bridge linkers and immunoconjugates and methods of using them

INVENTOR(S): Zhao, Robert Yongxin; Yang, Qingliang; Huang, Yuanyuan; Gai, Shun; Zhao, Linyao; Ye, Hangbo; Guo, Huihui; Tong, Qianqian; Cao, Minjun; Jia, Junxiang; Yang, Chengyu; Li, Wenjun; Zhou, Xiaomai; Xie, Hongsheng; Lin, Chen; Guo, Zhixiang; Ye, Zhicang

PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China; Hangzhou Dac Biotech Co, Ltd.

SOURCE: PCT Int. Appl., 246pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

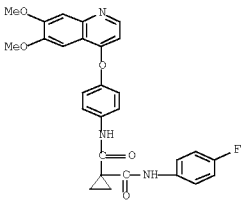
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016059622	A2	20160421	WO 2016-IB50580	20160204

WO 2016059622 A3 20161208
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
PRIORITY APPLN. INFO.: WO 2016-IB50580 20160204
OTHER SOURCE(S): CASREACT 164:531226; MARPAT 164:531226
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to novel linkers contg. a 2,3-disubstituted succinic group, or 2-monosubstituted, or 2,3-disubstituted fumaric or maleic (trans (E)- or cis (Z)-butenedioic) group, e.g., (I), for conjugation of two or more compds./cytotoxic agents per linker to a cell-binding mol., through bridge linking pairs of thiols (reduced from the interchain disulfide bonds of the cell-binding agent by a reducing agent, such as dithiothreitol, dithioerythritol, L-glutathione and tris(2-carboxyethyl)phosphine (TCEP), or/and β-mercaptoethanol) on the cell-binding mol. specifically. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by treating reaction with drugs and to their use for cancers, infections and autoimmune disorders. Thus, linker I was prepared by cyclization of 2,3-dibromosuccinic acid in CH2Cl2 in the presence of P2O5. RlCOCHBrCHBrCOR (II) was prepared in 3 steps from I and R1-H (preparation given) using R = H (preparation given). A herceptin antibody conjugate with II was prepared by reacting herceptin with and TCEP and II. Select conjugates of the invention were evaluated for their in vitro cytotoxicity against a human gastric carcinoma N87 cells. Five-week-old female BALB/c Nude mice inoculated s.c. in the area under the right shoulder with N-87 carcinoma cells treated with select conjugates of the invention had completely no tumor measurable at day 18 till day 68 (the end of experiment) in an in vivo antitumor activity study.
IT 849217-68-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of specific conjugation bridge linkers and immunoconjugates)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

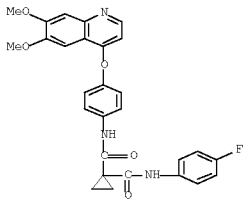


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 123 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:617203 CAPLUS Full-text
DOCUMENT NUMBER: 164:507400
TITLE: Cabozantinib malate compound and pharmaceutical composition thereof
INVENTOR(S): Chen, Qingcai; Zhao, Xiaowei; Zhao, Jun; Li, Zhen
PATENT ASSIGNEE(S): Jiangsu Aosaikang Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

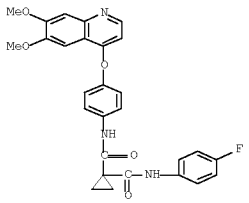
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105503717	A	20160420	CN 2014-10495691	20140924

PRIORITY APPLN. INFO.: CN 2014-10495691 20140924
AB The invention provides cabozantinib malate compd. of new cryst. form and preparation method thereof. Said cabozantinib malate compound of new crystalline form has good stability and no obvious change in highest individual impurity content and total impurity content under the conditions of high temperature (40℃), high humidity, and illumination.
IT 849217-68-1P, Cabozantinib 1140909-48-3P
RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cabozantinib malate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of specific conjugation bridge linkers and immunoconjugates

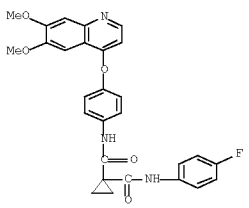
L4 ANSWER 122 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:625629 CAPLUS Full-text
DOCUMENT NUMBER: 165:40582
TITLE: Primary RET-mutated lung neuroendocrine carcinoma in MEN2B: response to RET-targeted therapy
AUTHOR(S): Geiger, Jessica L.; Chiosea, Simion I.; Challinor, Sue M.; Nikiforova, Marina N.; Bauman, Julie E.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Internal Medicine, University of Pittsburgh Cancer Institute, Pittsburgh, PA, 15232, USA
SOURCE: Endocrine-Related Cancer (2015), 22(5), L19-L22
CODEN: ERCAE9; ISSN: 1351-0088
DIGITAL OBJECT ID: 10.1530/ERC-15-0307
PUBLISHER: BioScientifica Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB This article deals with primary RET-mutated lung neuroendocrine carcinoma in Multiple endocrine neoplasia type 2B (MEN2B). Nonsmoking male patient with known MEN2B who presented with advanced, primary pulmonary neuroendocrine carcinoma harboring only his germline RET mutation was reported. Serial computed tomog. (CT) imaging, morphol. and immunohistochem. anal. were performed . Author conclude that the patient failed to respond to conventional chemotherapy, however responded dramatically to cabozantinib, a RET-targeted therapy approved for medullary thyroid carcinoma.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonsmoking male patient with known multiple endocrine neoplasia type 2B and primary pulmonary neuroendocrine carcinoma harboring only his germline RET mutation failed to respond to responded to cabozantinib, RET-targeted therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

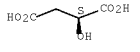
CRN 849217-68-1
CMF C28 H24 F N3 O5



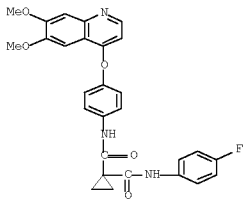
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 124 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:559516 CAPLUS Full-text
DOCUMENT NUMBER: 165:267870
TITLE: Cabozantinib is selectively cytotoxic in acute myeloid leukemia cells with FLT3-internal tandem duplication (FLT3-ITD)
AUTHOR(S): Lu, Jeng-Wei; Wang, An-Ni; Liao, Heng-An; Chen, Chien-Yuan; Hou, Hsin-An; Hu, Chung-Yi; Tien, Hwei-Fan; Ou, Da-Liang; Lin, Liang-In
CORPORATE SOURCE: Department of Clinical Laboratory Sciences and Medical Biotechnology, National Taiwan University, Taipei, Taiwan
SOURCE: Cancer Letters (New York, NY, United States) (2016), 376(2), 218-225
CODEN: CALEDQ; ISSN: 0304-3835
DIGITAL OBJECT ID: 10.1016/j.canlet.2016.04.004
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is an oral multikinase inhibitor that exhibits anti-tumor activity in several cancers. We found that cabozantinib was significantly cytotoxic to MV4-11 and Molm-13 cells that harbored FLT3-ITD, resulting in IC50 values of 2.4 nM and 2.0 nM, resp. However, K562, OCI-AML3 and THP-1 (leukemia cell lines lacking FLT3-ITD) were resistant to cabozantinib, showing IC50 values in the micromolar range. Cabozantinib arrested MV4-11 cell growth at the G0/G1 phase within 24 h, which was associated with decreased phosphorylation of FLT3, STAT5, AKT and ERK. Addnl., cabozantinib induced MV4-11 cell apoptosis in a dose-dependent manner (as indicated by annexin V staining and high levels of cleaved caspase 3 and PARP-1), down-regulated the anti-apoptotic protein survivin and up-regulated the pro-apoptotic protein Bak. Thus, cabozantinib is selectively cytotoxic to leukemia cells with FLT3-ITD, causing cell-cycle arrest and apoptosis. In mouse xenograft model, cabozantinib significantly inhibited MV4-11 and Molm-13 tumor growth at a dosage of 10 mg/kg and showed longer survival rate. Clin. trials evaluating the efficacy of cabozantinib in acute myeloid leukemia (AML) with FLT3-ITD are warranted.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as selectively cytotoxic in acute myeloid leukemia cells with FLT3-internal tandem duplication)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

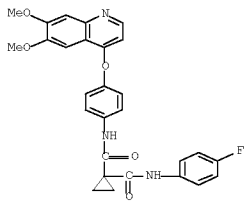


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 125 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:552052 CAPLUS Full-text
DOCUMENT NUMBER: 164:447096
TITLE: Pharmaceutical compositions comprising tyrosine kinase inhibitors for treating enveloped viruses
INVENTOR(S): Einav, Shirit; Neveu, Gregory; Barouch-Bentov, Rina
PATENT ASSIGNEE(S): The Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 38pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016054468	A1	20160407	WO 2015-US53638	20151002
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20170136021	A1	20170518	US 2015-14873339	20151002

PRIORITY APPLN. INFO.: US 2014-62059449 P 20141003
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Described are compns. such as tyrosine kinase inhibitors (e.g. erlotinib, sunitinib) and methods for treating an enveloped virus in a patient in need thereof. Exemplary enveloped viruses are those in the family Filoviridae and include Ebola virus.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. comprising tyrosine kinase inhibitors for treating enveloped viruses)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

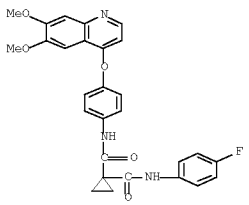


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 126 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:551762 CAPLUS Full-text
DOCUMENT NUMBER: 164:479060
TITLE: Prediction of response to PARP inhibitors and combinational therapy of cancer targeting c-Met and PARP1
INVENTOR(S): Hung, Mien-Chie; Du, Yi
PATENT ASSIGNEE(S): Board of Regent, The University of Texas System, USA
SOURCE: PCT Int. Appl., 103pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016054055	A1	20160407	WO 2015-US52966	20150929
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

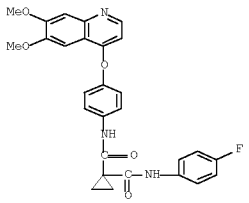
PRIORITY APPLN. INFO.: US 2014-62057037 P 20140929
AB Provided herein are methods for identifying and treating cancers that are resistant to PARP inhibition. Methods for sensitizing cancers to a PARP inhibitor therapy are also provided. In some aspects, PARP inhibitor cancers are treated with a PARP inhibitor therapy in combination with a c-Met inhibitor therapy.
IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prediction of response to PARP inhibitors and combinational therapy of cancer targeting c-met and PARP1 and treatment with other therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

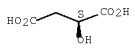
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

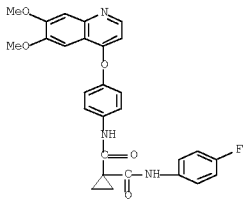


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 127 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:534801 CAPLUS Full-text
DOCUMENT NUMBER: 164:512966
TITLE: Quick-release medicine phosphatide compound and pharmaceutical composition thereof
INVENTOR(S): Li, Xinsong; Du, Yawei; Ling, Longbing; He, Ruiyu
PATENT ASSIGNEE(S): Southeast University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 54pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105457038	A	20160406	CN 2015-10756327	20151109

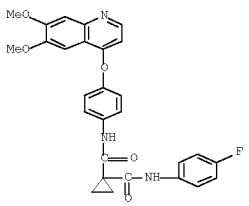
PRIORITY APPLN. INFO.: CN 2015-10756327 20151109
OTHER SOURCE(S): CASREACT 164:512966
AB The invention discloses a quick-release medicine phosphatide compd. and pharmaceutical composition thereof. In this compound I, medicine Y1 and Y2 are connected with quick-release hydrophobic spacer arm and enhancement type hydrophobic spacer arm through chemical bond. Two kinds of the spacer arms collaborate with each other and strengthen hydrophobic action to form hydrophobic lipophilic chain. Two hydrophobic chains are connected with phospholipid hydrophilic head to constitute amphipathic mol. Pharmaceutical composition is quick-release medicine phosphatide compound or combined medicinal combination of this compound and pharmaceutically acceptable carrier. The quick-release medicine phosphatide compound and lipidosome nanoparticle thereof can be used as liquid preparation, solid preparation, semi-solid preparation, sterilized preparation and sterile preparation with low toxicity, and can be used for the efficient treatment of diseases such as various tumors.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quick-release medicine phosphatide compound and pharmaceutical composition
thereof)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 128 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:501826 CAPLUS Full-text
DOCUMENT NUMBER: 164:433336
TITLE: Prediction of effect of a c-met inhibitor using mutation of KRAS or BRAF
INVENTOR(S): Shim, Seon Hui; Jung, Soo Yeon; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 126pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160090635	A1	20160331	US 2015-14869563	20150929
KR 2016037666	A	20160406	KR 2014-130560	20140929

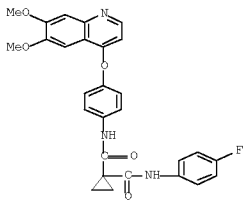
PRIORITY APPLN. INFO.: KR 2014-130560 A 20140929
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method for predicting and/or monitoring the efficacy of a c-Met inhibitor using a biomarker; a method for selecting a subject suitable for the application of a c-Met inhibitor using a biomarker; and a method for preventing and/or treating cancer comprising administering a c-Met inhibitor to the selected subject. In particular embodiments, provided are biomarkers for use in predicting and/or monitoring the therapeutic effect of a c-Met inhibitor or selecting a subject suitable for the application of a c-Met inhibitor, including IL-8, bIG-H3, KRAS or BRAF and nucleic acids encoding the proteins. Another embodiment provides a c-Met inhibitor or a pharmaceutical composition including a c-Met inhibitor, for use in inhibiting c-Met and/or treating a cancer in a subject, wherein the subject has a higher level of IL-8 or bIG-H3 compared to a reference sample in which a c-Met inhibitor is not effective, and/or has a mutation of KRAS and/or BRAF. KRAS protein comprises at least one amino acid mutation selected from the group consisting of G12A, G12D, G12R, G12C, G12S, G12V, A146T, A59T, L23R, G13N, G13D, I24F, Q61L, Q61H, G13C, and Q61K; and BRAF protein comprises at least one amino acid mutation selected from the group consisting of G596R, V600E, V600K, V600R, K601E, D594G, K601E, G469A, V600M, G469A, V600L, G466V, V600D, G469V, D594G, D594N, N581S, L597V, L597S, L597Q, K601N, G466V, G466E, G464V, and G469E.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prediction of effect of a c-met inhibitor in cancer therapy using mutation of KRAS or BRAF)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 129 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:467583 CAPLUS Full-text
DOCUMENT NUMBER: 164:424395
TITLE: Combination therapies for treatment of cancer
INVENTOR(S): Janes, Matthew Robert; Patricelli, Matthew Peter; Li, Liansheng; Ren, Pingda; Liu, Yi
PATENT ASSIGNEE(S): Araxes Pharma LLC, USA
SOURCE: PCT Int. Appl., 397pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

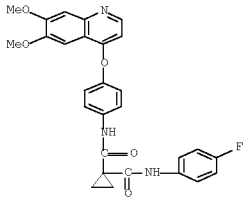
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016044772	A1	20160324	WO 2015-US51030	20150918
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20160166571	A1	20160616	US 2015-14858766	20150918
AR 101982	A1	20170125	AR 2015-103030	20150918

PRIORITY APPLN. INFO.: US 2014-62052332 P 20140918
US 2015-62195633 P 20150722
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 164:424395; MARPAT 164:424395
AB Combination therapies for treatment of cancers assocd. with mutations in the KRAS gene are provided. Compns. comprising therapeutic agents for treatment of cancers associated with mutations in the KRAS gene are also provided.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapies for treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



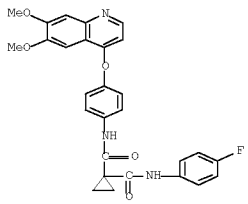
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 130 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:448327 CAPLUS Full-text
DOCUMENT NUMBER: 165:338869
TITLE: Expression profiling of small intestinal neuroendocrine tumors identifies subgroups with clinical relevance, prognostic markers and therapeutic targets
AUTHOR(S): Andersson, Ellinor; Arvidsson, Yvonne; Swaerd, Christina; Hofving, Tobias; Waengberg, Bo; Kristiansson, Erik; Nilsson, Ola
CORPORATE SOURCE: Sahlgrenska Cancer Center, Department of Pathology, Institute of Biomedicine, Sahlgrenska Academy at the University of Gothenburg, Goeteborg, Swed.
SOURCE: Modern Pathology (2016), 29(6), 616-629
CODEN: MODPEO; ISSN: 0893-3952
DIGITAL OBJECT ID: 10.1038/modpathol.2016.48
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB We wanted to define the transcriptome of small intestinal neuroendocrine tumors in order to identify clin. relevant subgroups of tumors, prognostic markers and novel targets for treatment. Genome-wide expression profiling was conducted on tumor biopsies from 33 patients with well-differentiated neuroendocrine tumors of the distal ileum and metastatic disease at the time of diagnosis. Unsupervised hierarchical clustering anal. identified three groups of tumors. The largest group, comprising half of the tumors, was characterized by longer patient survival and higher expression of neuroendocrine markers, including SSTR2. Tumors with higher grade (G2/3) or gain of chromosome 14 were associated with shorter patient survival and increased expression of cell cycle-promoting genes. Pathway anal. predicted the prostaglandin E receptor 2 (PTGER2) as the most significantly activated regulator in tumors of higher grade, whereas Forkhead box M1 (FOXM1) was the most significantly activated regulator in tumors with gain of chromosome 14. Druggable genes identified from expression profiles included clin. proven SSTR2 and also novel targets, for example, receptor tyrosine kinases (RET, FGFR1/3, PDGFRB and FLT1), epigenetic regulators, mol. chaperones and signal transduction mols. Evaluation of candidate drug targets on neuroendocrine tumors cells (GOT1) showed significant inhibition of tumor cell growth after treatment with tyrosine kinase inhibitors or inhibitors of HDAC, HSP90 and AKT. In conclusion, we have defined the transcriptome of small intestinal neuroendocrine tumors and identified novel subgroups with clin. relevance. We found specific gene expression patterns associated with tumor grade and chromosomal alterations. Our data also suggest novel prognostic biomarkers and therapies for these patients.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression profiling of small intestinal neuroendocrine tumors identifies subgroups with clin. relevance, prognostic markers and therapeutic targets)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 131 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:388457 CAPLUS Full-text
DOCUMENT NUMBER: 165:481256
TITLE: Evolving molecularly targeted therapies for advanced-stage thyroid cancers
AUTHOR(S): Bible, Keith C.; Ryder, Mabel
CORPORATE SOURCE: Division of Medical Oncology, Department of Oncology, and Endocrine Malignancies Disease Oriented Group, Mayo Clinic Cancer Center, Mayo Clinic, Rochester, MN, 55905, USA
SOURCE: Nature Reviews Clinical Oncology (2016), 13(7), 403-416
CODEN: NRCOAA; ISSN: 1759-4774
DIGITAL OBJECT ID: 10.1038/nrclinonc.2016.19
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Increased understanding of disease-specific mol. targets of therapy has led to the regulatory approval of two drugs (vandetanib and cabozantinib) for the treatment of medullary thyroid cancer (MTC), and two agents (sorafenib and lenvatinib) for the treatment of radioactive- iodine refractory differentiated thyroid cancer (DTC) in both the USA and in the EU. The effects of these and other therapies on overall survival and quality of life among patients with thyroid cancer, however, remain to be more-clearly defined. When applied early in the disease course, intensive multimodality therapy seems to improve the survival outcomes of patients with anaplastic thyroid cancer (ATC), but salvage therapies for ATC are of uncertain benefit. Addnl. innovative, rationally designed therapeutic strategies are under active development both for patients with DTC and for patients with ATC, with multiple phase II and phase III randomized clin. trials currently ongoing. Continued effort is being made to identify further signalling pathways with potential therapeutic relevance in thyroid cancers, as well as to elaborate on the complex interactions between signalling pathways, with the intention of translating these discoveries into effective and personalized therapies. Herein, we summarize the progress made in mol. medicine for advanced-stage thyroid cancers of different histotypes, analyze how these developments have altered - and might further refine - patient care, and identify open questions for future research.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evolving molecularly targeted therapies for advanced-stage thyroid cancers)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

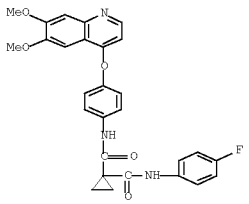
L4 ANSWER 132 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:381187 CAPLUS Full-text
DOCUMENT NUMBER: 164:368125
TITLE: Biomarker for predicting sensitivity to protein kinase inhibitor and use thereof
INVENTOR(S): Kim, Tae Won; Jin, Dong Hoon; Hong, Seung Woo; Moon, Jai Hee; Shin, Jae Sik; Lee, Ha Reum; Choi, Eun Kyoung; Kim, Seung Mi; Jung, Soo A.; Ha, Seung Hee; Jung, Ha Na; Lee, Dae Hee; Jung, Seang Hwan; Lee, Jung Shin; Choi, Eun Kyung; Lee, Jae Lyun; Hong, Yong Sang; Kim, Kyu Pyo; Kim, Jeong Eun; Park, Seong Joon; Kim, Bong Choel
PATENT ASSIGNEE(S): CJ HealthCare Corporation, S. Korea
SOURCE: PCT Int. Appl., 60pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016036172	A1	20160310	WO 2015-KR9322	20150903
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
KR 2016028399	A	20160311	KR 2015-125055	20150903

PRIORITY APPLN. INFO.: KR 2014-116787 A 20140903
AB The present invention relates to a biomarker for predicting the sensitivity of cells to a protein kinase inhibitor and a use thereof, a composition, a kit, and a prediction method. The biomarker comprises splicing variant or mutant of RON gene. According to the present invention, an effect of predicting sensitivity to a protein kinase inhibitor is excellent, and thus the present invention can be useful for cancer treatment.
IT 1140909-48-3, XL-184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active RON-containing biomarker for predicting cell sensitivity to protein kinase inhibitor)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

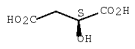
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

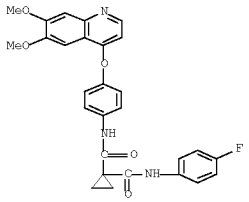
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



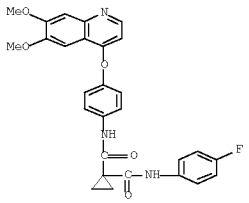
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 133 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:352953 CAPLUS Full-text
DOCUMENT NUMBER: 164:501384
TITLE: Delineation of Polypharmacology across the Human Structural Kinome Using a Functional Site Interaction Fingerprint Approach
AUTHOR(S): Zhao, Zheng; Xie, Li; Xie, Lei; Bourne, Philip E.
CORPORATE SOURCE: National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, MD, 20894, USA
SOURCE: Journal of Medicinal Chemistry (2016), 59(9), 4326-4341
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/acs.jmedchem.5b02041
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Targeted polypharmacol. of kinases has emerged as a promising strategy to design efficient and safe therapeutics. Here, we perform a systematic study of kinase-ligand binding modes for the human structural kinome at scale (208 kinases, 1777 unique ligands, and their complexes) by integrating chemical genomics and structural genomics data and by introducing a functional site interaction fingerprint (Fs-IFP) method. New insights into kinase-ligand binding modes were obtained. We establish relationships between the features of binding modes, the ligands, and the binding pockets, resp. We also drive the intrinsic binding specificity and which correlation with amino acid conservation. Third, we explore the landscape of the binding modes and highlight the regions of "selectivity pocket" and "selectivity entrance". Finally, we demonstrate that Fs-IFP similarity is directly correlated to the exptl. determined profile. These improve our understanding of kinase-ligand interactions and contribute to the design of novel polypharmacol. therapies targeting kinases.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delineation of polypharmacol. across structural kinome using functional site interaction fingerprint approach)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



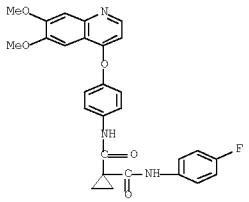
OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 135 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:333433 CAPLUS Full-text
DOCUMENT NUMBER: 166:223117
TITLE: Population pharmacokinetic/pharmacodynamic modeling of tumor growth kinetics in medullary thyroid cancer patients receiving cabozantinib
AUTHOR(S): Miles, Dale R.; Wada, David R.; Jumbe, Nelson L.; Lacy, Steven A.; Nguyen, Linh T.
CORPORATE SOURCE: Exelixis Inc., San Francisco, CA, USA
SOURCE: Anti-Cancer Drugs (2016), 27(4), 328-341
CODEN: ANTDEV; ISSN: 0959-4973
DIGITAL OBJECT ID: 10.1097/CAD.0000000000000330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Nonlinear mixed effects models were developed to describe the relationship between cabozantinib exposure and target lesion tumor size in a phase III study of patients with progressive metastatic medullary thyroid cancer. These models used cabozantinib exposure ests. from a previously published population pharmacokinetic model for cabozantinib in cancer patients that was updated with data from healthy-volunteer studies. Semi-mechanistic models predict well for tumors with static, increasing, or decreasing growth over time, but they were not considered adequate for predicting tumor sizes in medullary thyroid cancer patients, among whom an early reduction in tumor



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 134 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:342498 CAPLUS Full-text
DOCUMENT NUMBER: 164:380608
TITLE: Exploiting Temporal Collateral Sensitivity in Tumor Clonal Evolution
AUTHOR(S): Zhao, Boyang; Sedlak, Joseph C.; Srinivas, Raja; Creixell, Pau; Pritchard, Justin R.; Tidor, Bruce; Lauffenburger, Douglas A.; Hemann, Michael T.
CORPORATE SOURCE: Computational and Systems Biology Program, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SOURCE: Cell (Cambridge, MA, United States) (2016), 165(1), 234-246
CODEN: CELLB5; ISSN: 0092-8674
DIGITAL OBJECT ID: 10.1016/j.cell.2016.01.045
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The prevailing approach to addressing secondary drug resistance in cancer focuses on treating the resistance mechanisms at relapse. However, the dynamic nature of clonal evolution, along with potential fitness costs and cost compensations, may present exploitable vulnerabilities-a notion that we term "temporal collateral sensitivity.". Using a combined pharmacol. screen and drug resistance selection approach in a murine model of Ph+ acute lymphoblastic leukemia, we indeed find that temporal and/or persistent collateral sensitivity to non-classical BCR-ABL1 drugs arises in emergent tumor subpopulations during the evolution of resistance toward initial treatment with BCR-ABL1-targeted inhibitors. We determined the sensitization mechanism via genotypic, phenotypic, signaling, and binding measurements in combination with computational models and demonstrated significant overall survival extension in mice. Addnl. stochastic math. models and small-mol. screens extended our insights, indicating the value of focusing on evolutionary trajectories and pharmacol. profiles to identify new strategies to treat dynamic tumor vulnerabilities.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exploiting temporal collateral sensitivity in tumor clonal evolution)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

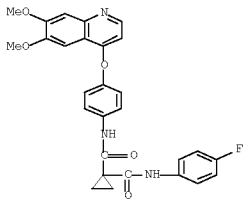
L4 ANSWER 136 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:295556 CAPLUS Full-text
DOCUMENT NUMBER: 166:313971
TITLE: Cabozantinib (XL184) Inhibits Growth and Invasion of Preclinical TNBC Models
AUTHOR(S): Sameni, Mansoureh; Tovar, Elizabeth A.; Essenburg, Curt J.; Chalasani, Anita; Linklater, Erik S.; Borgman, Andrew; Cherba, David M.; Anbalagan, Arulselvi; Winn, Mary E.; Graveel, Carrie R.; Sloane, Bonnie F.
CORPORATE SOURCE: Department of Pharmacology, Wayne State University School of Medicine, Detroit, MI, USA
SOURCE: Clinical Cancer Research (2016), 22(4), 923-934

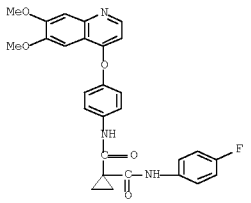
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-0187
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: Triple-neg. breast cancer (TNBC) is an aggressive breast cancer subtype that is associated with poor clin. outcome. There is a vital need for effective targeted therapeutics for TNBC patients, yet treatment strategies are challenged by the significant intertumoral heterogeneity within the TNBC subtype and its surrounding microenvironment. Receptor tyrosine kinases (RTK) are highly expressed in several TNBC subtypes and are promising therapeutic targets. In this study, we targeted the MET receptor, which is highly expressed across several TNBC subtypes. Exptl. Design: Using the small-mol. inhibitor cabozantinib (XL184), we examined the efficacy of MET inhibition in preclin. models that recapitulate human TNBC and its microenvironment. To analyze the dynamic interactions between TNBC cells and fibroblasts over time, we utilized a 3D model referred to as MAME (Mammary Architecture and Microenvironment Engineering) with quant. image anal. To investigate cabozantinib inhibition in vivo, we used a novel xenograft model that expresses human HGF and supports paracrine MET signaling. Results: XL184 treatment of MAME cultures of MDA-MB-231 and HCC70 cells (± HGF-expressing fibroblasts) was cytotoxic and significantly reduced multicellular invasive outgrowths, even in cultures with HGF-expressing fibroblasts. Treatment with XL184 had no significant effects on METneg breast cancer cell growth. In vivo assays demonstrated that cabozantinib treatment significantly inhibited TNBC growth and metastasis. Conclusions: Using preclin. TNBC models that recapitulate the breast tumor microenvironment, we demonstrate that cabozantinib inhibition is an effective therapeutic strategy in several TNBC subtypes. Clin Cancer Res; 22(4); 923-34. ©2015 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib inhibits growth and invasion of triple-neg. breast cancer models including human MDA-MB-231, HCC70 cells and mouse model)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





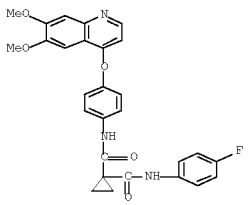
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 138 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:249149 CAPLUS Full-text
DOCUMENT NUMBER: 164:320714
TITLE: The discovery of 2-substituted phenol quinazolines as potent RET kinase inhibitors with improved KDR selectivity
AUTHOR(S): Newton, Rebecca; Bowler, Katherine A.; Burns, Emily M.; Chapman, Philip J.; Fairweather, Emma E.; Fritzl, Samantha J. R.; Goldberg, Kristin M.; Hamilton, Niall M.; Holt, Sarah V.; Hopkins, Gemma V.; Jones, Stuart D.; Jordan, Allan M.; Lyons, Amanda J.; Nikki March, H.; McDonald, Neil Q.; Maguire, Laura A.; Mould, Daniel P.; Purkiss, Andrew G.; Small, Helen F.; Stowell, Alexandra I. J.; Thomson, Graeme J.; Waddell, Ian D.; Waszkowycz, Bohdan; Watson, Amanda J.; Ogilvie, Donald J.
CORPORATE SOURCE: Cancer Research UK Manchester Institute, Drug Discovery Unit, University of Manchester, Withington, M20 4BX, UK
SOURCE: European Journal of Medicinal Chemistry (2016), 112, 20-32
CODEN: EJMCA5; ISSN: 0223-5234
DIGITAL OBJECT ID: 10.1016/j.ejmech.2016.01.039
PUBLISHER: Elsevier Masson SAS
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 164:320714

AB Deregulation of the receptor tyrosine kinase RET has been implicated in medullary thyroid cancer, a small percentage of lung adenocarcinomas, endocrine-resistant breast cancer and pancreatic cancer. There are several clin. approved multi-kinase inhibitors that target RET as a secondary pharmacol. but addnl. activities, most notably inhibition of KDR, lead to dose-limiting toxicities. There is, therefore, a clin. need for more specific RET kinase inhibitors. Herein we report our efforts towards identifying a potent and selective RET inhibitor using vandetanib 1 as the starting point for structure-based drug design. Phenolic anilinoquinazolines exemplified by 6 showed improved affinities towards RET but, unsurprisingly, suffered from high metabolic clearance. Efforts to mitigate the metabolic liability of the phenol led to the discovery that a flanking substituent not only improved the hepatocyte stability, but could also impart a significant gain in selectivity. This culminated in the identification of 36, a potent RET inhibitor with much improved selectivity against KDR.

IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenol quinazolines preparation as RET kinase inhibitors with improved KDR selectivity and potential as antitumor agents)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 139 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:237680 CAPLUS Full-text
DOCUMENT NUMBER: 165:91020
TITLE: Patterns in target-directed breast cancer research
AUTHOR(S): Torres, Sofia; Simmons, Christine; Boileau, Jean-Francois; McLeod, Deanna; Martins, Ilidio; Trudeau, Maureen
CORPORATE SOURCE: Sunnybrook Health Sciences Centre, Toronto, ON, M4N 3M5, Can.
SOURCE: SpringerPlus (2016), 5(1), 1-15
CODEN: SPRIFB; ISSN: 2193-1801
DIGITAL OBJECT ID: 10.1186/s40064-016-1736-1
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 137 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:264676 CAPLUS Full-text
DOCUMENT NUMBER: 165:480869
TITLE: Skeletal metastases and impact of anticancer and bone-targeted agents in patients with castration-resistant prostate cancer
AUTHOR(S): Vignani, Francesca; Bertaglia, Valentina; Buttigliero, Consuelo; Tucci, Marcello; Scagliotti, Giorgio V.; Di Maio, Massimo
CORPORATE SOURCE: Division of Medical Oncology, Department of Oncology, University of Turin at San Luigi Gonzaga Hospital, Turin, Italy
SOURCE: Cancer Treatment Reviews (2016), 44, 61-73
CODEN: CTREDJ; ISSN: 0305-7372
DIGITAL OBJECT ID: 10.1016/j.ctrv.2016.02.002
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Incidence of bone metastases is very high in advanced prostate cancer patients. Bone metastases likely have a significant impact on functional status and quality of life, not only related to pain, but also to the relevant risk of skeletal-related events. A better understanding of mechanisms associated with bone metastatic disease secondary to prostate cancer and more specifically to the cross-talk between tumor cells and bone microenvironment in metastatic progression represented the background for the development of new effective bone-targeted therapies. Furthermore, a better knowledge of biol. mechanisms driving disease progression led to significant advances in the treatment of castration-resistant prostate cancer, with the development and approval of new effective drugs. Aim of this review is to outline the physiopathol. of bone metastases in prostate cancer and summarize the main results of clin. trials conducted with different drugs to control morbidity induced by skeletal metastases and bone disease progression. For each agent, therapeutic effect on bone metastases has been measured in terms of pain control and/or incidence of skeletal-related events, usually defined as a composite endpoint, including the need for local treatment (radiation therapy or surgery), spinal cord compression, pathol. bone fractures. In details, data obtained with chemotherapy (mitoxantrone, docetaxel, cabazitaxel), new generation hormonal agents (abiraterone, enzalutamide), radium-223, bone-targeted agents (zoledronic acid, denosumab) and with several exptl. agents (cabozantinib, dasatinib, anti-endothelin and other agents) in patients with castration-resistant prostate cancer are reviewed.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skeletal metastases and impact of anticancer and bone-targeted agents in patients with castration-resistant prostate cancer)

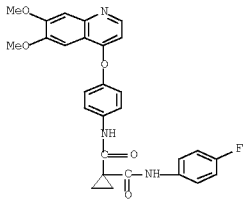
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

AB We undertake an anal. of ongoing BC targeted therapy trials registered to CT.gov to describe patterns of ongoing clin. research, highlight gaps in current research programs and identify ways of optimizing ongoing initiatives. A search of clinicaltrials.gov was conducted on Sept. 4, 2013 to identify ongoing randomized phase II and III trials of targeted therapies in BC. A total of 280 trials were analyzed, the majority conducted in either human epidermal growth factor receptor 2 (HER2)-pos. (n = 79, 28.2 %) or hormone receptor (HR)-pos. (n = 104, 37.1 %) populations. Less than half of all trials were conducted in populations selected to match the agent under investigation (n = 126, 45 %). HER2-directed therapy is the single most investigated class of targeted agents (n = 73, 26.1 %), but trials investigating anti-angiogenic agents are also common (n = 49, 17.5 %). The most common new classes of agents under investigation in HR-pos. and triple neg. (TN)/BRCA-pos. disease, are non-receptor protein kinase-inhibitors (n = 12; 11.5 %) and poly (ADP-ribose) polymerase inhibitors (n = 6; 30 %), resp. The majority of regimens combine new targeted agents with either chemotherapy (n = 164, 58.6 %) or endocrine therapy (n = 113, 40.4 %); a total of 8 trials (2.8 %) investigated peptide-drug conjugates. The most frequently utilized end-points were pathol. complete response in the neo-adjuvant setting (n = 36, 52.9 %) and time-to-event end-points in the adjuvant and advanced settings (77.3 and 72.6 %, resp.). Our findings suggest a need for more target-matched agent development, maintenance of a value-based focus in research and a need for the clin. development of agents to treat TN/BRCA-pos. and HR-pos. BC.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(patterns in target-directed breast cancer research)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 140 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:226918 CAPLUS Full-text

DOCUMENT NUMBER: 164:550430

TITLE: Chemical Proteomics Reveals Ferrochelatase as a Common Off-target of Kinase Inhibitors

AUTHOR(S): Klaeger, Susan; Gohlke, Bjoern; Perrin, Jessica; Gupta, Vipul; Heinzlmeir, Stephanie; Helm, Dominic; Qiao, Huichao; Bergamini, Giovanna; Handa, Hiroshi; Savitski, Mikhail M.; Bantscheff, Marcus; Medard, Guillaume; Preissner, Robert; Kuster, Bernhard

CORPORATE SOURCE: Chair of Proteomics and Bioanalytics, Technical University of Munich, Freising, Germany

SOURCE: ACS Chemical Biology (2016), 11(5), 1245-1254
CODEN: ACBCCT; ISSN: 1554-8929

DIGITAL OBJECT ID: 10.1021/acschembio.5b01063

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal; (online computer file)

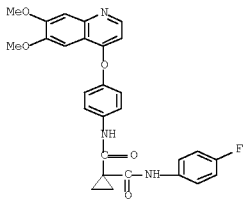
LANGUAGE: English

AB Many protein kinases are valid drug targets in oncol. because they are key components of signal transduction pathways. The number of clin. kinase inhibitors is on the rise, but these mols. often exhibit polypharmacol., potentially eliciting desired and toxic effects. Therefore, a comprehensive assessment of a compound's target space is desirable for a better understanding of its biol. effects. The enzyme ferrochelatase (FECH) catalyzes the conversion of protoporphyrin IX into heme and was recently found to be an off-target of the BRAF inhibitor Vemurafenib, likely explaining the phototoxicity associated with this drug in melanoma patients. This raises the question of whether FECH binding is a more general feature of kinase inhibitors. To address this, we applied a chemical proteomics approach using kinobeads to evaluate 226 clin. kinase inhibitors for their ability to bind FECH. Surprisingly, low or submicromolar FECH binding was detected for 29 of all compds. tested and isothermal dose response measurements confirmed target engagement in cells. We also show that Vemurafenib, Linsitinib, Neratinib, and MK-2461 reduce heme levels in K562 cells, verifying that drug binding leads to a loss of FECH activity. Further biochem. and docking expts. identified the protoporphyrin pocket in FECH as one major drug binding site. Since the genetic loss of FECH activity leads to photosensitivity in humans, our data strongly suggest that FECH inhibition by kinase inhibitors is the mol. mechanism triggering photosensitivity in patients. We therefore suggest that a FECH assay should generally be part of the preclin. mol. toxicol. package for the development of kinase inhibitors.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical proteomics reveals ferrochelatase as a common off-target of kinase inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 141 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:224790 CAPLUS Full-text

DOCUMENT NUMBER: 164:293822

TITLE: Drug combinations to treat multiple myeloma

INVENTOR(S): Aftab, Dana T.; Lamb, Peter

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016022697	A1	20160211	WO 2015-US43825	20150805
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2015301097	A1	20170302	AU 2015-301097	20150805
KR 2017031786	A	20170321	KR 2017-7006288	20150805
CN 106573042	A	20170419	CN 2015-80042010	20150805

PRIORITY APPLN. INFO.: US 2014-62033386 P 20140805
WO 2015-US43825 W 20150805

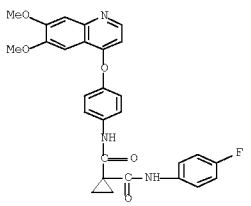
OTHER SOURCE(S): CASREACT 164:293822; MARPAT 164:293822

AB This invention relates to the combination of a C-Met inhibitor and a proteasome inhibitor to treat cancer, particularly multiple myeloma.

IT 849217-68-1P
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug combinations to treat multiple myeloma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



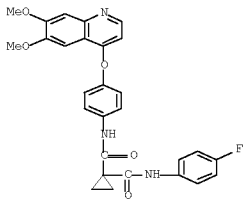
IT 1140909-48-3P 1365530-43-3P 1634653-27-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug combinations to treat multiple myeloma)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

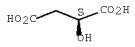
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

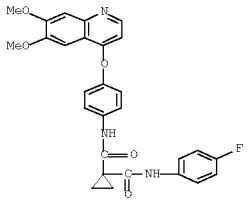
Absolute stereochemistry. Rotation (-).



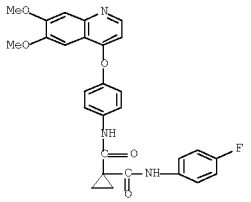
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

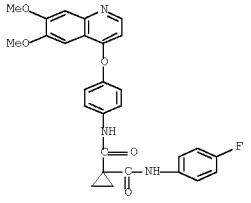


IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations to treat multiple myeloma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 142 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:222043 CAPLUS Full-text
DOCUMENT NUMBER: 164:270659
TITLE: Interaction of new kinase inhibitors cabozantinib and tofacitinib with human serum alpha-1 acid glycoprotein. A comprehensive spectroscopic and molecular Docking approach
AUTHOR(S): Ajmal, Mohammad Rehan; Abdelhameed, Ali Saber; Alam, Parvez; Khan, Rizwan Hasan
CORPORATE SOURCE: Interdisciplinary Biotechnology Unit, Aligarh Muslim University, Aligarh, 202002, India
SOURCE: Spectrochimica Acta, Part A: Molecular and Biomolecular Spectroscopy (2016), 159, 199-208
CODEN: SAMCAS; ISSN: 1386-1425
DIGITAL OBJECT ID: 10.1016/j.saa.2016.01.049
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In the current study we have investigated the interaction of newly approved kinase inhibitors namely Cabozantinib (CBZ) and Tofacitinib (TFB) with human Alpha-1 acid glycoprotein (AAG) under simulated physiol. conditions using fluorescence quenching measurements, CD, dynamic light scattering and mol. docking methods. CBZ and TFB binds to AAG with significant affinity and the calculated binding constant for the drugs lie in the order of 104. With the increase in temperature the binding constant values decreased for both CBZ and TFB. The fluorescence resonance energy transfer (FRET) from AAG to CBZ and TFB suggested the fluorescence intensity of AAG was quenched by the two studied drugs via the formation of a non-fluorescent complex in the static manner. The mol. distance r value calculated from FRET is around 2 nm for both drugs, fluorescence spectroscopy data was employed for the study of thermodn. parameters, standard Gibbs free energy change at 300K was calculated as - 5.234 kcal mol- 1 for CBZ-AAG interaction and - 6.237 kcal mol- 1 for TFB-AAG interaction, standard enthalpy change and standard entropy change for CBZ-AAG interaction are - 9.553 kcal mol- 1 and - 14.618 cal mol- 1K- 1 resp. while for AAG-TFB interaction, standard enthalpy and standard entropy change was calculated as 4.019 kcal mol- 1 and 7.206 cal mol- 1K- 1 resp. Protein binding of the two drugs caused the tertiary structure alterations. Dynamic light scattering measurements demonstrated the reduction in the hydrodynamic radii of the protein. Furthermore mol. docking results suggested the Hydrophobic interaction and hydrogen bonding were the interactive forces in the binding process of CBZ to AAG while in case of TFB only hydrophobic interactions were found to be involved, overlap of the binding site for two studied drugs on the AAG mol. was revealed by docking results.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor drugs cabozantinib and tofacitinib interaction with serum α1-acid glycoprotein)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



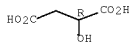
OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 143 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:219788 CAPLUS Full-text
DOCUMENT NUMBER: 166:260118
TITLE: Phase 1 dose escalation trial of the safety and pharmacokinetics of cabozantinib concurrent with temozolomide and radiotherapy or temozolomide after radiotherapy in newly diagnosed patients with high-grade gliomas
AUTHOR(S): Schiff, David; Desjardins, Annick; Cloughesy, Timothy;

CM 2

CRN 636-61-3
CMF C4 H6 O5

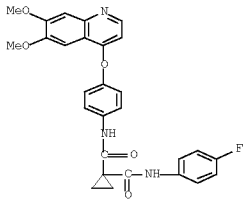
Absolute stereochemistry. Rotation (+).



RN 1634653-27-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

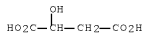
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 6915-15-7
CMF C4 H6 O5

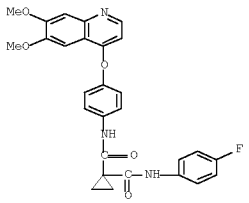


Mikkelsen, Thomas; Glantz, Michael; Chamberlain, Marc C.; Reardon, David A.; Wen, Patrick Y.
CORPORATE SOURCE: Department of Neurology, Neuro-Oncology Center, University of Virginia Medical Center, Charlottesville, VA, USA
SOURCE: Cancer (Hoboken, NJ, United States) (2016), 122(4), 582-587
CODEN: CANCAR; ISSN: 0008-543X
DIGITAL OBJECT ID: 10.1002/cncr.29798
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Cabozantinib inhibits mesenchymal-epithelial transition factor (MET) and vascular endothelial growth factor receptor 2 (VEGFR2) and has demonstrated activity in patients with recurrent glioblastoma, warranting evaluation of the addition of cabozantinib to radiotherapy (RT) and temozolomide (TMZ) for patients with newly diagnosed high-grade glioma. Cabozantinib doses of 40 mg and 60 mg were explored. Patients on the concurrent treatment arm received cabozantinib daily with standard TMZ and after RT continued cabozantinib daily with adjuvant TMZ. In the maintenance arm, patients who completed RT and ≥1 adjuvant cycle of TMZ continued adjuvant TMZ with added cabozantinib (3 schedules: days 1-28, days 1-14, or days 8-21). RESULTS : A total of 26 patients (25 with recurrent glioblastoma and 1 patient with anaplastic astrocytoma) aged 30 to 72 years were enrolled (10 to the concurrent arm and 16 to the maintenance arm). The median number of post-RT TMZ cycles was 4.5 (range, 0-14 cycles) in the concurrent arm and 5.5 (range, 1-12 cycles) in the maintenance arm. Cabozantinib at a dose of 60 mg daily was the maximum administered dose and a dose of 40 mg daily was determined to be the maximum tolerated dose for both treatment arms (schedule of days 1-28). The most frequent grade 3/4 adverse events were thrombocytopenia (31% of patients), leukopenia (27% of patients, including 5 patients with neutropenia), and deep vein thrombosis and/or pulmonary embolism (23% of patients) (adverse events were graded according to the National Cancer Institute Common Terminol. Criteria for Adverse Events [version 3.0]). Cabozantinib at a dose of 40 mg daily with RT plus TMZ and post-RT TMZ for patients with newly diagnosed high-grade glioma was generally well tolerated, and demonstrated no pharmacokinetic interactions with concurrent TMZ. Given the strong theor. rationale for combining anti-VEGF and anti-MET activity with standard therapy, cabozantinib at a dose of 40 mg daily warrants evaluation in combination with standard therapy for patients with newly diagnosed glioblastoma.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase 1 dose escalation trial of safety and pharmacokinetics of cabozantinib concurrent with temozolomide and radiotherapy or temozolomide after radiotherapy in newly diagnosed patients with high-grade gliomas)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 144 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:196080 CAPLUS Full-text
DOCUMENT NUMBER: 164:318691
TITLE: Hydrophilic drug phospholipid, its pharmaceutical composition and application
INVENTOR(S): Li, Xinsong; Xu, Chen; Du, Yawei; Ling, Longbing; Hou, Yongpeng
PATENT ASSIGNEE(S): Southeast University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 38pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 105288648	A	20160203	CN 2015-10661316	20151014

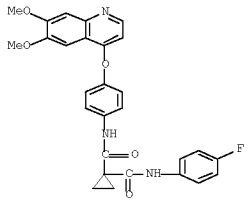
PRIORITY APPLN. INFO.: CN 2015-10661316 20151014
OTHER SOURCE(S): CASREACT 164:318691; MARPAT 164:318691

AB The present invention discloses a hydrophilic drug phospholipid, its pharmaceutical composition and application. the pharmaceutical composition is hydrophilic drug phospholipid or the composition of the combination drug of hydrophilic drug phospholipid and pharmacodynamic acceptable carrier, it can be liquid formulation, solid prepns., semi-solid formulation, capsules, granules, gels, injection. the pharmaceutical composition is liposomal nanoparticle formed by hydrophilic drug phospholipid or hydrophilic drug phospholipid and additives, the particle size is 10-1000 nm. the hydrophilic drug phospholipid and its liposomal nanoparticles can be used as the liquid formulations, solid prepns., semi-solid formulation, sterilized prepns. and sterile preparation, have low toxicity, can be used effective treatment for various tumors.

IT 849217-68-1, Cabozantinib
RL: NANO (Nanomaterial); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic drug phospholipid, its pharmaceutical composition and application)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 145 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:193681 CAPLUS Full-text
DOCUMENT NUMBER: 164:245721
TITLE: Use of HSP90 as marker for predicting efficacy of c-Met inhibitor in treatment of cancer
INVENTOR(S): Lee, Ji Min; Kim, Bo Gyou; Oh, Seung Ja; Kim, Kyung Ah; Lee, Saet Byoul; Hwang, Jae Woong
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 94pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

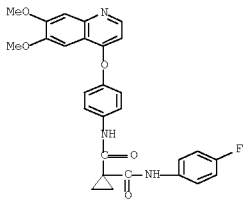
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20160030559	A1	20160204	US 2015-14814278	20150730
KR 2016015076	A	20160212	KR 2014-97560	20140730

PRIORITY APPLN. INFO.: KR 2014-97560 A 20140730
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to the use of heat shock protein 90 (Hsp90) as marker for predicting an efficacy of a c-Met inhibitor, selecting a subject for application of a c-Met inhibitor, or monitoring an efficacy of a c-Met inhibitor, and a relevant method of using Hsp90 for treatment of cancer.

IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of HSP90 as marker for predicting efficacy of c-Met inhibitor in treatment of cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 146 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:188602 CAPLUS Full-text
DOCUMENT NUMBER: 164:277127
TITLE: Preparation of acetylcyclopentylmethylaminopyridopyrimidinone derivatives for use as CDK small-molecule inhibitors
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 117pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015597	A1	20160204	WO 2015-CN84983	20150723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294681	A	20160203	CN 2015-10439329	20150723
CN 105294682	A	20160203	CN 2015-10439488	20150723
CN 105294736	A	20160203	CN 2015-10443167	20150724

PRIORITY APPLN. INFO.: CN 2014-10361634 A 20140726
CN 2015-10076030 A 20150212
OTHER SOURCE(S): CASREACT 164:277127; MARPAT 164:277127
GI

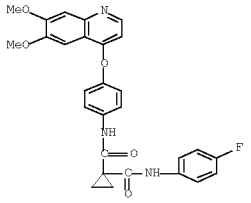
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [B = Ph, pyridazinyl, pyrimidinyl, pyrazinyl, etc.; L = bond, CH2, CH2CH2, CH2NHCH2, etc.; R1 and R2 independently = H, F, Cl, Br, OH, alkyl, etc.; R3 = H, heteroaryl, cycloalkyl, heterocyclyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as CDK small-mol. inhibitors. Thus, e.g., II was prepared by a multistep procedure (preparation given). Select I were evaluated in CDK4 and CDK6 enzymic inhibition activity assays, e.g., II demonstrated IC50 values of 18 nM and 35 nM, resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of acetylcyclopentylmethylaminopyridopyrimidinone derivs. for use as CDK small-mol. inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 147 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:186216 CAPLUS Full-text

DOCUMENT NUMBER: 164:277126

TITLE: 2-Aminopyrido[2,3-d]pyrimidin-7(8H)-one derivatives as CDK inhibitors and their preparation

INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China

SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

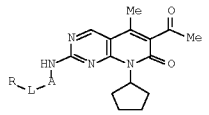
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015598	A1	20160204	WO 2015-CN84984	20150723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294681	A	20160203	CN 2015-10439329	20150723
CN 105294682	A	20160203	CN 2015-10439488	20150723
CA 2954189	A1	20160204	CA 2015-2954189	20150723
AU 2015296322	A1	20170112	AU 2015-296322	20150723
KR 2017032244	A	20170322	KR 2016-7037000	20150723
CN 105294736	A	20160203	CN 2015-10443167	20150724
US 20170121323	A1	20170504	US 2016-15318366	20161213
PRIORITY APPLN. INFO.:			CN 2014-10361634 A	20140726
			CN 2015-10076030 A	20150212
			WO 2015-CN84984 W	20150723

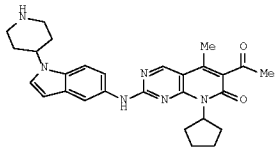
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 164:277126; MARPAT 164:277126

GI



I



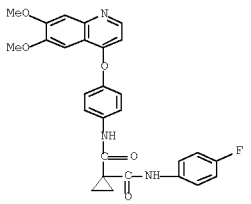
II

AB The invention provides substituted 2-aminopyrido[2,3-d]pyrimidin-7(8H)-one compds. of formula I, which can be used for treating inflammation and cell proliferation diseases. The compound of the invention is a powerful cyclin-dependent kinase 4 (CDK 4) or cyclin-dependent kinase 6 (CDK 6) inhibitor. Compds. of formula I wherein L is a bond, (un)substituted C0-4 alkylene, (un)substituted amino-C0-4 alkyl, (un)substituted O-C0-4 alkyl, etc.; A is bicyclic heteroaryl, and bicyclic heterocyclyl; R is H, C3-9 cycloalkyl, C1-9 heteroaryl, C2-9 heterocyclyl, etc.; and stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). The invention compds. were evaluated for their CDK inhibitory activity. From the assay, it was determined that compound II exhibited IC50 values of 6.8 nM and 29.2 nM toward CDK4 and CDK6, resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of aminopyridopyrimidinone derivs. as CDK inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 148 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:185751 CAPLUS Full-text

DOCUMENT NUMBER: 164:277125

TITLE: 6-[2-(Pyridinyl-2-ylamino)pyrimidin-4-yl]imidazole compounds as CDK inhibitors and their preparation

INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China

SOURCE: PCT Int. Appl., 278pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015605	A1	20160204	WO 2015-CN85036	20150724
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294683	A	20160203	CN 2015-10444529	20150724
CN 105294655	A	20160203	CN 2015-10447867	20150724
PRIORITY APPLN. INFO.:			CN 2014-10362374 A	20140726
			CN 2015-10015255 A	20150113

OTHER SOURCE(S): CASREACT 164:277125; MARPAT 164:277125

GI

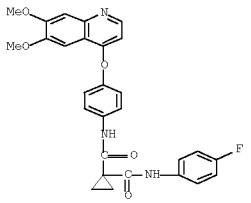
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides substituted 6-[2-(pyridinyl-2-ylamino)pyrimidin-4-yl]imidazole compds. of formula I, which can be used for treating inflammation and cell proliferation diseases. The compound of the invention is a powerful cyclin-dependent kinase 4 (CDK 4) or cyclin-dependent kinase-6 (CDK 6) inhibitor. Compds. of formula I wherein R1 and R2 are independently H, F, Cl, Br, OH, C1-4 alkyl, etc.; L1 is a bond, (un)substituted C0-4 alkylene, (un)substituted C0-4 alkoxy-C0-4 alkylene, (un)substituted C0-4 alkylamino-C0-4 alkyl, etc.; R3 is (spiro/bridge/fused) C5-12 heterobicyclyl, C1-9 heteroaryl, C6-12 aryl, etc.; and stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). The invention compds. were evaluated for their CDK inhibitory activity (some data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of [(pyridinylamino)pyrimidinyl]benzimidazoles as CDK inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

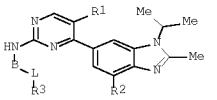


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

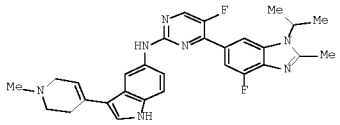
L4 ANSWER 149 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:185021 CAPLUS Full-text
DOCUMENT NUMBER: 164:264663
TITLE: Preparation of isopropylmethylbenzoimidazolylpyrimidine derivatives for use as CDK small-molecule inhibitors
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Nie, Linlin; Bai, Shun; Guan, Mingyu; Li, Xuke; Cheng, Changchung
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 125pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016015604	A1	20160204	WO 2015-CN85034	20150724
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 105294683	A	20160203	CN 2015-10444529	20150724
CN 105294655	A	20160203	CN 2015-10447867	20150724

PRIORITY APPLN. INFO.: CN 2014-10362374 A 20140726
CN 2015-10015255 A 20150113
OTHER SOURCE(S): CASREACT 164:264663; MARPAT 164:264663
GI

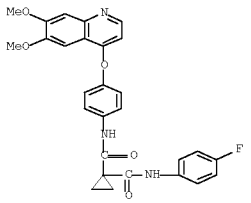


I



II

AB Title compds. I [B = Ph, pyridazinyl, pyrimidinyl, pyrazinyl, etc.; L = bond, CH2, CH2CH2, CH2NHCH2, etc.; R1 and R2 independently = H, F, Cl, Br, OH, alkyl, etc.; R3 = H, heteroaryl, cycloalkyl, heterocyclyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as CDK small-mol. inhibitors. Thus, e.g., II was prepared by amination of 6-(2-chloro-5-fluoropyrimidin-4-yl)-4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazole with 3-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)-1H-indol-5-amine. Select I were evaluated in enzymic inhibition activity assays (data given).
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of isopropylmethylbenzoimidazolylpyrimidine derivs. for use as CDK small-mol. inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

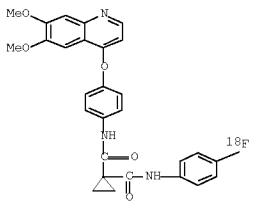
L4 ANSWER 150 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:184907 CAPLUS Full-text
DOCUMENT NUMBER: 164:251528
TITLE: Method of preparing fluorine-18 labeled cabozantinib and its analogs
INVENTOR(S): Xu, Wei; Donnelly, David J.; Chow, Patrick L.; Henley, Benjamin J.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2016019285	A1	20160204	WO 2015-US43195	20150731
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

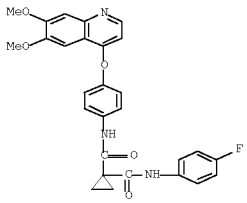
PRIORITY APPLN. INFO.: US 2014-62031471 P 20140731
OTHER SOURCE(S): CASREACT 164:251528; MARPAT 164:251528
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a method of prepg. compds. of I [wherein R1 and R2 = independently alkoxy or haloalkoxy; R3 = H, F, Cl, etc.; R4 = F, 18F, Cl, etc.] such as cabozantinib II, R4 = F, and [18F]-II, R4 = 18F, comprising the reaction of 4-aminophenol with 4-chloro-6,7-dimethoxyquinoline yielding the ether intermediate, III, which undergoes coupling with 1-carboxycyclopropanecarbonyl chloride providing IV, followed by amidation of IV with 4-fluoroaniline or [18F]-4-fluoroaniline under microwave heating yielding cabozantinib or [18F]-labeled cabozantinib. [18F]-II was administered to mice implanted with U87 tumors (glioblastoma) and to tumor-free animals. PET imaging resulted in visualization of the tumors in the brains of the tumor bearing animals and little or no uptake of [18F]-II in control animals suggesting [18F]-II does not cross the blood brain barrier in tumor-free mice but has significant uptake in U87 implanted mice.
IT 1870906-64-1P
RL: DGN (Diagnostic use); IMF (Industrial manufacture); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of preparing fluorine-18 labeled cabozantinib and its analogs)
RN 1870906-64-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-[4-(fluoro-18F)phenyl]- (CA INDEX NAME)



IT 849217-68-1P, Cabozantinib
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of preparing fluorine-18 labeled cabozantinib and its analogs)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



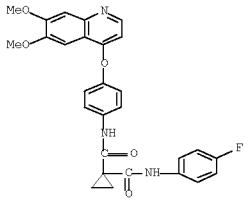
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 151 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:145922 CAPLUS Full-text
DOCUMENT NUMBER: 166:140561
TITLE: A Phase II Trial of the Multitargeted Tyrosine Kinase Inhibitor Lenvatinib (E7080) in Advanced Medullary Thyroid Cancer
AUTHOR(S): Schlumberger, Martin; Jarzab, Barbara; Cabanillas, Maria E.; Robinson, Bruce; Pacini, Furio; Ball, Douglas W.; McCaffrey, Judith; Newbold, Kate; Allison, Roger; Martins, Renato G.; Licitra, Lisa F.; Shah, Manisha H.; Bodenner, Donald; Elisei, Rossella; Burmeister, Lynn; Funahashi, Yasuhiro; Ren, Min; O'Brien, James P.; Sherman, Steven I.
CORPORATE SOURCE: Department of Nuclear Medicine and Endocrine Oncology, Institut Gustave-Roussy and University Paris-Sud, Villejuif, Fr.
SOURCE: Clinical Cancer Research (2016), 22(1), 44-53
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-1127
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: Pos. results of phase I studies evaluating lenvatinib in solid tumors, including thyroid cancer, prompted a phase II trial in advanced medullary thyroid carcinoma (MTC). Exptl. Design: Fifty-nine patients with unresectable progressive MTC per Response Evaluation Criteria In Solid Tumors (RECIST) v1.0 within the prior 12 mo received lenvatinib (24-mg daily, 28-day cycles) until disease progression, unmanageable toxicity, withdrawal, or death. Prior anti-VEGFR therapy was permitted. The primary endpoint was objective response rate (ORR) by RECIST v1.0 and independent imaging review. Results: Lenvatinib ORR was 36% [95% confidence interval (CI), 24%-49%]; all partial responses. ORR was comparable between patients with (35%) or without (36%) prior anti-VEGFR therapy. Disease control rate (DCR) was 80% (95% CI, 67%-89%); 44% had stable disease. Among responders, median time to response (TTR) was 3.5 mo (95% CI, 1.9-3.7). Median progression-free survival (PFS) was 9.0 mo (95% CI, 7.0-not evaluable). Common toxicity criteria grade 3/4 treatment-emergent adverse events included diarrhea (14%), hypertension (7%), decreased appetite (7%), fatigue, dysphagia, and increased alanine aminotransferase levels (5% each). Ret proto-oncogene status did not correlate with outcomes. Low baseline levels of angiopoietin-2, hepatocyte growth factor, and IL8 were associated with tumor reduction and prolonged PFS. High baseline levels of VEGF, soluble VEGFR3, and platelet-derived growth factor BB, and low baseline levels of soluble Tie-2, were associated with tumor reduction Conclusions: Lenvatinib had a high ORR, high DCR, and a short TTR in patients with documented progressive MTC. Toxicities were managed with dose modifications and medications. Clin Cancer Res; 22(1); 44-53. ©2015 AACR.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and safety of multitargeted tyrosine kinase inhibitor lenvatinib was evaluated for treatment of advanced medullary thyroid cancer in patients)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



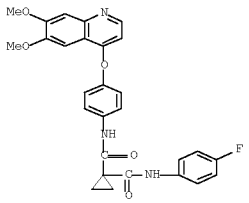
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 152 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:145903 CAPLUS Full-text
DOCUMENT NUMBER: 166:140556
TITLE: Integrating Murine and Clinical Trials with Cabozantinib to Understand Roles of MET and VEGFR2 as Targets for Growth Inhibition of Prostate Cancer
AUTHOR(S): Varkaris, Andreas; Corn, Paul G.; Parikh, Nila U.; Efstathiou, Eleni; Song, Jian H.; Lee, Yu-Chen; Aparicio, Ana; Hoang, Anh G.; Gaur, Sanchaika; Thorpe, Lynnelle; Maity, Sankar N.; Bar Eli, Menashe; Czerniak, Bogdan A.; Shao, Yiping; Alauddin, Mian; Lin, Sue-Hwa; Logothetis, Christopher J.; Gallick, Gary E.
CORPORATE SOURCE: Department of Genitourinary Medical Oncology, David H. Koch Center for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Clinical Cancer Research (2016), 22(1), 107-121
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-0235
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: We performed parallel investigations in cabozantinib-treated patients in a phase II trial and simultaneously in patient-derived xenograft (PDX) models to better understand the roles of MET and VEGFR2 as targets for prostate cancer therapy. Exptl. Design: In the clin. trial, radiog. imaging and serum markers were examined, as well as mol. markers in tumors from bone biopsies. In mice harboring PDX intrafemurally or s.c., cabozantinib effects on tumor growth, MET, PDX in which MET was silenced, VEGFR2, bone turnover, angiogenesis, and resistance were examined Results: In responsive patients and PDX, islets of viable pMET-pos. tumor cells persisted, which rapidly regrew after drug withdrawal. Knockdown of MET in PDX did not affect tumor growth in mice nor did it affect cabozantinib-induced growth inhibition but did lead to induction of FGFR1. Inhibition of VEGFR2 and MET in endothelial cells reduced the vasculature, leading to necrosis. However, each islet of viable cells surrounded a VEGFR2-neg. vessel. Reduction of bone turnover was observed in both cohorts. Conclusions: Our studies demonstrate that MET in tumor cells is not a persistent therapeutic target for metastatic castrate-resistant prostate cancer (CRPC), but inhibition of VEGFR2 and MET in endothelial cells and direct effects on osteoblasts are responsible for cabozantinib-induced tumor inhibition. However, vascular heterogeneity represents one source of primary therapy resistance, whereas induction of FGFR1 in tumor cells suggests a potential mechanism of acquired resistance. Thus, integrated cross-species investigations demonstrate the power of combining preclin. models with clin. trials to understand mechanisms of activity and resistance of investigational agents. Clin Cancer Res; 22(1); 107-21. ©2015 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib treatment-induced inhibition of VEGFR2, FGFR1 and MET signaling which responsible for tumor inhibition in in-vitro human prostate cancer cells and in in-vivo mouse model)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



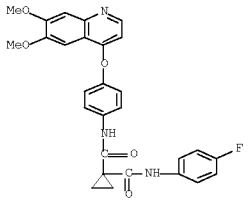
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 153 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:126388 CAPLUS Full-text
DOCUMENT NUMBER: 164:244992
TITLE: AutoT&T v.2: An Efficient and Versatile Tool for Lead Structure Generation and Optimization
AUTHOR(S): Li, Yan; Zhao, Zhixiong; Liu, Zhihai; Su, Minyi; Wang, Renxiao
CORPORATE SOURCE: State Key Laboratory of Bioorganic and Natural Products Chemistry, Collaborative Innovation Center of Chemistry for Life Sciences, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Journal of Chemical Information and Modeling (2016), 56(2), 435-453
CODEN: JCISD8; ISSN: 1549-9596
DIGITAL OBJECT ID: 10.1021/acs.jcim.5b00691
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB In structure-based drug design, automated de novo design methods are helpful tools for lead discovery as well as lead optimization. In a previous study the authors reported a new de novo design method, namely, Automatic Tailoring and Transplanting (AutoT&T). It overcomes some intrinsic problems in conventional fragment-based buildup methods. In this study, the authors describe an upgraded version, namely, AutoT&T2. Structural operations conducted by AutoT&T2 have been largely optimized by introducing several new algorithms. As a result, its overall speed in multiround optimization jobs has been improved by a few thousand fold. With this improvement, it is now practical to conduct structural crossover among multiple lead mols. using AutoT&T2. Three different test cases are described in this study that demonstrate the new features and versatile applications of AutoT&T2. The AutoT&T2 software suite is available to the public. Besides, a Web portal for running AutoT&T2 online is provided at http://www.sioc-ccbg.ac.cn/software/att2 for testing.

IT 849217-68-1, Cabozantinib

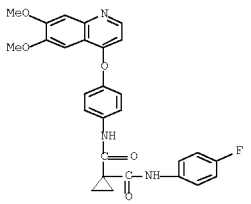
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AutoT&T v.2 is efficient and versatile tool for lead structure generation and optimization)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 154 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:125847 CAPLUS Full-text
TITLE: Research advances of FLT3 inhibitors in treatment of acute myeloid leukemia
AUTHOR(S): Li, Tonghui; Guo, Hao; Lu, Tao; Wang, Yue; Lu, Shuai; Tang, Weifang
CORPORATE SOURCE: Department of Organic Chemistry, China Pharmaceutical University, Nanjing, 211198, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2015), 46(2), 153-161
CODEN: ZHYXE9; ISSN: 1000-5048
DIGITAL OBJECT ID: 10.11665/j.issn.1000-5048.20150203
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 69 ref. is given on research advances of FLT3 inhibitors in treatment of acute myeloid leukemia. Acute myeloid leukemia (AML) is one of the most common acute leukemia in adults. Those patients with FLT3 mutations have a particularly poor prognosis. Recently, the emergence of a variety of targeted inhibitors has shown the capability of suppressing FLT3 signaling in vivo, which provided a new way to treat AML. In this paper, we reviewed those inhibitors based on their structures, which include indolone-related inhibitors, indolocarbazo-related inhibitors, benzimidazole/benzopyrazole-related inhibitors, quinoline/quinoxaline/quinazoline-related inhibitors, tricyclic inhibitors, pyrimidine-related inhibitors and others.
IT INDEXING IN PROGRESS

SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
EP 3145913 A1 20170329 EP 2015-728635 20150522
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
US 20170096395 A1 20170406 US 2016-15313191 20161122
PRIORITY APPLN. INFO.: IN 2014-CH2561 A 20140523
WO 2015-IB53765 W 20150522
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present disclosure provides novel cryst. forms of cabozantinib (S)-malate, designated as form-M1, M2, M3 and M4 and novel crystalline forms of cabozantinib free base, form-M1, M2 and M3 and methods of their production The present disclosure also provides processes for the preparation of crystalline cabozantinib (S)-malate form N-1.
IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(novel polymorph's of cabozantinib-S-malate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

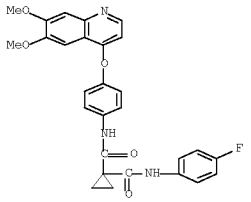


IT 1140909-48-3, Cabozantinib (S)-malate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(novel polymorph's of cabozantinib-S-malate)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

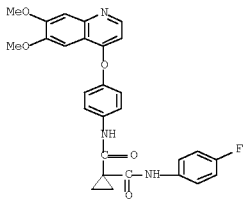
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(research advances of FLT3 inhibitors in treatment of acute myeloid leukemia)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 155 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:118025 CAPLUS Full-text
DOCUMENT NUMBER: 164:355574
TITLE: Novel polymorph's of cabozantinib-S-malate
INVENTOR(S): Jetti, Ramakoteswara Rao; Indukuri, Anjaneyaraju; Punde, Dnyandeo; Bohra, Chandersingh; Gadakar, Mahesh Kumar; Gore, Vinayak
PATENT ASSIGNEE(S): Mylan Laboratories Ltd., India
SOURCE: Indian Pat. Appl., 54pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2014CH02561	A	20160115	IN 2014-CH2561	20140523
WO 2015177758	A1	20151126	WO 2015-IB53765	20150522

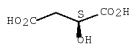
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



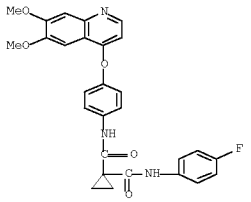
L4 ANSWER 156 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2016:117644 CAPLUS Full-text
DOCUMENT NUMBER: 165:256435
TITLE: Emerging targeted therapies in non-small cell lung cancer
AUTHOR(S): Khanal, Nabin; Ganti, Apar Kishor
CORPORATE SOURCE: Department of Internal Medicine, Creighton University Medical Center, Omaha, NE, USA
SOURCE: Expert Review of Anticancer Therapy (2016), 16(2), 177-187
CODEN: ERATBJ; ISSN: 1473-7140
DIGITAL OBJECT ID: 10.1586/14737140.2016.1126514
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Lung cancer is the leading cause of cancer-related deaths in United States, accounting for more than one-fourth of the deaths annually. Although comparatively rare and relatively less studied, genetic abnormalities other than epidermal growth factor receptor (EGFR) mutations, anaplastic lymphoma kinase (ALK) rearrangements, and Kirsten rat sarcoma (KRAS) mutations account for significant proportion of the driver mutations identified thus far. The targeted agents against B-rapidly accelerated fibrosarcoma (BRAF) V600E mutation, MNNG-HOS transforming gene (MET) pathway, ROS1 rearrangement, rearranged during transfection (RET) rearrangement, and HER2 pathways offer promising therapeutic options. Recruiting patients with

these rarer mutations to well-designed, large multicenter trials to further validate the use of targeted agents remains a challenge. The clin. data and ongoing trials with these agents are reviewed in this article.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emerging targeted therapies in non-small cell lung cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 157 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:117601 CAPLUS Full-text

DOCUMENT NUMBER: 164:421210

TITLE: A photoactivable multi-inhibitor nanoliposome for tumour control and simultaneous inhibition of treatment escape pathways

AUTHOR(S): Spring, Bryan Q.; Bryan Sears, R.; Zheng, Lei Zak; Mai, Zhiming; Watanabe, Reika; Sherwood, Margaret E.; Schoenfeld, David A.; Pogue, Brian W.; Pereira, Stephen P.; Villa, Elizabeth; Hasan, Tayyaba

CORPORATE SOURCE: Wellman Center for Photomedicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA

SOURCE: Nature Nanotechnology (2016), 11(4), 378-387
CODEN: NNAABX; ISSN: 1748-3387

DIGITAL OBJECT ID: 10.1038/nnano.2015.311

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; (online computer file)

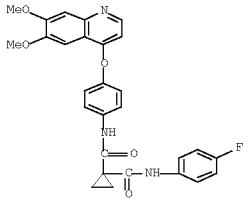
LANGUAGE: English

AB Nanoscale drug delivery vehicles can facilitate multimodal therapies of cancer by promoting tumor-selective drug release. However, few are effective because cancer cells develop ways to resist and evade treatment. Here, we introduce a photoactivable multi-inhibitor nanoliposome (PMIL) that imparts light-induced cytotoxicity in synchrony with a photoinitiated and sustained release of inhibitors that suppress tumor regrowth and treatment escape signaling pathways. The PMIL consists of a nanoliposome doped with a photoactivable chromophore (benzoporphyrin derivative, BPD) in the lipid bilayer, and a nanoparticle containing cabozantinib (XL184)-a multikinase inhibitor-encapsulated inside. Near-IR tumor irradiation, following i.v. PMIL administration, triggers photodynamic damage of tumor cells and microvessels, and simultaneously initiates release of XL184 inside the tumor. A single PMIL treatment achieves prolonged tumor reduction in two mouse models and suppresses metastatic escape in an orthotopic pancreatic tumor model. The PMIL offers new prospects for cancer therapy by enabling spatiotemporal control of drug release while reducing systemic drug exposure and associated toxicities.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(photoactivable multi-inhibitor nanoliposome for tumor control and simultaneous inhibition of treatment escape pathways)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 158 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:112224 CAPLUS Full-text

DOCUMENT NUMBER: 164:213920

TITLE: Preparation of substituted urea derivatives as protein kinase modulators

INVENTOR(S): Cheng, Changchung; Zhang, Yingjun; Liu, Bing; Long, Bohua; Chen, Yu; Cheng, Zhixin

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China

SOURCE: PCT Int. Appl., 182pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

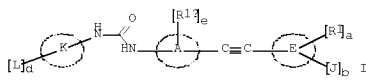
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2952083	A1	20160121	CA 2015-2952083	20150716
CN 105272930	A	20160127	CN 2015-10422604	20150716
AU 2015291522	A1	20161222	AU 2015-291522	20150716
KR 2017031669	A	20170321	KR 2016-7036774	20150716
US 20170114032	A1	20170427	US 2016-15314938	20161129
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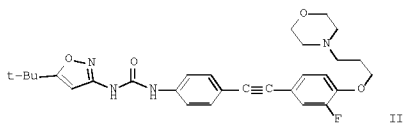
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 164:213920; MARPAT 164:213920

GI



I



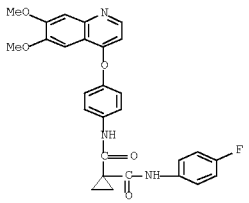
II

AB The title compds. I [ring A and ring E = (independently) C6-10 aryl or C1-12 heteroaryl; each J = G(CH2)nR2;each G = (independently) O, S(O)t, S, C(O), etc.; R1, R1a = H, F, Cl, Br, etc.; R2 = alkyl, cycloalkyl, heterocyclyl, etc.; ring K = 5-6 membered heteroaryl;each L = (independently) NH2, NO2, alkylthio, alkyl, etc.; each a and e = (independently) 0-4; each n, d and b = (independently) 1-4; and each t = (independently) 0-2], useful for preventing, managing, treating or lessening a proliferative disease, and modulating the activity of protein kinase, were prepared and claimed. E.g., a multi-step synthesis of the urea II, starting from 2-fluoro-4-iodophenol and N-(3-chloropropyl)morpholine, was described. Exemplified compds. I were tested for their activity against FLT3 kinase (data given for representative compds. I). Pharmaceutical compns. comprising compound I, alone or in combination with other therapeutic agents, were disclosed.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. as protein kinase modulators)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 159 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2016:44006 CAPLUS Full-text

TITLE: Purification of cabozantinib malate

INVENTOR(S): Reddy, Bandi Parthasaradhi; Reddy, Kura Rathnakar; Reddy, Dasari Muralidhara; Rao, Thungathurthy Srinivasa; Bandi, Vamsi Krishna

PATENT ASSIGNEE(S): Hetero Research Foundation, India

SOURCE: Indian Pat. Appl., 32pp.
CODEN: INXXBQ

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

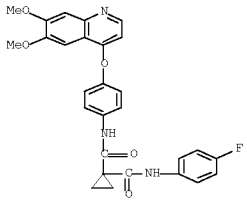
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2014CH01967	A	20160101	IN 2014-CH1967	20140415
PRIORITY APPLN. INFO.:			IN 2014-CH1967	20140415

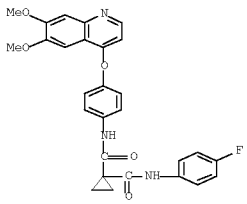
AB The present invention relates a novel cryst. form of Cabozantinib and Cabozantinib malate, process for its preparation and pharmaceutical compns. comprising it.

IT INDEXING IN PROGRESS

IT 849217-68-1, Cabozantinib
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(purification of cabozantinib malate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

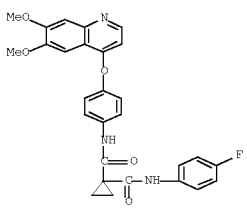


L4 ANSWER 160 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:2073656 CAPLUS Full-text
DOCUMENT NUMBER: 165:360261
TITLE: Hepatocyte growth factor and Met in drug discovery
AUTHOR(S): Sakai, Katsuya; Aoki, Shunsuke; Matsumoto, Kunio
CORPORATE SOURCE: Division of Tumor Dynamics and Regulation, Cancer Research Institute, Kanazawa University, Kanazawa, 920-1192, Japan
SOURCE: Journal of Biochemistry (2015), 157(5), 271-284
CODEN: JOBIAO; ISSN: 0021-924X
DIGITAL OBJECT ID: 10.1093/jb/mvv027
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of the hepatocyte growth factor (HGF) -Met pathway evokes dynamic biol. responses that support the morphogenesis, regeneration and survival of cells and tissues. A characterization of conditional Met knockout mice indicates that the HGF-Met pathway plays important roles in the regeneration, protection and homeostasis of cells such as hepatocytes, renal tubular cells and neurons. Preclin. studies in disease models have indicated that recombinant HGF protein and expression plasmid for HGF are biol. drug candidates for the treatment of patients with diseases or injuries that involve impaired tissue function. The phase-I and phase-I/II clin. trials of the intrathecal administration of HGF protein for the treatment of patients with amyotrophic lateral sclerosis and spinal cord injury, resp., are ongoing. Biol. actions of HGF that promote the dynamic movement, morphogenesis and survival of cells also closely participate in invasion-metastasis and resistance to the mol.-targeted drugs in tumor cells. Different types of HGF-Met pathway inhibitors are now in clin. trials for treatment of malignant tumors. Basic research on HGF and Met has lead to drug discoveries in regenerative medicine and tumor biol.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatocyte growth factor and Met in drug discovery)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 161 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:2060169 CAPLUS Full-text
DOCUMENT NUMBER: 166:36659
TITLE: Cabozantinib Inhibits Abiraterone's Upregulation of IGFIR Phosphorylation and Enhances Its Anti-Prostate Cancer Activity
AUTHOR(S): Wang, Xiaodong; Huang, Ying; Christie, Amanda; Bowden, Michaela; Lee, Gwo-Shu Mary; Kantoff, Philip W.; Sweeney, Christopher J.
CORPORATE SOURCE: Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SOURCE: Clinical Cancer Research (2015), 21(24), 5578-5587
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-15-0824
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Abiraterone improves the overall survival of men with metastatic castration-resistant prostate cancer. However, de novo or adaptive resistance to abiraterone limits its activity. Rational combinations of drugs with different mechanisms of action that overcome resistance mechanisms may improve the efficacy of therapy. To that end, we studied the mol. and phenotypic effects of the combination of cabozantinib plus abiraterone. Exptl. Design: Three prostate cancer cell lines were used to interrogate the in vitro mol. and antiproliferative effects of the single agents and combination of cabozantinib and abiraterone. The in vivo impact of the combination was assessed using the LAPC4-CR xenograft mouse model. Results: In vitro proliferation studies demonstrated single-agent doses between 2 μmol/L and 10 μmol/L for abiraterone and cabozantinib inhibit prostate cancer cell proliferation in a dose-dependent manner, and the anticancer activity of abiraterone is enhanced when combined with cabozantinib. In vivo LAPC4-CR xenograft mouse studies also showed that cabozantinib can improve the antitumor activity of abiraterone. Cabozantinib, a multiple receptor tyrosine kinase inhibitor, enhances the ability of abiraterone to inhibit AR activity in a cell line-dependent manner. In addition, our cell line studies demonstrate abiraterone-stimulated insulin-like growth factor I receptor (IGFIR) phosphorylation with downstream activation of MEK1/2 and ERK1/2, and that this potential adaptive resistance mechanism was inhibited by cabozantinib. Conclusions: Cabozantinib can enhance the efficacy of abiraterone by blocking multiple compensatory survival mechanisms, including IGFIR activation, and supports the assessment of the combination in a clin. trial. Clin Cancer Res; 21(24); 5578-87. ©2015 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib inhibits abiraterone's upregulation of IGFIR phosphorylation and enhances its anti-prostate cancer activity in LAPC4-CR xenograft mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

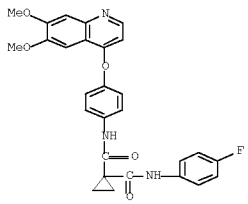
L4 ANSWER 162 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:2059342 CAPLUS Full-text
DOCUMENT NUMBER: 164:119066
TITLE: Methods and devices for treating posterior ocular disorders
INVENTOR(S): Noronha, Glenn; Brooks, Christopher John; Andino, Rafael Victor; Patel, Samirkumar; White, Daniel
PATENT ASSIGNEE(S): Clearside Biomedical, Inc., USA
SOURCE: PCT Int. Appl., 175pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015195842	A1	20151223	WO 2015-US36299	20150617
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2952822	A1	20151223	CA 2015-2952822	20150617
IL 249602	A	20170131	IL 2015-249602	20150617
AU 2015277133	A1	20170202	AU 2015-277133	20150617
KR 2017039128	A	20170410	KR 2017-7001356	20150617
EP 3157463	A1	20170426	EP 2015-808944	20150617
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
IN 201637044187	A	20170505	IN 2016-37044187	20161224

PRIORITY APPLN. INFO.:		
US 2014-62013209	P	20140617
US 2014-62018148	P	20140627
US 2014-62063792	P	20141014
US 2015-62155367	P	20150430
US 2015-62156802	P	20150504
WO 2015-US36299	W	20150617

AB The present invention relates to a methods and devices for treating uveitis, macular edema associated with uveitis and macular edema associated with retinal vein occlusion in a human subject in need thereof. In certain aspects, devices provided herein include a medicament container defining a lumen configured to contain a medicament, a distal end portion of the medicament container including a coupling portion configured to be removably coupled to a needle assembly, a proximal end portion of the medicament container including a flange and a longitudinal shoulder; a piston assembly including a distal end portion movably disposed within the lumen of the medicament container; and a handle coupled to a proximal end portion of the piston assembly.
IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(methods and devices for treating posterior ocular disorders)
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

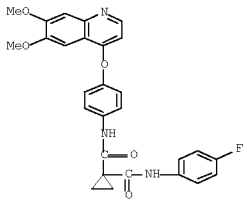
L4 ANSWER 163 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:2015841 CAPLUS Full-text
DOCUMENT NUMBER: 164:99265
TITLE: Anti-human Tumor endothelial marker TEM8 antibodies and other molecularly targeted agent for combination therapy of cancer
INVENTOR(S): Saha, Saurabh; Zhang, Xiaoyan M.; Dimitrov, Dimiter; Zhu, Zhongyu; St. Croix, Brad; Zudaire, Enrique
PATENT ASSIGNEE(S): Biomed Valley Discoveries, Inc., USA; Untied States Dept. of Health and Human Services
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015191610	A2	20151217	WO 2015-US34941	20150609
WO 2015191610	A3	20160204		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

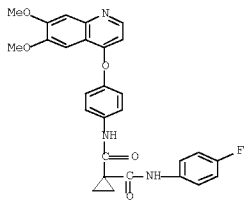
US 20170095575 A1 20170406 US 2016-15317079 20161207
PRIORITY APPLN. INFO.: US 2014-62009371 P 20140609
WO 2015-US34941 W 20150609

AB The present invention provides, inter alia, methods for treating or ameliorating the effects of a disease, such as cancer, in a subject. The methods include: administering to a subject in need thereof (a) a therapeutically effective amount of a molecularly targeted agent; and (b) a therapeutically effective amount of a monoclonal antibody or antigen binding fragment thereof, wherein the monoclonal antibody contains: (i) a heavy chain variable region (VH), which includes an amino acid sequence selected from SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, and SEQ ID NO:7; and (ii) a light chain variable region (VL), which includes an amino acid sequence selected from SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8. Compns., including pharmaceutical compns., and kits for treating diseases, such as cancer, are also provided herein.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human Tumor endothelial marker TEM8 antibodies and other molecularly targeted agent for combination therapy of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 164 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:2008346 CAPLUS Full-text
DOCUMENT NUMBER: 164:136379
TITLE: Bioluminescent kinase strips: A novel approach to targeted and flexible kinase inhibitor profiling
AUTHOR(S): Hennek, J.; Alves, J.; Yao, E.; Goueli, S. A.; Zegzouti, H.
CORPORATE SOURCE: R&D Department, Promega Corporation, Madison, WI, 53711, USA
SOURCE: Analytical Biochemistry (2016), 495, 9-20
CODEN: ANBCA2; ISSN: 0003-2697
DIGITAL OBJECT ID: 10.1016/j.ab.2015.11.007
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB In addn. to target efficacy, drug safety is a major requirement during the drug discovery process and is influenced by target specificity. Therefore, it is imperative that every new drug candidate be profiled against various liability panels that include protein kinases. Here, an effective methodol. to streamline kinase inhibitor profiling is described. An accessible standardized profiling system for 112 protein kinases covering all branches of the kinome was developed. This approach consists of creating different sets of kinases and their corresponding substrates in multi-tube strips. The kinase stocks are pre-standardized for optimal kinase activity and used for inhibitor profiling using a bioluminescent ADP detection assay. The authors show that these strips can routinely generate inhibitor selectivity profiles for small or broad kinase family panels. Lipid kinases were also assembled in strip format and profiled together with protein kinases. The authors identified two specific PI3K inhibitors that have off-target effects on CK2 that were not reported before and would have been missed if compds. were not profiled against lipid and protein kinases simultaneously. To validate the accuracy of the data generated by this method, the authors confirmed that the inhibition potencies observed are consistent with published values produced by more complex technologies such as radioactivity assays.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioluminescent kinase strips as novel approach to targeted and flexible kinase inhibitor profiling)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



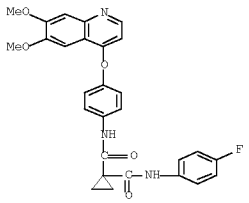
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 165 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:2005012 CAPLUS Full-text
DOCUMENT NUMBER: 165:218414
TITLE: A chemical screening approach to identify novel key mediators of erythroid enucleation
AUTHOR(S): Wolwer, Christina B.; Pase, Luke B.; Pearson, Helen B.; Godde, Nathan J.; Lackovic, Kurt; Huang, David C. S.; Russell, Sarah M.; Humbert, Patrick O.
CORPORATE SOURCE: Cell Cycle and Cancer Genetics, Peter MacCallum Cancer Centre, Melbourne, Australia
SOURCE: PLoS One (2015), 10(11), e0142655/1-e0142655/12
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0142655
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Erythroid enucleation is crit. for terminal differentiation of red blood cells, and involves extrusion of the nucleus by orthochromatic erythroblasts to produce reticulocytes. Due to the difficulty of synchronizing erythroblasts, the mol. mechanisms underlying the enucleation process remain poorly understood. To elucidate the cellular program governing enucleation, we utilized a novel chemical screening approach whereby orthochromatic cells primed for enucleation were enriched ex vivo and subjected to a functional drug screen using a 324 compound library consisting of structurally diverse, medicinally active and cell permeable drugs. Using this approach, we have confirmed the role of HDACs, proteasomal regulators and MAPK in erythroid enucleation and introduce a new role for Cyclin-dependent kinases, in particular CDK9, in this process. Importantly, we demonstrate that when coupled with imaging anal., this approach provides a powerful means to identify and characterize rate limiting steps involved in the erythroid enucleation process.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical screening approach to identify novel key mediators of erythroid enucleation)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

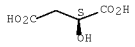
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

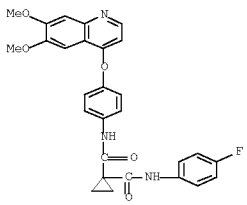
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 166 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1965343 CAPLUS Full-text
DOCUMENT NUMBER: 164:566304
TITLE: Repurposing of anticancer drugs: in vitro and in vivo activities against Schistosoma mansoni
AUTHOR(S): Cowan, Noemi; Keiser, Jennifer
CORPORATE SOURCE: Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, CH-4002, Switz.
SOURCE: Parasites & Vectors (2015), 8, 1-9
CODEN: PVAEAK; ISSN: 1756-3305
DIGITAL OBJECT ID: 10.1186/s13071-015-1023-y
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Drug discovery for the neglected tropical disease schistosomiasis has a high priority. Anticancer drugs, especially protein kinase inhibitors, might serve as a starting point for drug discovery owing to the importance of protein kinases in helminth growth and development. Furthermore, the Schistosoma mansoni genome encodes several genes for targets of drugs marketed for human use, including several anticancer drugs. Methods: In this study, we screened the approved oncol. drug set of the National Cancer Institute's Developmental Therapeutic Program for antischistosomal activity. Drugs were tested in vitro against the larval and adult stage of S. mansoni. IC50 values and albumin binding were determined for active compds. Lead compds. were tested in the chronic S. mansoni mouse model. Results: Eleven of the 114 compds. tested revealed IC50 values ≤ 10 μM against both S. mansoni stages. Five of these lost activity against adult S. mansoni in the presence of serum albumin. Of 6 compds. studied in vivo, the highest activity was observed from two kinase inhibitors trametinib, and vandetanib, which reduced worm burden by 63.6 and 48.1 % resp., after a single oral dose of 400 mg/kg body weight Conclusion: Our study has confirmed that oncol. drugs possess antischistosomal activity. There is space for further investigation, including elucidation of the mechanisms of action of schistosome-active cancer drugs, application of different treatment courses, and structure-activity relationship studies for improving drug potency.
IT 849217-68-1, Cabozantinib

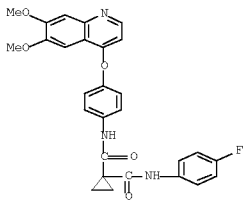
as targets for drugs already approved by the US Food and Drug Administration (FDA) for use in humans. In this context, we defined here the kinome of S. haematobium using a refined bioinformatic pipeline. We classified, curated and annotated predicted kinases, and assessed the developmental transcription profiles of kinase genes. Then, we prioritised a panel of kinases as potential drug targets and inferred chems. that bind to them using an integrated bioinformatic pipeline. Most kinases of S. haematobium are very similar to those of its congener, S. mansoni, offering the prospect of designing chems. that kill both species. Overall, this study provides a global insight into the kinome of S. haematobium and should assist the repurposing or discovery of drugs against schistosomiasis.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(defining Schistosoma haematobium kinome enables prediction of essential kinases as anti-schistosome drug targets)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 112 THERE ARE 112 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 168 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1916188 CAPLUS Full-text
DOCUMENT NUMBER: 166:252975
TITLE: Clinical observation of liver cancer patients treated with axitinib and cabozantinib after failed sorafenib treatment: a case report and literature review
AUTHOR(S): Zhang, Bin; Zhang, Xia; Zhou, Tao; Liu, Jiwei
CORPORATE SOURCE: Department of Oncology, The First Affiliated Hospital of Dalian Medical University, Dalian, Peop. Rep. China
SOURCE: Cancer Biology & Therapy (2015), 16(2), 215-218
CODEN: CBTAAO; ISSN: 1555-8576
DIGITAL OBJECT ID: 10.4161/15384047.2014.962318
PUBLISHER: Taylor & Francis Ltd.

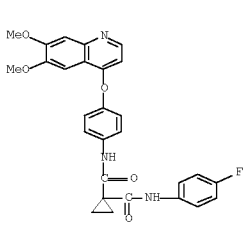
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro drug testing against larval and adult stage of Schistosoma mansoni and determination of IC50 values and albumin binding for active compds., also lead compds. were tested in chronic Schistosoma mansoni mouse model)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 167 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1955534 CAPLUS Full-text
DOCUMENT NUMBER: 165:359865
TITLE: Defining the Schistosoma haematobium kinome enables the prediction of essential kinases as anti-schistosome drug targets
AUTHOR(S): Stroehlein, Andreas J.; Young, Neil D.; Jex, Aaron R.; Sternberg, Paul W.; Tan, Patrick; Boag, Peter R.; Hofmann, Andreas; Gasser, Robin B.
CORPORATE SOURCE: Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Parkville, Australia
SOURCE: Scientific Reports (2015), 5, 17759
CODEN: SRCEC3; ISSN: 2045-2322
DIGITAL OBJECT ID: 10.1038/srep17759
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The blood fluke Schistosoma haematobium causes urogenital schistosomiasis, a neglected tropical disease (NTD) that affects more than 110 million people. Treating this disease by targeted or mass administration with a single chemical, praziquantel, carries the risk that drug resistance will develop in this pathogen. Therefore, there is an imperative to search for new drug targets in S. haematobium and other schistosomes. In this regard, protein kinases have potential, given their essential roles in biol. processes and

DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Hepatocellular carcinoma (HCC) is a major pathol. type of primary liver cancer. Sorafenib has demonstrated definite efficacy in targeted therapy for HCC. However, when treatment with sorafenib fails, suitable drugs must be found for further treatment. This article reports a case of an HCC patient who was treated with angiogenesis inhibitor axitinib and c-Met inhibitor cabozantinib following treatment with sorafenib. The report focuses on clin. treatment and toxicity. Rational application of targeted therapy is also explored.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. observation of liver cancer patients treated with axitinib and cabozantinib after failed sorafenib treatment)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 169 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1897715 CAPLUS Full-text
DOCUMENT NUMBER: 166:321338
TITLE: Cabozantinib: an orphan drug for thyroid cancer
AUTHOR(S): Viola, D.; Cappagli, V.; Matrone, A.; Mazzeo, S.; Elisei, R.
CORPORATE SOURCE: Endocrine Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56124, Italy
SOURCE: Expert Opinion on Orphan Drugs (2015), 3(12), 1469-1477
CODEN: EOODAJ; ISSN: 2167-8707
DIGITAL OBJECT ID: 10.1517/21678707.2015.1112789
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)

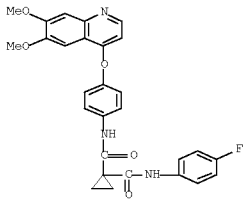
LANGUAGE: English

AB Until recently, no therapeutic options were available for the treatment of advanced medullary thyroid cancer (MTC). Cabozantinib (XL184) is a novel tyrosine kinase inhibitor (TKI) that inhibits several tyrosine kinase receptors, in particular those coded by MET, VEGFR-2 and RET oncogenes that are considered to be involved in the pathogenesis of MTC. This article provides an overview of the phase I and III trials that demonstrated the efficacy of cabozantinib in two cohorts of advanced MTC patients who were naive or previously treated with other TKIs. The benefits in terms of progression-free survival (PFS), overall survival (OS) and the demog. clin. and mutational status of the two cohorts of MTC patients are reported and discussed. The possibility to have a therapeutic option for the treatment of patients with advanced and progressive MTC and, in particular, the evidence that the drug can be active also in those patients who already experienced disease progression while taking another TKI is a great opportunity as demonstrated in cases treated with cabozantinib after vandetanib such as the one reported in this paper.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib, an orphan drug for thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 170 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1892326 CAPLUS Full-text

DOCUMENT NUMBER: 163:709974

TITLE: Novel polymorphs of cabozantinib (S)-malate and cabozantinib free base

INVENTOR(S): Jetti, Ramakoteswara Rao; Indukuri, Anjaneyaraju; Punde, Dnyandeo; Bohra, Chandersingh; Gadakar, Mahesh Kumar; Gore, Vinayak

PATENT ASSIGNEE(S): Mylan Laboratories Ltd., India

SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015177758	A1	20151126	WO 2015-IB53765	20150522
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
IN 2014CH02561	A	20160115	IN 2014-CH2561	20140523
EP 3145913	A1	20170329	EP 2015-728635	20150522
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20170096395	A1	20170406	US 2016-15313191	20161122

PRIORITY APPLN. INFO.: IN 2014-CH2561 A 20140523
WO 2015-IB53765 W 20150522

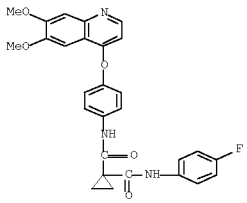
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present disclosure provides novel cryst. forms of cabozantinib (S)-malate, designated as form-M1, M2, M3 and M4 and novel crystalline forms of cabozantinib free base, form-M1, M2 and M3 and methods of their production The present disclosure also provides processes for the preparation of crystalline cabozantinib (S)-malate form N-1. Formula (I).

IT 849217-68-1, Cabozantinib
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(novel polymorphs of cabozantinib (S)-malate and cabozantinib free base)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



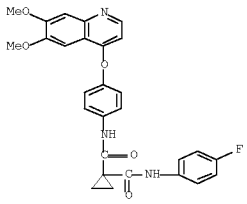
IT 1140909-48-3P, Cabozantinib (S)-malate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(novel polymorphs of cabozantinib (S)-malate and cabozantinib free base)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

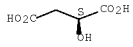
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 171 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1833484 CAPLUS Full-text

DOCUMENT NUMBER: 164:370558

TITLE: Identification of Bone-Derived Factors Conferring De Novo Therapeutic Resistance in Metastatic Prostate Cancer

AUTHOR(S): Lee, Yu-Chen; Lin, Song-Chang; Yu, Guoyu; Cheng, Chien-Jui; Liu, Bin; Liu, Hsuan-Chen; Hawke, David H.; Parikh, Nila U.; Varkaris, Andreas; Corn, Paul; Logothetis, Christopher; Satcher, Robert L.; Yu-Lee, Li-Yuan; Gallick, Gary E.; Lin, Sue-Hwa

CORPORATE SOURCE: Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

SOURCE: Cancer Research (2015), 75(22), 4949-4959
CODEN: CNREA8; ISSN: 0008-5472

DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-15-1215

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

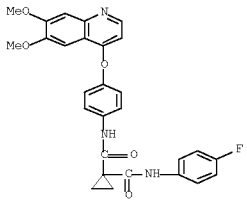
AB Resistance to currently available targeted therapies significantly hampers the survival of patients with prostate cancer with bone metastasis. Here we demonstrate an important resistance mechanism initiated from tumor-induced bone. Studies using an osteogenic patient-derived xenograft, MDA-PCa-118b, revealed that tumor cells resistant to cabozantinib, a Met and VEGFR-2 inhibitor, reside in a "resistance niche" adjacent to prostate cancer-induced bone. We performed secretome anal. of the conditioned medium from tumor-induced bone to identify proteins (termed "osteocrines") found within this resistance niche. In accordance with previous reports demonstrating that activation of integrin signaling pathways confers therapeutic resistance, 27 of the 90 osteocrines identified were integrin ligands. We found that following cabozantinib treatment, only tumor cells positioned adjacent to the newly formed woven bone remained viable and expressed high levels of pFAK-Y397 and pTalin-S425, mediators of integrin signaling. Accordingly, treatment of C4-2B4 cells with integrin ligands resulted in increased pFAK-Y397 expression and cell survival, whereas targeting integrins with FAK inhibitors PF-562271 or defactinib inhibited FAK phosphorylation and reduced the survival of PC3-mm2 cells. Moreover, treatment of MDA-PCa-118b tumors with PF-562271 led to decreased tumor growth, irresp. of initial tumor size. Finally, we show that upon treatment cessation, the combination of PF-562271 and cabozantinib delayed tumor recurrence in contrast to cabozantinib treatment alone. Our studies suggest that identifying paracrine de novo resistance mechanisms may significantly contribute to the generation of a broader set of potent therapeutic tools

that act combinatorially to inhibit metastatic prostate cancer. Cancer Res; 75(22); 4949-59. ©2015 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(paracrine de novo resistance factors significantly contribute to generation of bone formation, therapeutic resistance and inhibit metastatic prostate cancer cells and in human and mouse model)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 172 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1805828 CAPLUS Full-text

DOCUMENT NUMBER: 163:694481

TITLE: Acetylenedicarboxyl linkers and their uses in specific conjugation of a cell-binding molecule

INVENTOR(S): Zhao, Robert Yongxin

PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China

SOURCE: U.S. Pat. Appl. Publ., 80pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

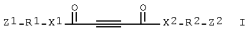
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150322155	A1	20151112	US 2015-14799666	20150715

PRIORITY APPLN. INFO.: US 2015-14799666 20150715

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 163:694481; MARPAT 163:694481

GI

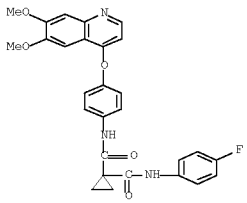


AB Provided are novel acetylenedicarboxyl linkers used for the specific conjugation of compds./cytotoxic agents to a cell-binding mol., through bridge linking pairs of thiols on the cell-binding mol. Also provided are methods of making such linkers, and of using such linkers in making homogeneous conjugates, as well as of application of the conjugates in treatment of cancers, infections and autoimmune disorders. Particularly provided is a bridge linker compound of the Formula (I), wherein:The acetylenedicarboxyl group is capable of reacting with a pair of sulfur atoms of the cell-binding agent; Z1 and Z2 are the same or different a function group that enables to react with a cytotoxic drug; R1 and R2 are the same or different linear alkyl; X1 and X2 are independently selected from NH, N(R3), O, S or CH2; R3 is H, linear alkyl.

IT 849217-68-1, Cabozan-tinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-therapy with; acetylenedicarboxyl linkers and their uses in specific conjugation of cell-binding mol.)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 173 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1783974 CAPLUS Full-text

DOCUMENT NUMBER: 166:119601

TITLE: New molecularly targeted therapies against advanced hepatocellular carcinoma: From molecular pathogenesis to clinical trials and future directions

AUTHOR(S): Chuma, Makoto; Terashita, Katsumi; Sakamoto, Naoya

CORPORATE SOURCE: Department of Gastroenterology and Hepatology, Hokkaido University, Sapporo, Japan

SOURCE: Hepatology Research (2015), 45(10), E1-E11
CODEN: HPRSFM; ISSN: 1386-6346

DIGITAL OBJECT ID: 10.1111/hepr.12459

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; General Review; (online computer file)

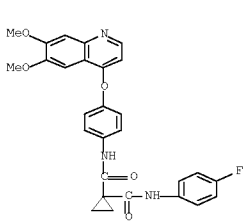
LANGUAGE: English

AB Hepatocellular carcinoma (HCC) can be lethal due to its aggressive course and lack of effective systemic therapies for advanced disease. Sorafenib is the only systemic therapy that has demonstrated an overall survival benefit in patients with advanced HCC, and new agents for treatment of advanced HCC are needed. The multiple pathways involved in HCC oncogenesis, proliferation and survival provide many opportunities for the development of molecularly targeted therapies. Mol. targets of interest have expanded from angiogenesis to cancer cell-directed oncogenic signaling pathways for treatment of advanced HCC. Agents targeting vascular endothelial growth factor receptor, epidermal growth factor receptor, fibroblast growth factor receptor, platelet-derived growth factor receptor, c-mesenchymal-epithelial transition factor-1 and mammalian target of rapamycin signaling have been actively explored. This article focuses on the evaluation of mol. agents targeting pathogenic HCC and provides a review of recently completed phase III drug studies (e.g. involving sorafenib, sunitinib, brivanib, linifanib, erlotinib, everolimus, ramucirumab or orantinib) and ongoing drug studies (e.g. involving lenvatinib, regorafenib, tivantinib or cabozantinib) of molecularly targeted agents in advanced HCC, including a brief description of the biol. rationale behind these agents.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of sorafenib, sunitinib, brivanib, linifanib, erlotinib, everolimus, ramucirumab/orantinib and lenvatinib, regorafenib, tivantinib/cabozantinib of molecularly targeted agents in patients with advanced hepatocellular carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 174 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1783428 CAPLUS Full-text

DOCUMENT NUMBER: 163:681013

TITLE: Cabozantinib for the treatment of progressive metastatic medullary thyroid cancer

AUTHOR(S): Krajewska, Jolanta; Olczyk, Tomasz; Jarzab, Barbara

CORPORATE SOURCE: Nuclear Medicine and Endocrine Oncology Department, M.Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Pol.

SOURCE: Expert Review of Clinical Pharmacology (2016), 9(1), 69-79
CODEN: ERCPAG; ISSN: 1751-2433

DIGITAL OBJECT ID: 10.1586/17512433.2016.1102052

PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

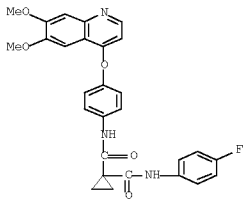
LANGUAGE: English

AB A review. Cabozantinib (XL-184) is a potent inhibitor of MET, VEGFR 2/KDR, RET and other receptor tyrosine kinases, such as KIT, AXL and FLT3. Its efficacy against MTC has been demonstrated in a prospective, randomized, placebo-controlled study (EXAM). Cabozantinib comparing to placebo significantly prolonged progression free survival both in hereditary and sporadic MTC, 11.2 vs. 4.0 mo, resp. Final anal. showed no global differences in overall survival (OS) between cabozantinib and placebo. However, in a subgroup with RET M918T mutation the difference in OS was significant: 44.3 vs. 18.9 mo, resp. Among the most frequent cabozantinib-related adverse events (AEs), observed in >30% of patients were diarrhea, palmar-plantar erythrodysesthesia, decreased weight, decreased appetite, nausea, fatigue, dysgeusia, hair color changes and hypertension. Expert Commentary: Cabozantinib constitutes an effective treatment option with acceptable toxicity in MTC patients showing either germinal or sporadic tumor RET M918T mutation as the drug prolonged OS in these subjects.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of progressive metastatic medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



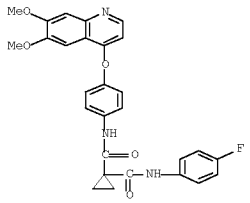
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 175 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1726025 CAPLUS Full-text
DOCUMENT NUMBER: 163:628844
TITLE: Method of treating lung adenocarcinoma
INVENTOR(S): Aftab, Dana T.; Yu, Peiwen
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015164869	A1	20151029	WO 2015-US27800	20150427
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2946416	A1	20151029	CA 2015-2946416	20150427
AR 100191	A1	20160914	AR 2015-101255	20150427
AU 2015249232	A1	20161110	AU 2015-249232	20150427
KR 2016147934	A	20161223	KR 2016-7033010	20150427
IL 248408	A	20161229	IL 2015-248408	20150427
EP 3134084	A1	20170301	EP 2015-721100	20150427
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 106488768	A	20170308	CN 2015-80022580	20150427
US 20170042880	A1	20170216	US 2016-15305854	20161021

PRIORITY APPLN. INFO.: US 2014-61984599 P 20140425
WO 2015-US27800 W 20150427
OTHER SOURCE(S): CASREACT 163:628844; MARPAT 163:628844
AB This invention is directed to the treatment of cancer in a patient, particularly a patient with lung adenocarcinoma, and more particularly a patient with SLC34A2-ROS1, CD74-ROS1, or FIG-ROS1 fusion-pos. non-small cell lung cancer, with an inhibitor of MET, VEGFR2, and ROS1.
IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(treating lung adenocarcinoma)

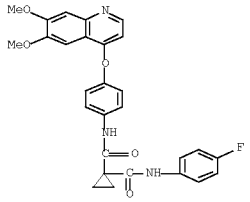
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treating lung adenocarcinoma)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

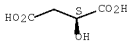
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

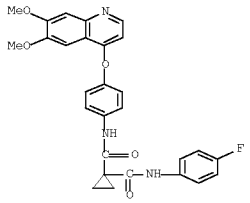
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating lung adenocarcinoma)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

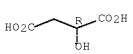
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

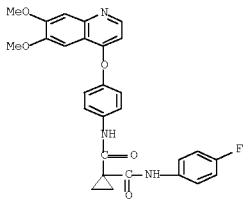


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 176 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1723003 CAPLUS Full-text
DOCUMENT NUMBER: 163:632038
TITLE: Hepatocyte growth factor as marker of prognosis in small cell lung cancer (SCLC)
INVENTOR(S): Arriola Aperribay, Edurne; Canadas Castillo, Israel; Rovira Guerin, Ana; Albanell Mestres, Joan
PATENT ASSIGNEE(S): Fundacio Institut Mar d'Investigacions Mediques (IMIM), Spain
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015161885	A1	20151029	WO 2014-EP58375	20140424
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20160327559	A1	20161110	US 2016-15108249	20160624

PRIORITY APPLN. INFO.: WO 2014-EP58375 W 20140424
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention relates to a new marker, the hepatocyte growth factor (HGF) in serum or plasma for the prognosis of small-cell lung cancer (SCLC). The invention also provides methods for selecting subjects suffering from SCLC that are candidate to respond to certain substances inhibiting certain kinases expressed in the tumors. There are also encompassed the use of immunoassay and nucleic acid reagents for detecting HGF in serum or plasma, said reagents for carrying out the prognostic method.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatocyte growth factor in serum or plasma as prognostic marker of small-cell lung cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

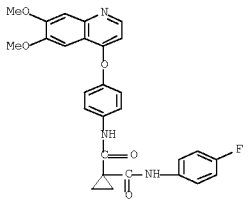
L4 ANSWER 177 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1694942 CAPLUS Full-text
DOCUMENT NUMBER: 163:596944
TITLE: Methods for treating cancer using TOR kinase inhibitor combination therapy
INVENTOR(S): Fultz, Kimberly Elizabeth; Tran, Tam Minh; Xu, Shuichan; Xu, Weiming; Trowe, Torsten; Filvaroff, Ellen
PATENT ASSIGNEE(S): Signal Pharmaceuticals, LLC, USA
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015160868	A1	20151022	WO 2015-US25843	20150415
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
NZ 629860	A	20160129	NZ 2014-629860	20140902
US 20150297590	A1	20151022	US 2015-14686872	20150415
EP 3131552	A1	20170222	EP 2015-780570	20150415
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

PRIORITY APPLN. INFO.: US 2014-61980124 P 20140416
WO 2015-US25843 W 20150415
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Provided are methods for treating or preventing cancer, comprising administering an effective amount of a 3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one TOR kinase inhibitor and an effective amount of a second active agent to a patient. Cancers treated by the method include solid tumors of the head, neck, breast, lung, ovaries, colon, rectum, stomach, prostate, urinary bladder, uterine, cervix, and other reproductive organs, wherein the tumors include relapsed, refractory or advanced solid tumors.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy using pyrazinopyrazine TOR kinase inhibitors for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

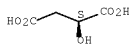
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

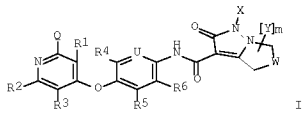


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

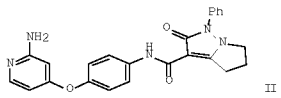
L4 ANSWER 178 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1694572 CAPLUS Full-text
DOCUMENT NUMBER: 163:601731
TITLE: Preparation of bicyclic pyrazolone compounds for inhibiting or modulating the activity of receptor tyrosine kinases
INVENTOR(S): Xi, Ning; Wu, Yanjun
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: U.S. Pat. Appl. Publ., 52pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150299219	A1	20151022	US 2015-14687992	20150416
WO 2015164161	A1	20151029	WO 2015-US26062	20150416
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 3134088	A1	20170301	EP 2015-782304	20150416
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

PRIORITY APPLN. INFO.: US 2014-61982729 P 20140422
WO 2015-US26062 W 20150416
OTHER SOURCE(S): CASREACT 163:601731; MARPAT 163:601731
GI

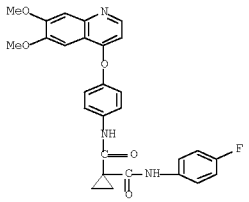


I



II

AB The title compds. I [Q = H, (un)substituted OH, NH2, etc.; U = CR7 or N; X = H, alkyl, cycloalkyl, etc.; Y = alkyl, cycloalkyl, aryl, etc.; m = 0-4; W = (CH2)n, (CH2)nO, (CH2)nNH, (CH2)nS (wherein n = 0-4); R1-R7 = H, F, Cl, Br, etc.; with the provisos], which are used to inhibit or modulate the activity of receptor tyrosine kinases, especially Axl, Mer, c-Met and Ron, were prepared E.g., a multi-step synthesis of II, starting from phenylhydrazine and 4-chlorobutanoyl chloride, was described. Exemplified compds. I were tested for their biol. activity (data given for representative compds. I). The invention also provides pharmaceutical compns. comprising the compound I, and a method of preventing, treating or lessening the severity of a proliferative disorder in a patient with the compds. I or the pharmaceutical compns. comprising I.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of bicyclic pyrazolone compds. for inhibiting or modulating the activity of receptor tyrosine kinases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

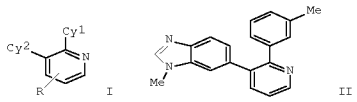


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

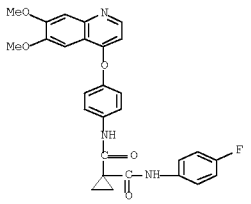
L4 ANSWER 179 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1654358 CAPLUS Full-text
DOCUMENT NUMBER: 163:601695
TITLE: 2,3-Disubstituted pyridine compounds as TGF-beta inhibitors and their preparation
INVENTOR(S): Singh, Rajinder; Bhamidipati, Somasekhar; Ding, Pingyu; Payan, Donald; Gelman, Marina; Kinsella, Todd
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 406pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015157093	A1	20151015	WO 2015-US24146	20150402
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 3129367	A1	20170215	EP 2015-716690	20150402
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 106536507	A	20170322	CN 2015-80030111	20150402
AR 99991	A1	20160831	AR 2015-101066	20150408
US 20170096409	A1	20170406	US 2016-15128051	20160921
IN 201617032604	A	20170120	IN 2016-17032604	20160923

PRIORITY APPLN. INFO.: US 2014-61976880 P 20140408
US 2014-62019577 P 20140701
WO 2015-US24146 W 20150402
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 163:601695; MARPAT 163:601695
GI



AB The invention described compds. of formula I and a method of treating cancer comprising administering to a subject having cancer one of the compds. in conjunction with another therapeutic treatment of cancer. The compds. I inhibit signaling by a member of the TGF-β superfamily such as nodal or activin. Compds. of formula I wherein Cyl is (un)substituted Ph, benzofuranyl, (un)substituted C1-3 alkyl, etc.; Cy2 is pyrazolo[1,5-a]pyrimidinyl, benzothiazolyl, imidazo[1,2-a]pyridinyl, (un)substituted phenylsulfonyl, etc.; R is (un)substituted Ph, (un)substituted heteroaryl and (un)substituted heterocycloalkyl; and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by cross-coupling of 2-chloro-2-(3-methylphenyl)pyridine with 1-methyl-1H-benzimidazole-6-boronic acids. The invention compds. were evaluated for their TGF-β inhibitory activity (some data given).
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of disubstituted pyridine compds. as TGF-β inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

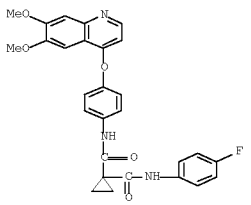
L4 ANSWER 180 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1650548 CAPLUS Full-text
DOCUMENT NUMBER: 163:585951
TITLE: Preparation of bridge linkers used for specific conjugation of two or more cytotoxic agents to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin; Zhao, Robert
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015155753	A2	20151015	WO 2015-IB56083	20150810
WO 2015155753	A3	20160630		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150284416	A1	20151008	US 2015-14740403	20150616

PRIORITY APPLN. INFO.: US 2015-14740403 TO 20150616
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 163:585951; MARPAT 163:585951
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to novel linkers contg. a 2,3-disubstituted succinic group, or 2-monosubstituted, or 2,3-disubstituted fumaric or maleic (trans (E)- or cis (Z)-butenedioic) group, e.g., (I), for conjugation of two or more compds./cytotoxic agents per linker to a cell-binding mol., through bridge linking pairs of thiols (reduced from the interchain disulfide bonds of the cell-binding agent by a reducing agent, such as dithiothreitol, dithioerythritol, L-glutathione and tris(2-carboxyethyl)phosphine (TCEP), or/and β-mercaptoethanol) on the cell-binding mol. specifically. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by treating reaction with drugs and to their use for cancers, infections and autoimmune disorders. Thus, linker I was prepared by cyclization of 2,3-dibromosuccinic acid in CH2Cl2 in the presence of P2O5. R1-COCHBrCHBrCO-R (II) was prepared in 3 steps from I and R1-H (preparation given) using R = H (preparation given). A herceptin antibody conjugate with II was prepared by reacting herceptin with and TCEP and II. The resulting conjugate was evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 889 and for SK-OV-3 cell was over 800. Five-week-old female BALB/c Nude mice inoculated s.c. in the area under the right shoulder with N-87 carcinoma cells treated with the conjugate had completely no tumor measurable at day 13 till day 60 (the end of experiment) in an in vivo antitumor activity study.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of two or more cytotoxic agents to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of two or more cytotoxic agents to a cell-binding mol.

L4 ANSWER 181 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1646639 CAPLUS Full-text
DOCUMENT NUMBER: 163:612041
TITLE: Method for screening antitumor drug biomarkers, and application thereof
INVENTOR(S): Xiong, Lei
PATENT ASSIGNEE(S): HTS Biotechnology (Shanghai) Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 23pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

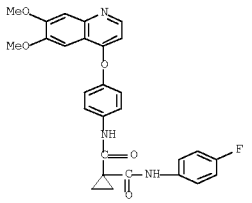
CN 104975063	A	20151014	CN 2014-10130154	20140401
PRIORITY APPLN. INFO.:			CN 2014-10130154	20140401

AB The invention discloses method for screening antitumor drug biomarkers, and application thereof. The method comprises the steps of: (1) providing tumor cells as starting cells, and tumor cells are from identical tumor tissue of the same object, (2) performing passage of the starting cells, establishing cell lines, and detecting genomic information of the cell lines so as to obtain at least 5 tumor cell lines that have genomic differences and are highly homologous, (3) performing antitumor drug sensitivity testing of the tumor cell lines, and typing the tumor cell lines based on the testing results, and (4) based on the typing results, analyzing the genomic information of the tumor cell lines to determine anti-tumor drug biomarkers. The method can maximally reduce background noise between different tumor cell lines, and can help to efficiently and accurately screen biomarkers of antitumor drugs.

IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); BUU (Biological use, unclassified); PAC (Pharmacological activity); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(method for screening antitumor drug biomarkers, and application thereof)

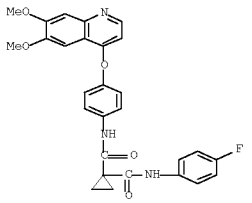
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 182 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER:	2015:1640328 CAPLUS Full-text
DOCUMENT NUMBER:	163:618028
TITLE:	Preparation of bicyclopyrazolone compounds as tyrosine kinase inhibitors
INVENTOR(S):	Xi, Ning; Wu, Yanjun
PATENT ASSIGNEE(S):	Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE:	Faming Zhuanli Shenqing, 81pp. CODEN: CNXXEV
DOCUMENT TYPE:	Patent
LANGUAGE:	Chinese



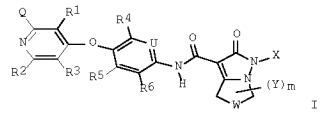
L4 ANSWER 183 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER:	2015:1635205 CAPLUS Full-text
DOCUMENT NUMBER:	164:550339
TITLE:	Selective targeting of CTNNB1-, KRAS- or MYC-driven cell growth by combinations of existing drugs
AUTHOR(S):	Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; Spijkers-Hagelstein, Jill A. P.; de Vetter, Judith R. F.; de Man, Jos; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE:	Netherlands Translational Research Center B.V., Oss, Neth.
SOURCE:	PLoS One (2015), 10(5), e0125021/1-e0125021/22 CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID:	10.1371/journal.pone.0125021
PUBLISHER:	Public Library of Science
DOCUMENT TYPE:	Journal; (online computer file)
LANGUAGE:	English

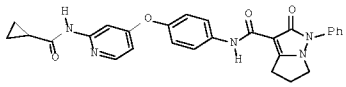
AB The aim of combination drug treatment in cancer therapy is to improve response rate and to decrease the probability of the development of drug resistance. Preferably, drug combinations are synergistic rather than additive, and, ideally, drug combinations work synergistically only in cancer cells and not in non-malignant cells. We have developed a workflow to identify such targeted synergies, and applied this approach to selectively inhibit the proliferation of cell lines with mutations in genes that are difficult to modulate with small mols. The approach is based on curve shift anal., which we demonstrate is a more robust method of determining synergy than combination matrix screening with Bliss-scoring. We show that the MEK inhibitor trametinib is more synergistic in combination with the BRAF inhibitor dabrafenib than with vemurafenib, another BRAF inhibitor. In addition, we show that the combination of MEK and BRAF inhibitors is synergistic in BRAF-mutant melanoma cells, and additive or antagonistic in, resp., BRAF-wild type melanoma cells and non-malignant fibroblasts. This combination exemplifies that synergistic action of drugs can depend on cancer genotype. Next, we used curve shift anal. to identify new drug combinations that specifically inhibit cancer cell proliferation driven by difficult-to-drug cancer genes. Combination studies were performed with compds. that as single agents showed preference for inhibition of cancer cells with mutations in either the CTNNB1 gene (coding for β-catenin), KRAS,

FAMILY ACC. NUM. COUNT:	1				
PATENT INFORMATION:					
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CN 104974162	A	20151014	CN 2015-10167125		20150409
PRIORITY APPLN. INFO.:			CN 2014-10141156	A	20140409
OTHER SOURCE(S):	MARPAT 163:618028				

GI



I



II

AB The invention provides bicyclopyrazolone compds. I [wherein Q = H, (un)substituted OH, NH2, etc.; U = (un)substituted CH or N; X = H, alkyl, alkenyl, alkynyl, etc.; Y = independently H, alkyl, alkenyl, etc.; W = (CH2)n, (CH2)nO, (CH2)nNH, or (cH2)nS; n = 0-4; R1-R6 = independently H, F, Cl, Br, CN, N3, etc.; m = 1-4; with provisos], stereoisomers, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts, or prodrugs thereof for suppressing the activity of receptor tyrosine kinase, especially Axl, Mer, c-Met and Ron kinases. The invention also provides pharmaceutical compns. comprising the title compds., and application of the title compds. and pharmaceutical compns. for preventing and treating proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 3 and 26 nM against Mer and c-Met tyrosine kinases, resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of bicyclopyrazolone compds. as tyrosine kinase inhibitors)

RN 849217-68-1 CAPLUS

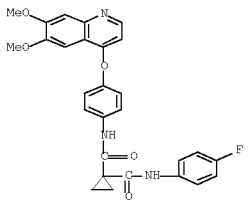
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

or cancer cells expressing increased copy nos. of MYC. We demonstrate that the Wnt-pathway inhibitor ICG-001 and trametinib acted synergistically in Wnt-pathway-mutant cell lines. The ERBB2 inhibitor TAK-165 was synergistic with trametinib in KRAS-mutant cell lines. The EGFR/ERBB2 inhibitor neratinib acted synergistically with the spindle poison docetaxel and with the Aurora kinase inhibitor GSK-1070916 in cell lines with MYC amplification. Our approach can therefore efficiently discover novel drug combinations that selectively target cancer genes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective targeting of CTNNB1-, KRAS-or MYC-driven human cancer cell growth by combinations of existing drugs)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT:	2	THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT:	62	THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 184 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

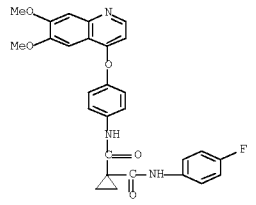
ACCESSION NUMBER:	2015:1634096 CAPLUS Full-text
DOCUMENT NUMBER:	164:469140
TITLE:	Pharmacokinetic interaction study of combining cabozantinib with erlotinib in rats by UPLC-MS/MS
AUTHOR(S):	Wang, Zhiyi; Zhang, Qingwei; Zhang, Meiling; Wu, Haiya; Zhang, Yuan
CORPORATE SOURCE:	The Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, 325000, Peop. Rep. China
SOURCE:	Latin American Journal of Pharmacy (2015), 34(2), 313-318 CODEN: LAJPA9; ISSN: 0326-2383
PUBLISHER:	Colegio de Farmaceuticos de la Provincia de Buenos Aires
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB This study examd. whether oral administration of erlotinib to rats with cabozantinib led to any pharmacokinetic interactions or not. Twenty four rats were randomly divided into 3 groups, cabozantinib group (cabozantinib 30 mg/kg, n = 8), erlotinib group (erlotinib 25 mg/kg, n = 8) and co-administration group (erlotinib 25 mg/kg and cabozantinib 30 mg/kg, n = 8). The concentration of cabozantinib and erlotinib in rat plasma was determined by a sensitive and simple UPLC-MS/MS method. There was statistical pharmacokinetics difference for cabozantinib in the cabozantinib group and co-administration group, when co-oral administration cabozantinib with erlotinib, the AUC(0-t) and Cmax increased ($p < 0.01$). There was statistical pharmacokinetics difference for erlotinib in the erlotinib group and co-administration group, when co-oral administration erlotinib with cabozantinib, the AUC(0-t) increased and CL decreased ($p < 0.05$). These data indicate erlotinib could influence the pharmacokinetic profile of cabozantinib in rats, and vice versa, which might cause drug-drug interactions when using cabozantinib with erlotinib.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic interaction study of combining cabozantinib with erlotinib in rats by ultra-performance liquid chromatog.-mass spectrum/mass spectrum)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 185 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1626773 CAPLUS Full-text

DOCUMENT NUMBER: 165:121630

TITLE: Evaluation of the effect of food and gastric pH on the single-dose pharmacokinetics of cabozantinib in healthy adult subjects

AUTHOR(S): Nguyen, Linh; Holland, Jaymes; Mamelok, Richard; Laberge, Marie-Kristine; Grenier, Julie; Swearingen, Dennis; Armas, Danielle; Lacy, Steven

CORPORATE SOURCE: Exelixis, Inc., San Francisco, CA, USA

SOURCE: Journal of Clinical Pharmacology (2015), 55(11), 1293-1302
CODEN: JCPCBR; ISSN: 0091-2700

DIGITAL OBJECT ID: 10.1002/jcph.526

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; (online computer file)

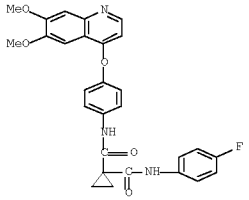
LANGUAGE: English

AB Cabozantinib is a small mol. tyrosine kinase inhibitor that has been approved for the treatment of patients with progressive, metastatic medullary thyroid cancer. Cabozantinib exhibits a pH-dependent solubility profile in vitro. Two phase 1 clin. pharmacol. studies were conducted in healthy subjects to evaluate whether factors that may affect cabozantinib solubility and gastric pH could alter cabozantinib bioavailability: a food effect study (study 1) and a drug-drug interaction (DDI) study with the proton pump inhibitor (PPI) esomeprazole (study 2). Following a high-fat meal (study 1), cabozantinib Cmax and AUC were increased (40.5% and 57%, resp.), and the median tmax was delayed by 2 h. Cabozantinib should thus not be taken with food (patients should not eat for at least 2 h before and at least 1 h after administration). In the DDI study (study 2), the 90% confidence intervals (CIs) around the ratio of least-squares means of cabozantinib with esomeprazole vs. cabozantinib alone for AUC0-inf were within the 80%-125% limits; the upper 90%CI for Cmax was 125.1%. Because of the low apparent risk of a DDI, concomitant use of PPIs or weaker gastric pH-altering agents with cabozantinib is not contraindicated.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of effect of food and gastric hydrogen ion concentration on single-dose pharmacokinetics of cabozantinib in healthy adult subjects)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 186 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1623830 CAPLUS Full-text

DOCUMENT NUMBER: 163:553993

TITLE: Preparation of cytotoxic auristatin analogs and their conjugates with cell-binding molecules

INVENTOR(S): Liang, Qingliang; Zhao, Robert Y.; Ye, Hangbo; Gai, Shun; Jia, Junxiang; Huang, Yuanyuan; Li, Xing; Guo, Huihui; Xie, Hongsheng; Li, Wenjun; Zhou, Xiaomai; Yang, Chengyu; Zhuo, Xiaotao; Zhao, Linyao; Cao, Minjun; Lin, Chen; Peng, Jie; Ye, Zhicang; Xu, Jun

PATENT ASSIGNEE(S): Hangzhou DAC Biotech Co, Ltd., Peop. Rep. China

SOURCE: PCT Int. Appl., 127pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151079	A2	20151008	WO 2015-IB54653	20150620
WO 2015151079	A3	20160506		

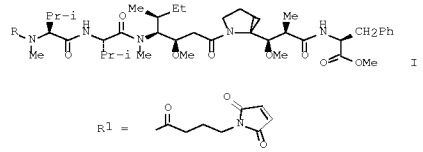
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

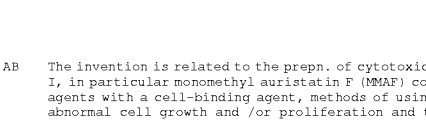
PRIORITY APPLN. INFO.: WO 2015-IB54653 20150620

OTHER SOURCE(S): CASREACT 163:553993; MARPAT 163:553993

GI



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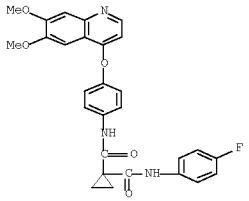
I

AB The invention is related to the prepn. of cytotoxic auristatin analogs, e.g., I, in particular monomethyl auristatin F (MMAF) conjugates of such cytotoxic agents with a cell-binding agent, methods of using them to arrest or retard abnormal cell growth and /or proliferation and to their use for targeted treatment of cancer, autoimmune disease, and infectious diseases. Thus, I [R = H] was prepared and coupled to 4-maleimidobutyric acid to provide I [R = R1] linker drug conjugate. A herceptin antibody-I [R = R1] conjugate was prepared and evaluated for its in vitro potency against N-87 human gastric carcinoma cells.

IT 849217-68-1, Cabozantinib 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug, synergistic agent; preparation of auristatin analogs and their conjugates with cell-binding mols. useful as antiproliferative and antitumor agents)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

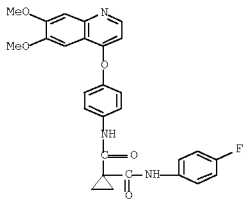


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

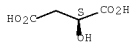
CRN 849217-68-1
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

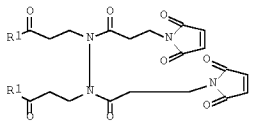


L4 ANSWER 187 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1623829 CAPLUS Full-text
DOCUMENT NUMBER: 163:553992
TITLE: Preparation of bridge linkers used for specific conjugation of a cytotoxic agent to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 112pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

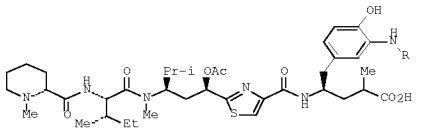
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151081	A2	20151008	WO 2015-IB55264	20150712
WO 2015151081	A3	20160602		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20150314017 A1 20151105 US 2015-14799712 20150715
PRIORITY APPLN. INFO.: WO 2015-IB55264 T0 20150712
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 163:553992; MARPAT 163:553992
GI

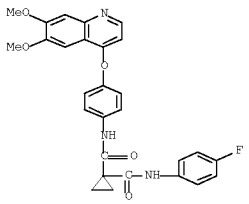


I



II

AB The invention is related to the prepn. of novel linkers contg. a hydrazine unit, e.g., I, used for the specific conjugation in particular cytotoxic agents to a cell-binding mol., through bridge linking a pair of thiols on the cell-binding mol. The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by reaction with drugs and to their use for treating especially cancer. Thus, the linker I [R1 = OH] was prepared by a multi-step synthesis starting from O-benzylhydroxylamine hydrochloride and tert-Bu acrylate using tert-Bu 3-aminopropanoate and 3-maleimidopropanoic acid. Reaction of I with oxalyl chloride, and treatment of the diacid dichloride with II [R = H] gave I [R1 = II wherein R is absent]. A herceptin antibody-I [R1 = II wherein R is absent] conjugate was prepared and evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 105 and for SK-OV-3 cell was over 3136.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 188 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1623828 CAPLUS Full-text
DOCUMENT NUMBER: 163:585947
TITLE: Preparation of novel bridge linkers containing an acetylenedicarbonyl group for specific conjugation of a cytotoxic agent to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 113pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

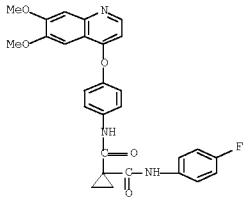
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151080	A2	20151008	WO 2015-IB55051	20150704
WO 2015151080	A3	20160602		

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2015-IB55051 20150704
OTHER SOURCE(S): CASREACT 163:585947; MARPAT 163:585947
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of novel bridge linkers contg. an acetylenedicarboxylic group, e.g., I, to link two drugs to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (cytotoxic agent) conjugates in a specific manner comprising either modification of drugs with these linkers first, followed by reaction with prepared cell-binding agents; or modification of cell-binding agents with these linkers first, followed by reaction with drugs and to their use for treating especially cancer. Thus, I [R = 2,5-dioxopyrrolidin-1-yloxy] was prepared by reacting 13-amino-bis(4,7,10-trioxadodecanoic acid) (preparation given) with bis(2,5-dioxopyrrolidin-1-yl)but-2-ynedioate (preparation given) and treatment of the tetraacid with NHS. Amidation of I [R = 2,5-dioxopyrrolidin-1-yloxy] with tubulysin analog R1-H gave R1-I [R = absent] containing 4 tubulysins analog per bridge linker. A herceptin antibody-R1-I [R = absent] conjugate was prepared and evaluated for its in vitro cytotoxicity against a human gastric carcinoma N87 cells, human ovarian carcinoma SK-OV-3 cells and promyelocytic leukemia HL-60 cells. The specificity of the conjugate for N87 cell was over 270 (IC50>10/IC50 = 0.037), and for SK-OV-3 cell was over 344.
IT 849217-68-1
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.

L4 ANSWER 189 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1623827 CAPLUS Full-text
DOCUMENT NUMBER: 163:553991
TITLE: Preparation of hydrophilic linkers for the conjugation of a cytotoxic agent or a chromophore to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

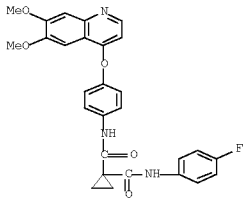
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015151078	A2	20151008	WO 2015-IB54521	20150615
WO 2015151078	A3	20160310		

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2015-IB54521 20150615
OTHER SOURCE(S): MARPAT 163:553991
GI

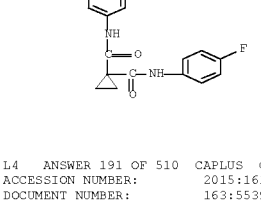
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of hydrophilic linkers contg. phosphamide, phosphinate, sulfonamide, sulfonyl, sulfonimide, and/or sulfoxide groups, e.g., I, to link drugs, in particular, cytotoxic agents or a chromophore mols. to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (e.g. cytotoxic agent) conjugates comprising either modification of the drugs with these hydrophilic linkers first, followed by reaction with cell-binding agents; or modification of cell-binding agents with these hydrophilic linkers first, followed by reaction with drugs. Thus, linker I was prepared from N-methylethane-1,2-diamine and succinic anhydride using POCl3, 3-(methylamino)propanoic acid and NHS. Conjugation of I with the tubulysin analog II [R = H] gave the drug-linker conjugate II [R = Rl]. An antiHer2-II [R= Rl] antibody conjugate of was prepared and evaluated for its in vitro cytotoxicity. The specificity of the conjugate for N87 cell was over 1315 (IC50> 50/IC50= 0.038), and for SK-OV-3 cell was over 1560.
IT 849217-68-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.

L4 ANSWER 190 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1619209 CAPLUS Full-text
DOCUMENT NUMBER: 165:434458
TITLE: Drug Lineup for Kidney Cancer May Change
AUTHOR(S): Anon.
CORPORATE SOURCE: USA
SOURCE: Cancer Discovery (2015), 5(10), OF2
CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID: 10.1158/2159-8290.CD-NB2015-116
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB The early findings from two studies may shuffle the treatment lineup for patients with renal cell carcinoma. Both cabozantinib and nivolumab show advantages in progression-free and overall survival when compared with everolimus, the most commonly used second-line treatment for patients with the disease.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug Lineup for Kidney Cancer May Change)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 191 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1617130 CAPLUS Full-text
DOCUMENT NUMBER: 163:553989
TITLE: Preparation of hydrophilic linkers for the conjugation of a cytotoxic agent or a chromophore to a cell-binding molecule
INVENTOR(S): Zhao, Robert Yongxin
PATENT ASSIGNEE(S): Suzhou M-Conj Biotech Co., Ltd., Peop. Rep. China
SOURCE: U.S. Pat. Appl. Publ., 69 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

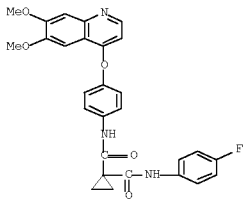
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150284416	A1	20151008	US 2015-14740403	20150616
WO 2015155753	A2	20151015	WO 2015-IB56083	20150810
WO 2015155753	A3	20160630		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2015-14740403 T0 20150616
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 163:553989
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to the prepn. of hydrophilic linkers contg. phosphamide, phosphinate, sulfonamide, sulfonyl, sulfonimide, and/or sulfoxide groups, e.g., I, to link drugs, in particular, cytotoxic agents or a chromophore mols. to a cell-binding agent (e.g., an antibody). The invention is also related to methods of making cell-binding agent-drug (e.g. cytotoxic agent) conjugates comprising either modification of the drugs with these hydrophilic linkers first, followed by reaction with cell-binding agents; or modification of cell-binding agents with these hydrophilic linkers first, followed by reaction with drugs. Thus, linker I was prepared from N-methylethane-1,2-diamine and succinic anhydride using POCl3, 3-(methylamino)propanoic acid and NHS. Conjugation of I with the tubulysin analog II [R = H] gave the drug-linker conjugate II [R = Rl]. An antiHer2-II [R= Rl] antibody conjugate of was prepared and evaluated for its in vitro cytotoxicity. The specificity of the conjugate for N87 cell was over 1315 (IC50> 50/IC50= 0.038), and for SK-OV-3 cell was over 1560.
IT 849217-68-1P, Cabozantinib
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(codrug; preparation of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; prepn. of bridge linkers for specific conjugation of a cytotoxic agent to a cell-binding mol.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 192 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1617114 CAPLUS Full-text
DOCUMENT NUMBER: 163:551060
TITLE: Combination therapy comprising anti-angiogenesis agents and OX40 binding agonists
INVENTOR(S): Walsh, Kevin; De Almeida, Patricia; Du, Changchun; Kim, Jeong; Zhu, Jing; Bevers, Jack; Andya, James; Shen, Ye
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 166pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015153514	A1	20151008	WO 2015-US23434	20150330
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2943834	A1	20151008	CA 2015-2943834	20150330
US 20150307617	A1	20151029	US 2015-14673792	20150330
AU 2015241038	A1	20161013	AU 2015-241038	20150330
CN 106132439	A	20161116	CN 2015-80015619	20150330
IL 248004	A	20161130	IL 2015-248004	20150330
KR 2016146747	A	20161221	KR 2016-7029911	20150330
EP 3126386	A1	20170208	EP 2015-721059	20150330
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20170015755	A1	20170119	US 2016-15280586	20160929

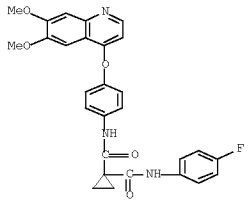
PRIORITY APPLN. INFO.:
US 2014-61973193 P 20140331
US 2014-61989448 P 20140506
US 2014-62073873 P 20141031
US 2014-62080171 P 20141114
US 2015-62113345 P 20150206
WO 2015-US23434 W 20150330

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The authors disclose a cancer treatment method comprising the administering of an anti-angiogenesis agent and an OX40 binding agonist. In the one example, anti-VEGF antibody treatment resulted in reduced tumor growth, compared to anti-gp120 (control), in a syngeneic mouse colon carcinoma model. Anti-OX40 antibody treatment exhibited little activity alone. Anti-OX40 treatment in combination with anti-VEGF treatment demonstrated superior tumor growth inhibition when compared to single agent administration or anti-gp120 treatment.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-angiogenesis agents in combination with OX40 agonists for treatment of cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 193 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1613854 CAPLUS Full-text
DOCUMENT NUMBER: 166:23804
TITLE: Screening method for multi-target drugs and/or drug combination
INVENTOR(S): Zhang, Hongyu; Yang, Qingyong; Quan, Yuan; Luo, Zhihui; Zhu, Lida
PATENT ASSIGNEE(S): Huazhong Agricultural University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 23pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

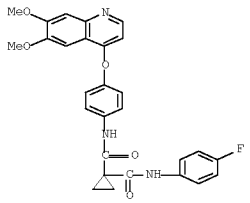
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104965998	A	20151007	CN 2015-10288863	20150529
WO 2016192191	A1	20161208	WO 2015-CN85114	20150724
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: CN 2015-10288863 A 20150529

AB The present invention discloses a screening method for multi-target drugs and/or drug combination, and belongs to the tech. field of biol. medicine. The method comprises the steps of: (1) to find drug target database, aggregate medicines target and the research targets, and each target corresponding drugs, get target and drug correspondence data relationships; (2) systems genetics approach screening the target with a target in combination with associated; (3) according to the procedure target drug obtained in step (1) correspondence between the data and the step of the target with the target composition has an associated obtained in step (2) the screened multi-target drugs and/or drug combination. Screening method of the present invention has a low screening cost and high efficiency, and has broad application prospect in the field of relocation and development and design of medicines.

IT 849217-68-1, CABOZANTINIB
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(screening method for multi-target drugs and/or drug combination)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 194 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1604658 CAPLUS Full-text
DOCUMENT NUMBER: 163:569777
TITLE: Preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid salt and their crystal forms
INVENTOR(S): Chen, Minhua; Zhang, Yanfeng; Li, Jiaoyang; Zhang, Xiaoyu; Lu, Fei
PATENT ASSIGNEE(S): Crystal Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 14pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104961681	A	20151007	CN 2014-10641139	20141113

PRIORITY APPLN. INFO.: CN 2014-10641139 20141113

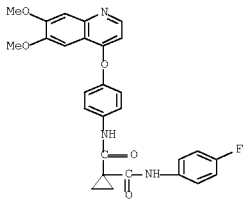
AB The title N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid salt has higher solubility than N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide malate, and plays important roles in improving the bioavailability, treatment effect, and safety of drug.

IT 1817759-89-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure; preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid and their crystal forms)

RN 1817759-89-9 CAPLUS
CN Galactaric acid, compd. with N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

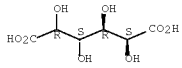
CRN 849217-68-1
CMF C28 H24 F N3 O5



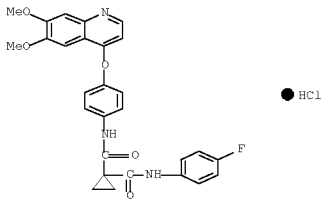
CM 2

CRN 526-99-8
CMF C6 H10 O8

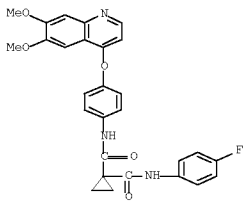
Relative stereochemistry.



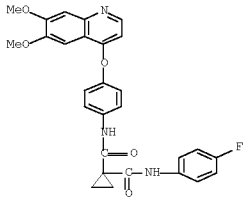
IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide mucic acid and their crystal forms)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 196 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1602738 CAPLUS Full-text
DOCUMENT NUMBER: 164:575620
TITLE: TAMing resistance to multi-targeted kinase inhibitors through Axl and Met inhibition
AUTHOR(S): Pinato, D. J.; Chowdhury, S.; Stebbing, J.
CORPORATE SOURCE: Department of Surgery and Cancer, Imperial College London, London, UK
SOURCE: Oncogene (2016), 35(21), 2684-2686
CODEN: ONCNES; ISSN: 0950-9232
DIGITAL OBJECT ID: 10.1038/onc.2015.374
PUBLISHER: Nature Publishing Group

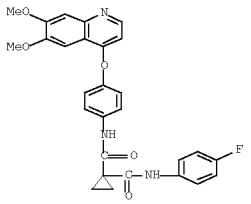


L4 ANSWER 195 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1604653 CAPLUS Full-text
DOCUMENT NUMBER: 163:569776
TITLE: Preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms
INVENTOR(S): Chen, Minhua; Zhang, Yanfeng; Li, Jiaoyang; Zhang, Xiaoyu; Lu, Fei
PATENT ASSIGNEE(S): Crystal Pharmatech Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104961680	A	20151007	CN 2014-10626255	20141107

PRIORITY APPLN. INFO.: CN 2014-10626255 20141107
AB The title N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride has higher solubility than N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide malate, and plays important roles in improving the bioavailability, treatment effect, and safety of drug.
IT 1817759-42-4
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure; preparation of N-(4-((6,7-bis(methoxy)quinolin-4-yl)oxy)phenyl)-N-(4-fluorophenyl)cyclopropane-1,1-diformamide hydrochloride and their crystal forms)
RN 1817759-42-4 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrochloride (1:1) (CA INDEX NAME)

DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB TAM (Tyro3-Axl-Mer) receptor tyrosine kinases and Met are implicated in several hallmarks of cancer progression including sustained angiogenesis, enhanced motility, tissue invasion and acquisition of metastatic potential through the upregulation of epithelial-to-mesenchymal transition. Increasing evidence has confirmed Axl and Met as emerging central drivers of adaptive resistance to targeted therapies across a wide variety of cancers. In this issue of Oncogene, Zhou et al. describe the mechanisms linking Axl and Met activation to acquired resistance to sunitinib in renal cell carcinoma (RCC), providing a pre-clin. rationale for the development of Axl and Met inhibitors including cabozantinib in anti-angiogenic resistant RCC.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TAMing resistance to multi-targeted kinase inhibitors through Axl and Met inhibition)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

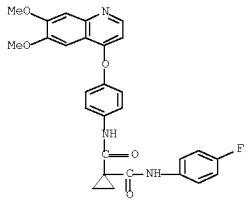
L4 ANSWER 197 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1593218 CAPLUS Full-text
DOCUMENT NUMBER: 163:673623
TITLE: Cabozantinib in Thyroid Cancer
AUTHOR(S): Fallahi, Poupak; Ferrari, Silvia M.; Di Bari, Flavia; Materazzi, Gabriele; Benvenga, Salvatore; Miccoli, Paolo; Antonelli, Alessandro
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56126, Italy
SOURCE: Recent Patents on Anti-Cancer Drug Discovery (2015), 10(3), 259-269
CODEN: RPADDY; ISSN: 1574-8928

DIGITAL OBJECT ID: 10.2174/1574892810666150708110816
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib is an oral once-daily multitarget tyrosine kinase inhibitor of MET, VEGFR2, RET, acting against KIT, AXL, FLT3 and Tie-2. Cabozantinib has shown anti-cancer effects in preclin. and clin. models of cancers derived from both epithelial and mesenchymal origins [prostate cancer, non small lung cancer, medullary thyroid cancer (MTC) and differentiated thyroid cancer (DTC), renal cell carcinoma, etc.]. In a Phase III clin. study, cabozantinib improved PFS (11.2 mo vs. 4.0 mo in the placebo group) of patients with MTC (independently of age, bone metastases, RET status and prior treatment). Cabozantinib was approved in 2012 by FDA for metastatic MTC and in 2013 by EMA. Cabozantinib has been also evaluated in metastatic DTC patients, because they have activation on tyrosine kinases, including MET, VEGFR2 and RET, suggesting the possible use of cabozantinib in metastatic DTC. Actually, two Phase II trials of cabozantinib in DTC patients resistant to RAI are ongoing. To increase the antineoplastic effect of cabozantinib, and to overcome the occurrence of drug resistance, combination studies with other anticancer agents are ongoing. In conclusion, cabozantinib has shown to exert an important therapeutic effect in patients with MTC improving PFS. In DTC patients, cabozantinib has shown promising results.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of tyrosine kinase inhibitor cabozantinib in thyroid cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



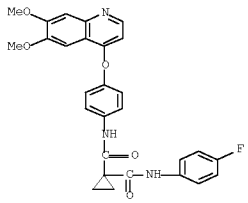
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 152 THERE ARE 152 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 198 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1592351 CAPLUS Full-text
DOCUMENT NUMBER: 165:90124
TITLE: Sensitivity of neuroblastoma to the novel kinase inhibitor cabozantinib is mediated by ERK inhibition
AUTHOR(S): Zhang, Linna; Scorsone, Kathleen; Woodfield, Sarah E.; Zage, Peter E.
CORPORATE SOURCE: Department of Pediatrics, Section of Hematology-Oncology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Cancer Chemotherapy and Pharmacology (2015), 76(5), 977-987
CODEN: CCPHDZ; ISSN: 0344-5704
DIGITAL OBJECT ID: 10.1007/s00280-015-2871-z
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Purpose: Children with high-risk neuroblastoma have poor survival rates, and novel therapies are needed. We hypothesized that cabozantinib would be effective against neuroblastoma tumor cells and tumors in preclin. models via inhibition of receptor tyrosine kinase signaling pathways. Methods: We determined neuroblastoma cell viability after treatment with cabozantinib alone and in combination with 13-cis-retinoic acid, topotecan, and temozolomide using MTT assays. Inhibition of RET and intracellular signaling was measured by Western blot anal. of treated and untreated cells. To investigate the efficacy of cabozantinib against neuroblastoma tumors in vivo, neuroblastoma cells were injected orthotopically into immunocompromised mice, and mice were treated with oral cabozantinib. Tumors were evaluated for growth by determination of in vivo luminescence and final tumor wts. Results: All neuroblastoma cell lines were sensitive to cabozantinib, and IC50 values ranged from 1.6 to 16.2 μM. Cabozantinib treatment was synergistic with 13-cis-retinoic acid and chemotherapy agents topotecan and temozolomide. Cabozantinib treatment inhibited RET phosphorylation in all cell lines and ERK phosphorylation in more sensitive neuroblastoma cell lines. In mice with neuroblastoma xenograft tumors, cabozantinib treatment significantly reduced tumor growth. Conclusions: Treatment of neuroblastoma tumor cells with cabozantinib inhibits RET and ERK phosphorylation and is effective against neuroblastoma tumor cell lines alone and in combination with 13-cis-retinoic acid, topotecan, and temozolomide. Cabozantinib treatment is also effective in reducing tumor growth in vivo. Cabozantinib therefore represents a novel therapeutic agent for neuroblastoma, and further preclin. and clin. studies are warranted.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of cabozantinib against neuroblastoma tumor cells and tumors in preclin. immunocompromised mouse models via inhibition of receptor tyrosine kinase signaling pathways)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



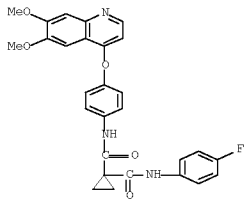
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 199 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1582731 CAPLUS Full-text
DOCUMENT NUMBER: 166:36339
TITLE: MET/HGF targeted drugs as potential therapeutic strategies in non-small cell lung cancer
AUTHOR(S): Perez-Ramirez, Cristina; Canadas-Garre, Marisa; Molina, Miguel Angel; Faus-Dader, Maria Jose; Calleja-Hernandez, Miguel Angel
CORPORATE SOURCE: Pharmacogenetics Unit, UGC Provincial de Farmacia de Granada, Instituto de Investigacion Biosanitaria de Granada, Complejo Hospitalario Universitario de Granada, Granada, Spain
SOURCE: Pharmacological Research (2015), 102, 90-106
CODEN: PHMREP; ISSN: 1043-6618
DIGITAL OBJECT ID: 10.1016/j.phrs.2015.09.016
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. This article discusses about MET pathway signaling and dysregulation development of MET inhibitors like tivantinib, cabozantinib, crizotinib and foretinib to block HGF/MET signaling pathway and use of c-Met protein /hepatocyte growth factor targeted drugs as potential therapeutic strategies in non-small cell lung cancer in human and mouse model.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of c-Met protein/hepatocyte growth factor targeted drugs as potential therapeutic strategies in non-small cell lung cancer in human and mouse model)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 202 THERE ARE 202 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 200 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1579900 CAPLUS Full-text
DOCUMENT NUMBER: 163:512733
TITLE: Cancer treatment with c-MET antagonists and correlation of the latter with HGF expression
INVENTOR(S): Yu, Wei; Shames, David; Koeppen, Hartmut; Phan, See; Rost, Sandra
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 178pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

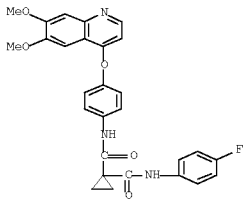
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015148531	A1	20151001	WO 2015-US22282	20150324
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2943329	A1	20151001	CA 2015-2943329	20150324
KR 2016137599	A	20161130	KR 2016-7029550	20150324
EP 3122900	A1	20170201	EP 2015-716253	20150324
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

MX 2016012285 A 20170123 MX 2016-12285 20160922
PRIORITY APPLN. INFO.: US 2014-61969706 P 20140324
US 2014-61985316 P 20140428
WO 2015-US22282 W 20150324

AB The present invention concerns cancer biomarkers. In particular, the invention concerns HGF as a biomarker for patient selection and patient prognosis in cancer, as well as methods of therapeutic treatment, articles of manufacture and methods for making them, diagnostic kits, methods of detection and methods of advertising related thereto. Cancer patients are treated with an anti-c-met antibody in combination with an anti-VEGF antibody.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer treatment with c-MET antagonists and correlation of the latter with HGF expression)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



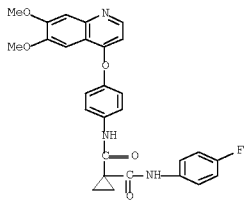
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 201 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1577497 CAPLUS Full-text
DOCUMENT NUMBER: 165:121781
TITLE: Rapid modification of the bone microenvironment following short-term treatment with Cabozantinib in vivo
AUTHOR(S): Haider, Marie-Therese; Hunter, Keith D.; Robinson, Simon P.; Graham, Timothy J.; Corey, Eva; Dear, T. Neil; Hughes, Russell; Brown, Nicola J.; Holen, Ingunn
CORPORATE SOURCE: Department of Oncology, University of Sheffield, Sheffield, UK
SOURCE: Bone (New York, NY, United States) (2015), 81, 581-592
CODEN: BONEDL; ISSN: 1873-2763
DIGITAL OBJECT ID: 10.1016/j.bone.2015.08.003
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Bone metastasis remains incurable with treatment restricted to palliative care. Cabozantinib (CBZ) is targeted against multiple receptor tyrosine kinases involved in tumor pathobiol., including hepatocyte growth factor receptor (MET) and vascular endothelial growth factor receptor 2 (VEGFR-2). CBZ has demonstrated clin. activity in advanced prostate cancer with resolution of lesions visible on bone scans, implicating a potential role of the bone microenvironment as a mediator of CBZ effects. We characterized the effects of short-term administration of CBZ on bone in a range of in vivo models to determine how CBZ affects bone in the absence of tumor. Studies were performed in a variety of in vivo models including male and female BALB/c nude mice (age 6-17-wk). Animals received CBZ (30 mg/kg, 5 × weekly) or sterile H2O control for 5 or 10 days. Effects on bone integrity (μCT), bone cell activity (PINP, TRAP ELISA), osteoblast and osteoclast number/mm trabecular bone surface, area of epiphyseal growth plate cartilage, megakaryocyte nos. and bone marrow composition were assessed. Effects of longer-term treatment (15-day & 6-wk administration) were assessed in male NOD/SCID and beige SCID mice. CBZ treatment had significant effects on the bone microenvironment, including reduced osteoclast and increased osteoblast nos. compared to control. Trabecular bone structure was altered after 8 administrations. A significant elongation of the epiphyseal growth plate, in particular the hypertrophic chondrocyte zone, was observed in all CBZ treated animals irresp. of administration schedule. Both male and female BALB/c nude mice had increased megakaryocyte nos./mm2 tissue after 10-day CBZ treatment, in addition to vascular ectasia, reduced bone marrow cellularity and extravasation of red blood cells into the extra-vascular bone marrow. All CBZ-induced effects were transient and rapidly lost following cessation of treatment. Short-term administration of CBZ induces rapid, reversible effects on the bone microenvironment in vivo highlighting a potential role in mediating treatment responses.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rapid modification of bone microenvironment following short-term treatment with cabozantinib in vivo)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



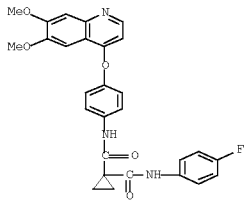
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 202 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1577278 CAPLUS Full-text
DOCUMENT NUMBER: 164:288433
TITLE: Stromal expression of VEGF-A and VEGFR-2 in prostate tissue is associated with biochemical and clinical recurrence after radical prostatectomy
AUTHOR(S): Nordby, Yngve; Andersen, Sigve; Richardsen, Elin; Ness, Nora; Al-Saad, Samer; Melbo-Jorgensen, Christian; Patel, Hiten R. H.; Donnem, Tom; Busund, Lill-Tove; Bremnes, Roy M.
CORPORATE SOURCE: Department Clinical Medicine, The Arctic University of Norway, Tromso, Norway
SOURCE: Prostate (Hoboken, NJ, United States) (2015), 75(15), 1682-1693
CODEN: PRSTDS; ISSN: 0270-4137
DIGITAL OBJECT ID: 10.1002/pros.23048
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Background : There is probably significant overtreatment of patients with prostate cancer due to a lack of sufficient diagnostic tools to predict aggressive disease. Vascular endothelial growth factors (VEGFs) and their receptors (VEGFRs) are potent mediators of angiogenesis and tumor proliferation, but have been examined to a limited extent in large prostate cancer studies. Meanwhile, recent promising results on VEGFR-2 inhibition have highlighted their importance, leading to the need for further investigations regarding their expression and prognostic impact. Design : Using tissue microarray and immunohistochem., the expression of VEGFs (VEGF-A and VEGF-C) and their receptors (VEGFR-2 and VEGFR-3) were measured in neoplastic tissue and corresponding stroma from radical prostatectomy specimens in 535 Norwegian patients. Their expression was evaluated semiquantatively and assocns. with event-free survival were calculated Results : High expression of VEGFR-2 in either stroma or epithelium was independently associated with a higher incidence of prostate cancer relapse (HR = 4.56, P = 0.038). A high combined expression of either VEGF-A, VEGFR-2 or both in stroma was independently associated with a higher incidence of biochem. failure (HR = 1.77, P = 0.011). Conclusions : This large study highlights the prognostic importance of VEGF-A and VEGFR-2 stromal expression. Analyses of these biomarkers may help distinguish which patients will benefit from radical treatment. Together with previous studies showing efficiency of targeting VEGFR-2 in prostate cancer, this study highlights its potential as a target for therapy, and may aid in future selection of prostate cancer patients for novel anti-angiogenic treatment. Prostate 75:1682-1693, 2015. 2015 Wiley Periodicals, Inc.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stromal expression of VEGF-A and VEGFR-2 in prostate tissue was associated with biochem. and clin. recurrence in human after radical prostatectomy)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 203 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1545892 CAPLUS Full-text
DOCUMENT NUMBER: 163:469529
TITLE: Target inhibition map system for combination antitumor therapy design and methods of using same
INVENTOR(S): Pal, Ranadip; Keller, Charles, III; Berlow, Noah E.; Seguin, Bernard
PATENT ASSIGNEE(S): Texas Tech University System, USA; Colorado State University Research Foundation
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

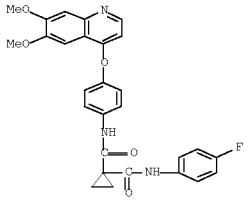
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150269307	A1	20150924	US 2015-14661918	20150318

PRIORITY APPLN. INFO.: US 2014-61955068 P 20140318
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed is a system and method for targeted therapy designs which model a cancer pathway for predicting the effectiveness of targeted anti-cancer drugs. The disclosed system and method includes utilization of a computer processor allowing for the selection of a set of drugs from available drugs using approximation algorithms utilizing cell viability data associated with a testable culture of a patient's tumor for generating a probabilistic target inhibition map (PTIM) from viability data for considering the selection of a set of drugs from available drugs, and further supports a wide variety of scenarios for personalized cancer therapy, related products and services.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

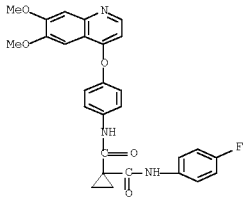
(target inhibition map system for combination therapy design and methods of using same)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

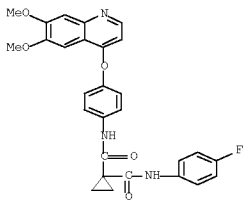
CRN 849217-68-1
CMF C28 H24 F N3 O5



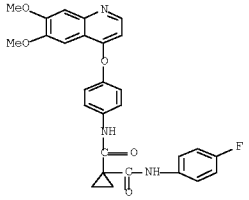
CM 2

CRN 97-67-6
CMF C4 H6 O5

RL: ANT (Analyte); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dosing of cabozantinib formulations)
RN 1809822-99-8 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, labeled with carbon-14 (CA INDEX NAME)



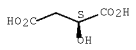
IT 1628542-34-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dosing of cabozantinib formulations)
RN 1628542-34-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, monohydroxy deriv. (CA INDEX NAME)



D1—OH

IT 1621681-63-7
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); THU

Absolute stereochemistry. Rotation (-).

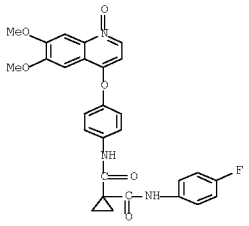


L4 ANSWER 204 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1542977 CAPLUS Full-text
DOCUMENT NUMBER: 163:469542
TITLE: Dosing of cabozantinib formulations
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy, Steven
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

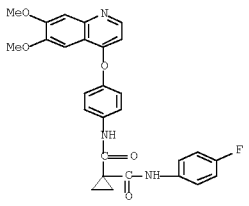
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015142928	A1	20150924	WO 2015-US21072	20150317
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 106255499	A	20161221	CN 2015-80023083	20150317
EP 3119476	A1	20170125	EP 2015-714340	20150317
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2017507995	T	20170323	JP 2016-558004	20150317
US 20170087143	A1	20170330	US 2016-15126767	20160916

PRIORITY APPLN. INFO.: US 2014-61954352 P 20140317
WO 2015-US21072 W 20150317
OTHER SOURCE(S): CASREACT 163:469542
AB The invention relates to administration of various pharmaceutical formulations of N-(4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1- dicarboxamide, (cabozantinib) a c-Met inhibitor, and its metabolites, to achieve desirable pharmacokinetic and pharmacodynamic effects.
IT 1809822-39-0P

(Therapeutic use); BIOL (Biological study); USES (Uses)
(dosing of cabozantinib formulations)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosing of cabozantinib formulations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



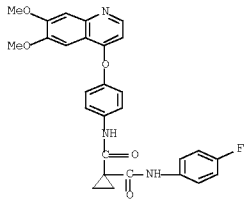
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
----L4 ANSWER 205 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
L4 ANSWER 205 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1518424 CAPLUS Full-text
DOCUMENT NUMBER: 163:693610

TITLE: Cabozantinib for the treatment of non-small cell lung cancer with KIF5B-RET fusion. An example of swift repositioning
AUTHOR(S): Song, Minsoo; Kim, Seong-Heon; Yoon, Suk Kyoon
CORPORATE SOURCE: New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Taegu, 701-310, S. Korea
SOURCE: Archives of Pharmacal Research (2015), 38(12), 2120-2123
CODEN: APHRDQ; ISSN: 0253-6269
DIGITAL OBJECT ID: 10.1007/s12272-015-0660-1
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A new chimeric fusion transcript of KIF5B (the kinesin family 5B gene) and the RET (Rearranged during Transcription) oncogene, KIF5B-RET, was found in 1-2 % of lung adenocarcinomas (LADCs) in 2012. Several related clin. trials for non-small cell lung cancer (NSCLC) with KIF5B-RET rearrangements using existing RET inhibitors, such as cabozantinib, lenvatinib, vandetanib, sunitinib, ponatinib, and AUY922, have been swiftly initiated by the discovery of the KIF5B-RET fusion gene. Anti-RET activity and the status of clin. development of cabozantinib for KIF5B-RET fusion-pos. NSCLC are discussed.

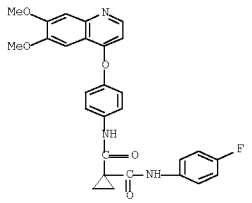
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of non-small cell lung cancer with KIF5B-RET fusion. An example of swift repositioning)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 206 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1496569 CAPLUS Full-text



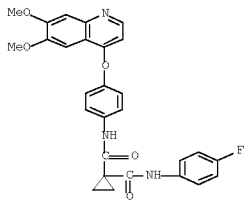
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 207 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1474667 CAPLUS Full-text
DOCUMENT NUMBER: 164:415926
TITLE: Antioxidant and Anticoagulant Status Were Improved by Personalized Dietary Intervention Based on Biochemical and Clinical Parameters in Cancer Patients
AUTHOR(S): Lee, Ga-Yi; Lee, Jong Jyun; Lee, Seung-Min
CORPORATE SOURCE: Program of Clinical Nutrition, Yonsei Graduate School of Human Environmental Sciences, Seoul, S. Korea
SOURCE: Nutrition and Cancer (2015), 67(7), 1083-1092
CODEN: NUCADQ; ISSN: 0163-5581
DIGITAL OBJECT ID: 10.1080/01635581.2015.1073754
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB We investigated whether personalized dietary intervention could improve clin. measurements such as immune cell-mediated cytotoxicity, serum albumin, derivs. of reactive oxygen metabolites (D-ROMS), D-dimer, and fibrinogen. Cancer patients received either a treatment support diet (TD, for those with chemotherapy), or a remission support diet (RD; for those in remission) for at least 3 wk (21-61 days). Both diets were low glycemic, low fat, and high plant protein diets; the diet for the TD group contained an addnl. 0.5 servings of protein. Based on clin. values, addnl. amts. of garlic, onion, tomato, shiitake, rice bran, kale, blueberry, pineapples, and/or turmeric powder were provided in regular meals. Estimated daily intake of protein, plant fat, garlic, onion, allicin, and quercetin was greater in the TD compared to the RD. An increased intake of vitamin A, vitamin C, vitamin E and selenium and a reduction in D-dimer were noted compared to baseline diets in both groups. A decrease in D-ROMS in the RD and an increase in albumin and an increased tendency in cytotoxicity in the TD were observed In conclusion, personalized diets with supplemented functional ingredients improved antioxidant status and/or anticoagulant activity in cancer patients undergoing chemotherapy and in remission.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant and anticoagulant status were improved by personalized dietary intervention based on biochem. and clin. parameters in cancer patients)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 208 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1456151 CAPLUS Full-text
DOCUMENT NUMBER: 163:418831
TITLE: Structural insight into selectivity and resistance profiles of ROS1 tyrosine kinase inhibitors
AUTHOR(S): Davare, Monika A.; Vellore, Nadeem A.; Wagner, Jacob P.; Eide, Christopher A.; Goodman, James R.; Drilon, Alexander; Deininger, Michael W.; O'Hare, Thomas; Druker, Brian J.
CORPORATE SOURCE: Knight Cancer Institute, Oregon Health & Science University, Portland, OR, 97239, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2015), 112(39), E5381-E5390
CODEN: PNASA6; ISSN: 0027-8424
DIGITAL OBJECT ID: 10.1073/pnas.1515281112
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Oncogenic ROS1 fusion proteins are mol. drivers in multiple malignancies, including a subset of non-small cell lung cancer (NSCLC). The phylogenetic proximity of the ROS1 and anaplastic lymphoma kinase (ALK) catalytic domains led to the clin. repurposing of the Food and Drug Administration (FDA)-approved ALK inhibitor crizotinib as a ROS1 inhibitor. Despite the antitumor activity of crizotinib observed in both ROS1- and ALK-rearranged NSCLC patients, resistance due to acquisition of ROS1 or ALK kinase domain mutations has been observed clin., spurring the development of

DOCUMENT NUMBER: 165:65305
TITLE: Oral adverse events in cancer patients treated with VEGFR-directed multitargeted tyrosine kinase inhibitors
AUTHOR(S): Yuan, Anna; Kurtz, Sharyn L.; Barysauskas, Constance M.; Pilotte, Amy P.; Wagner, Andrew J.; Treister, Nathaniel S.
CORPORATE SOURCE: Division of Oral Medicine, Brigham and Women's Hospital, Boston, MA, 02115, USA
SOURCE: Oral Oncology (2015), 51(11), 1026-1033
CODEN: EJCCER; ISSN: 1368-8375
DIGITAL OBJECT ID: 10.1016/j.oraloncology.2015.09.003
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB This study characterized the incidence and clin. features of oral adverse events among cancer patients who received VEGFR-directed multitargeted tyrosine kinase inhibitor (VR-TKI) therapies. Electronic medical records of adult cancer patients treated with sunitinib, sorafenib, regorafenib, pazopanib, cabozantinib, imatinib, and bevacizumab therapy at Dana-Farber Cancer Institute from 2009 to 2012 were reviewed. Data collected included patient characteristics, oral and non-oral adverse events, and time to onset. Time oral adverse event-free was the primary outcome.A total of 747 patients with 806 individual courses of therapy were treated for a median of 3.9 mo with sunitinib (n = 161), sorafenib (n = 172), regorafenib (n = 15), pazopanib (n = 132), cabozantinib (n = 23), imatinib (n = 144), or bevacizumab (n = 159) for lung cancer (21%), gastrointestinal stromal tumor (15%), and metastatic renal cell carcinoma (13%). An oral adverse event was reported in 23.7% of patients at a median of 1.9 mo after starting therapy. The most commonly reported oral adverse event was oral mucosal sensitivity (dysesthesia), occurring in 12% of patients, typically without clin. findings. Multivariate models showed patients who received VR-TKI therapy were at greater risk of any oral adverse event compared with patients treated with imatinib or bevacizumab. Patients receiving VR-TKI therapy who developed an oral adverse event were also at increased risk for hand-foot skin reaction (15.9%). VR-TKI associated oral adverse events are characterized primarily by dysesthesia with lack of clin. signs. Oral dysesthesia is more commonly associated with VR-TKIs than with bevacizumab or imatinib. Management is largely empirical and requires further investigation.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral adverse events in cancer patients treated with VEGFR-directed multitargeted tyrosine kinase inhibitors)

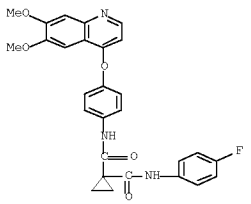
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

second-generation inhibitors. Here, we profile the sensitivity and selectivity of seven ROS1 and/or ALK inhibitors at various levels of clin. development. In contrast to crizotinib's dual ROS1/ALK activity, cabozantinib (XL-184) and its structural analog foretinib (XL-880) demonstrate a striking selectivity for ROS1 over ALK. Mol. dynamics simulation studies reveal structural features that distinguish the ROS1 and ALK kinase domains and contribute to differences in binding site and kinase selectivity of the inhibitors tested. Cell-based resistance profiling studies demonstrate that the ROS1-selective inhibitors retain efficacy against the recently reported CD74-ROS1G2032R mutant whereas the dual ROS1/ALK inhibitors are ineffective. Taken together, inhibitor profiling and stringent characterization of the structure-function differences between the ROS1 and ALK kinase domains will facilitate future rational drug design for ROS1- and ALK-driven NSCLC and other malignancies.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural insight into selectivity and resistance profiles of ROS1 tyrosine kinase inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L4 ANSWER 209 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1392691 CAPLUS Full-text

DOCUMENT NUMBER: 163:345656

TITLE: Use of ibrutinib to treat EGFR mutant cancer

INVENTOR(S): Fang, Bingliang; Roth, Jack A.; Wang, Michael; Wang, Li; Wu, Shuhong; Heymach, John V.; Swisher, Stephen G.; Hofstetter, Wayne L.

PATENT ASSIGNEE(S): The University of Texas System, USA

SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015127234	A1	20150827	WO 2015-US16859	20150220

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

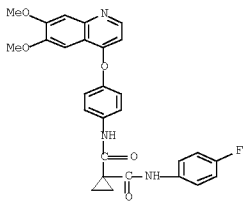
PRIORITY APPLN. INFO.: US 2014-61942255 P 20140220

AB Provided herein are methods of using irreversible BTK inhibitors, such as, for example, ibrutinib (PCI-32765), to treat EGFR mutant cancers, HER2 amplified cancers, and/or HER2 overexpressing cancers. In certain aspects, the method further comprises administering at least a second anticancer therapy to the subject.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of ibrutinib to treat EGFR mutant cancer and combination with other therapy)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 210 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1362724 CAPLUS Full-text

DOCUMENT NUMBER: 163:299275

TITLE: Preparation of crystalline solid forms of cabozantinib

INVENTOR(S): Aftab, Dana T.; Guz, Nathan; Lau, Stephen; Hamill, Noel; Walker, Tracy; Galbraith, Jana; Yau, Simon; Shah, Khalid

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015123639	A1	20150820	WO 2015-US16052	20150216

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2939546	A1	20150820	CA 2015-2939546	20150216
AU 2015218236	A1	20160915	AU 2015-218236	20150216
IL 247035	A	20160929	IL 2015-247035	20150216
KR 2016121544	A	20161019	KR 2016-7024184	20150216
CN 106068255	A	20161102	CN 2015-80012614	20150216
EP 3105204	A1	20161221	EP 2015-710315	20150216

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2017505796	T	20170223	JP 2016-551712	20150216
IN 201637026681	A	20160826	IN 2016-37026681	20160804
MX 2016010266	A	20170208	MX 2016-10266	20160808
US 20170044106	A1	20170216	US 2016-15118738	20160812

PRIORITY APPLN. INFO.: US 2014-61939985 P 20140214
WO 2015-US16052 W 20150216

AB The invention relates to novel cryst. solid forms of cabozantinib., and solvates thereof, including hydrates, that are useful for the treatment of cancer. Also disclosed are pharmaceutical compns. comprising the crystalline solid forms and processes for making the crystalline solid forms, as well as methods of using them for the treatment of cancer, particularly thyroid cancer, prostate cancer, hepatocellular cancer, renal cancer, and non-small cell lung carcinoma. The crystalline solid forms can be used to make the L-malate salt of cabozantinib.

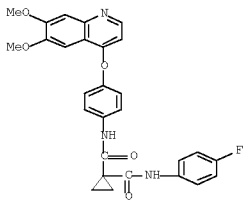
IT 1140909-48-3, Cabozantinib S-malate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystalline solid forms of cabozantinib)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

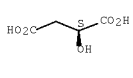
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

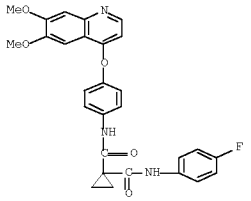
Absolute stereochemistry. Rotation (-).



IT 849217-68-1
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of crystalline solid forms of cabozantinib)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

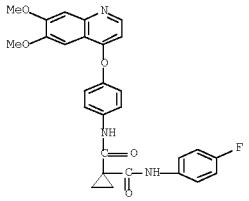


OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 211 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1349511 CAPLUS Full-text
DOCUMENT NUMBER: 163:449411
TITLE: Identification of triazolo[4,5-b]pyrazine derivatives as hepatocyte growth factor receptor inhibitors through structure-activity relationships and molecular docking simulations
AUTHOR(S): Dong, Minghui; Ren, Yujie; Gao, Xiaodong
CORPORATE SOURCE: School of Chemical and Environmental Engineering, Shanghai Institute of Technology, Shanghai, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2015), 25(19), 4118-4126
CODEN: BMCLE8; ISSN: 0960-894X
DIGITAL OBJECT ID: 10.1016/j.bmcl.2015.08.025
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB C-MET is a receptor tyrosine kinase and potential oncol. target for cancer therapy. The activities of 1,2,3-triazolo[4,5-b]pyrazine series of c-MET inhibitors were analyzed according to the three-dimensional quant. structure-activity relationship and mol. docking methods. The results indicated that the hydrophobic and electrostatic fields play key roles in activity and QSAR model was reliable enough for activity prediction. Moreover, the docking results do validate the predicted 3D-QSAR scores, vital residues Asp1222, Asp1231, Met1160, Tyr1259 and Tyr1230 found in binding site. Four new c-MET inhibitor analogs designed in this Letter which are being currently synthesized by our labs.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triazolo-pyrazine derivs. identification as HGFR inhibitors through SAR and mol. docking simulation)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

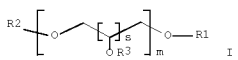
L4 ANSWER 212 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1315537 CAPLUS Full-text
DOCUMENT NUMBER: 163:323284
TITLE: Composition for vectorizing an anti-cancer agent
INVENTOR(S): Robic, Caroline; Mayer, Jean-Francois
PATENT ASSIGNEE(S): Guerbet, Fr.
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015118113	A1	20150813	WO 2015-EP52527	20150206
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
FR 3017295	A1	20150814	FR 2014-50972	20140207
CA 2938861	A1	20150813	CA 2015-2938861	20150206
AU 2015214230	A1	20160825	AU 2015-214230	20150206
KR 2016130992	A	20161115	KR 2016-7021534	20150206
EP 3102214	A1	20161214	EP 2015-704280	20150206

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

CN 106255503	A	20161221	CN 2015-80007327	20150206
JP 2017505326	T	20170216	JP 2016-550609	20150206
IN 201637026798	A	20160826	IN 2016-37026798	20160805
US 20160346202	A1	20161201	US 2016-15117109	20160805
MX 2016010217	A	20161205	MX 2016-10217	20160805

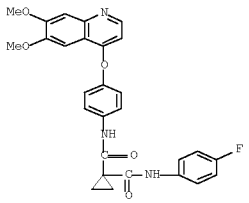
PRIORITY APPLN. INFO.: FR 2014-50972 A 20140207
WO 2015-EP52527 W 20150206
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
GI



I

AB The invention relates to a stable water-in-oil emulsion compn. contg.: 20% to 40% (volume/volume) aqueous phase in the form of droplets and containing an anti-cancer agent; and 60% to 80% (volume/volume) lipid phase containing an iodized oil and at least one surfactant, having formula I, in a proportion, of surfactant mass relative to the total volume of the composition, of 0.3% to 5%, formula II for said surfactant being the following in which: s has a value of 0 or 1; m is a whole number from 2 to 30; R1 is a formula I grouping wherein n is a whole number from 4 to 10, o is a whole number from 1 to 4, p is a whole number from 3 to 7; q is a whole number from 2 to 10, and r has a value of 0 or 1; R2 is a hydrogen atom or is identical to R1; and each R3 is, sep., a hydrogen atom or is identical to R1. The invention also relates to an emulsion obtained from said composition, to the preparing method thereof, and to the use thereof for treating cancer and the metastases thereof. An emulsion containing 50 mg doxorubicin, 1% PGPR in Lipidol, and 2.5 mL Xenetix 250 was prepared

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition for vectorizing anti-cancer agent)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



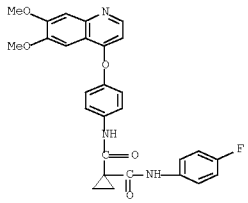
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 213 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1289334 CAPLUS Full-text
DOCUMENT NUMBER: 163:438199
TITLE: Response to MET Inhibitors in Patients with Stage IV Lung Adenocarcinomas Harboring MET Mutations Causing Exon 14 Skipping
AUTHOR(S): Paik, Paul K.; Drilon, Alexander; Fan, Pang-Dian; Yu, Helena; Rekhtman, Natasha; Ginsberg, Michelle S.; Borsu, Laetitia; Schultz, Nikolaus; Berger, Michael F.; Rudin, Charles M.; Ladanyi, Marc
CORPORATE SOURCE: Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Cancer Discovery (2015), 5(8), 842-849
CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID: 10.1158/2159-8290.CD-14-1467
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mutations in the MET exon 14 RNA splice acceptor and donor sites, which lead to exon skipping, deletion of the juxtamembrane domain containing the CBL E3-ubiquitin ligase-binding site, and decreased turnover of the resultant aberrant MET protein, were previously reported to be oncogenic in preclin. models. We now report responses to the MET inhibitors crizotinib and cabozantinib in four patients with stage IV lung adenocarcinomas harboring mutations leading to MET exon 14 skipping, highlighting a new therapeutic strategy for the 4% of lung adenocarcinoma patients whose tumors harbor this previously underappreciated genetic alteration. Significance: Oncogenic mutations in the MET exon 14 splice sites that cause exon 14 skipping occur in 4% of lung adenocarcinomas. We report responses to the MET inhibitors crizotinib and cabozantinib in patients with lung adenocarcinomas harboring MET exon 14 splice site mutations, identifying a new potential therapeutic target in this disease. Cancer Discov; 5(8); 842-9. ©2015 AACR. See related commentary by Ma, p. 802. See related article by Frampton et al., p. 850. This article is highlighted in the In This Issue feature, p. 783.

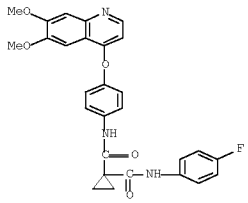
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(response to MET inhibitors in patients with stage IV lung adenocarcinomas harboring MET mutations causing exon 14 skipping)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



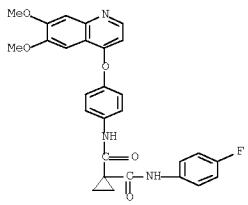
OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (24 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 214 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1265280 CAPLUS Full-text
DOCUMENT NUMBER: 164:501342
TITLE: Pharmacokinetic (PK) drug interaction studies of cabozantinib: Effect of CYP3A inducer rifampin and inhibitor ketoconazole on cabozantinib plasma PK and effect of cabozantinib on CYP2C8 probe substrate rosiglitazone plasma PK
AUTHOR(S): Nguyen, Linh; Holland, Jaymes; Miles, Dale; Engel, Caroline; Benrimoh, Natacha; O'Reilly, Terry; Lacy, Steven
CORPORATE SOURCE: Exelixis, Inc., So. San Francisco, CA, USA
SOURCE: Journal of Clinical Pharmacology (2015), 55(9), 1012-1023
CODEN: JCPCBR; ISSN: 0091-2700
DIGITAL OBJECT ID: 10.1002/jcph.510
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is a small-mol. tyrosine kinase inhibitor that has been approved for the treatment of patients with progressive, metastatic medullary thyroid cancer. In vitro data indicate that (1) cytochrome P 450 (CYP) 3A4 is the primary CYP isoenzyme involved in the metabolism of cabozantinib, and (2) CYP2C8 is the CYP isoenzyme most potently inhibited by cabozantinib with potential for in vivo inhibition at clin. relevant plasma exposures. Pharmacokinetic (PK) drug-drug interactions (DDIs) were evaluated clin. between cabozantinib and (1) a CYP3A inducer (rifampin) in healthy volunteers, (2) a CYP3A inhibitor (ketoconazole) in healthy volunteers, and (3) a CYP2C8 substrate (rosiglitazone) in patients with solid tumors. Compared with cabozantinib given alone, coadministration with rifampin resulted in a 4.3-fold higher plasma clearance (CL/F) of cabozantinib and a 77% decrease in cabozantinib plasma AUC0-inf, whereas coadministration with ketoconazole decreased cabozantinib CL/F by 29% and increased cabozantinib AUC0-inf by 38%. Chronic coadministration with cabozantinib resulted in no significant effect on rosiglitazone plasma Cmax, AUC0-24, or AUC0-inf. In summary, chronic use of strong CYP3A inducers and inhibitors should be avoided when cabozantinib is administered, and cabozantinib at clin. relevant exposures is not anticipated to markedly affect the PK of concomitant medications via CYP enzyme inhibition.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic drug interaction studies of cabozantinib, effect of CYP3A inducer rifampin and inhibitor ketoconazole on cabozantinib plasma PK and effect of cabozantinib on CYP2C8 probe substrate rosiglitazone plasma pharmacokinetics)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



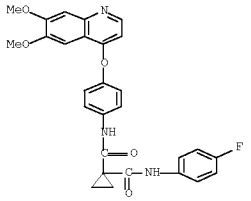
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 215 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1258933 CAPLUS Full-text
DOCUMENT NUMBER: 164:142494
TITLE: Small-molecule kinase inhibitors: an analysis of FDA-approved drugs
AUTHOR(S): Wu, Peng; Nielsen, Thomas E.; Clausen, Mads H.
CORPORATE SOURCE: Department of Chemistry, Technical University of Denmark, Kgs. Lyngby, DK-2800, Den.
SOURCE: Drug Discovery Today (2016), 21(1), 5-10
CODEN: DDTOFS; ISSN: 1359-6446
DIGITAL OBJECT ID: 10.1016/j.drudis.2015.07.008
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Small-mol. kinase inhibitors (SMKIs), 28 of which are approved by the US Food and Drug Administration (FDA), have been actively pursued as promising targeted therapeutics. Here, we assess the key structural and physicochem. properties, target selectivity and mechanism of function, and therapeutic indications of these approved inhibitors. Our anal. showed that >30% of approved SMKIs have a mol. weight (MW) exceeding 500 and all have a total ring count of between three and five. The assumption that type II inhibitors tend to be more selective than type I inhibitors has been proved to be unreliable. Although previous SMKI research was concentrated on tyrosine kinase inhibitors for cancer treatment, recent progress indicates diversification of SMKI research in terms of new targets, mechanistic types, and therapeutic indications.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural and physicochem. properties, target selectivity and mechanism of function therapeutic indications of FDA approved small-mol. kinase inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 216 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1256269 CAPLUS Full-text
DOCUMENT NUMBER: 164:524968
TITLE: 2ME2 inhibits the activated hypoxia-inducible pathways by cabozantinib and enhances its efficacy against medullary thyroid carcinoma
AUTHOR(S): Lin, Han; Jiang, Xian; Zhu, Huaqiang; Jiang, Wenjing; Dong, Xuesong; Qiao, Haiquan; Sun, Xueying; Jiang, Hongchi
CORPORATE SOURCE: Key Laboratory of Hepatosplenic Surgery, Department of General Surgery, The First Affiliated Hospital of Harbin Medical University, Harbin, 150001, Peop. Rep. China
SOURCE: Tumor Biology (2016), 37(1), 381-391
CODEN: TUMBEA; ISSN: 1010-4283
DIGITAL OBJECT ID: 10.1007/s13277-015-3816-1
PUBLISHER: Springer
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is a multi-targeted tyrosine kinase inhibitor targeting vascular endothelial growth factor (VEGF) receptor (VEGFR)-2, MET (c-Met, also called hepatocyte growth factor (HGF) receptor), and other receptor tyrosine kinases. Cabozantinib has recently been approved for treating advanced medullary thyroid carcinoma (MTC), but its long-term benefit remains uncertain and dose-dependent adverse events are very common. The present study has demonstrated that 2-methoxyestradiol (2ME2), an inhibitor of hypoxia-inducible factors (HIFs) and a promising anticancer agent under investigation in clin. trials, strengthens anticancer activities of cabozantinib against MTC cells in vitro and in vivo. The activated hypoxia-inducible pathways, which are mainly regulated by HIF-1, contribute to the resistance of hypoxic MTC cells to cabozantinib. Cabozantinib upregulated HIF-1α expression at translational levels and increased the expression of the downstream factors including VEGF, lactate dehydrogenase A (LDHA), HGF, and MET. 2ME2 corrected the activated pathways by cabozantinib through downregulating HIF-1α expression and inhibiting its nuclear translocation in hypoxic MTC cells. Administration of 2ME2 enhanced the efficacy of cabozantinib in suppressing the growth of MTC cell line xenografts and patient-derived xenografts established in mice. Given that 2ME2 targets insensitive hypoxic cancer cells to cabozantinib and can inhibit the activated pathways by cabozantinib, the present results warrant further investigation of 2ME2, particularly in combination with cabozantinib, for the treatment of MTC.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2ME2 inhibits activated hypoxia-inducible pathways by cabozantinib and enhances its efficacy against medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

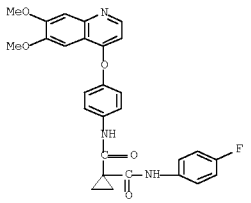


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 217 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1243654 CAPLUS Full-text
DOCUMENT NUMBER: 163:316612
TITLE: Biomarker TTF1 for predicting effect of c-met inhibitor
INVENTOR(S): Kim, Bo Gyou; Lee, Eunjin; Kim, Kyung Ah; Ahn, Tae Jin
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 92pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150212077	A1	20150730	US 2015-14604361	20150123
KR 2015088433	A	20150803	KR 2014-8733	20140124
PRIORITY APPLN. INFO.:			KR 2014-8733 A	20140124

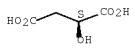
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method of predicting an effect of a c-Met inhibitor and/or selecting a subject for application of a c-Met inhibitor using trefoil factor 1 (TFF1), a method of monitoring an effect of a c-Met inhibitor using TFF1, and a method of treating and/or preventing cancer including administering a c-Met inhibitor to the selected subject. Herein, the effect of a c-Met inhibitor may refer to the prevention, improvement, alleviation, and/or treatment of a c-Met related disease such as cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biomarker TTF1 for predicting effect of c-met inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



CM 2

CRN 97-67-6
CMF C4 H6 O5

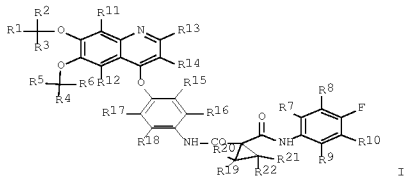
Absolute stereochemistry. Rotation (-).



L4 ANSWER 219 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1213912 CAPLUS Full-text
DOCUMENT NUMBER: 163:271103
TITLE: Preparation of deuterated cabozantinib derivatives and their application as anticancer agents
INVENTOR(S): Chen, Xinghai; Peng, Wei; Parker, Omar; Zheng, Feiming; Fu, Yong
PATENT ASSIGNEE(S): Shanghai Shengkao Pharmaceutical Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 35pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

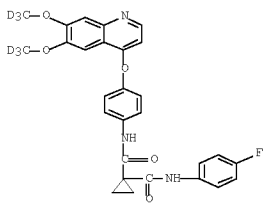
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104788372	A	20150722	CN 2014-10361351	20140725
PRIORITY APPLN. INFO.:			CN 2014-10361351	20140725

OTHER SOURCE(S): MARPAT 163:271103
GI

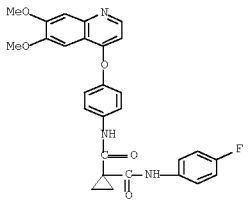


I

AB The invention is related to the prepn. of deuterated cabozantinib derivs. I and their application as anticancer agents. The invention compound I, wherein R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, and R22 are H or D independently and contain at least one D and their pharmaceutically acceptable salts, crystalline hydrates, solvates, prodrugs, single crystal or polymorph are claimed. Compound I was prepared by multi-step procedure (procedure given). The deuterated cabozantinib derivs. have slow decomposition in vivo, thereby reducing adverse metabolism of drugs. The invention compds. were evaluated for their anticancer activity.
IT 1802168-46-2P 1802168-48-4P 1802168-49-5P
1802168-50-8P 1802168-51-9P 1802168-52-0P
1802168-53-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of deuterated cabozantinib derivs. and their application as anticancer agents)
RN 1802168-46-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 1802168-48-4 CAPLUS

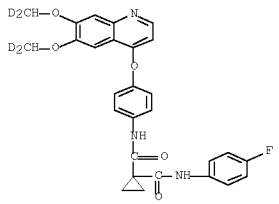


L4 ANSWER 218 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1226166 CAPLUS Full-text
TITLE: The study on synthetic technology of cabozantinib (S)-malate
AUTHOR(S): Qi, Baohui; He, Huan
CORPORATE SOURCE: Department of Bioengineering, Zhuhai Campus, Zunyi Medical College, Zhuhai, 519041, Peop. Rep. China
SOURCE: Guangdong Huagong (2014), 41(19), 22-23
CODEN: GHUAFI; ISSN: 1007-1865
PUBLISHER: Guangdong Huagong Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The cabozantinib(S)-malate, which was used for the treatment of locally advanced or metastatic progressive medullary thyroid cancer, was prepared from 3, 4-dimethoxyacetophenone by nitration, condensation, cyclization, chlorination and substitution, etc. In this synthetic route, raw materials were com. available, and reactive conditions were mild, and the operation was easy, and the yield was higher.
IT INDEXING IN PROGRESS
IT 1140909-48-3P, Cabozantinib (S)-malate
RL: SPN (Synthetic preparation); PREP (Preparation)
(study on synthetic technol. of cabozantinib S-malate)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

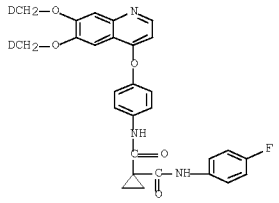
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

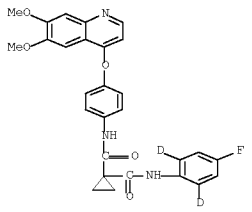
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d2)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



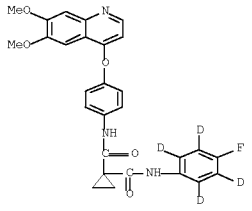
RN 1802168-49-5 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 1802168-50-8 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)- (CA INDEX NAME)



RN 1802168-53-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)- (CA INDEX NAME)

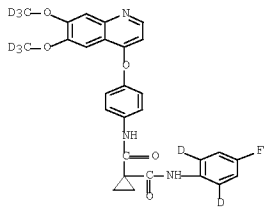


IT 1802168-54-2P 1802168-55-3P 1802168-56-4P
1802168-57-5P 1802168-58-6P 1802168-59-7P
1802168-60-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of deuterated cabozantinib derivs. and their application as anticancer agents)
RN 1802168-54-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

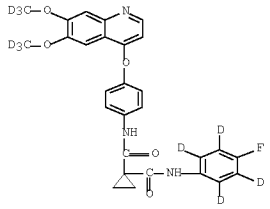
N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

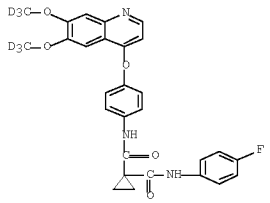
CRN 1802168-46-2
CMF C28 H18 D6 F N3 O5



RN 1802168-51-9 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)- (CA INDEX NAME)



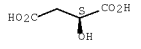
RN 1802168-52-0 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)- (CA INDEX NAME)



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

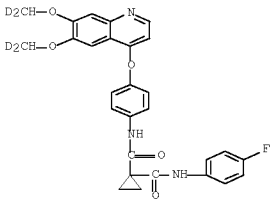


RN 1802168-55-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[[6,7-di(methoxy-d2)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

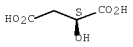
CRN 1802168-48-4
CMF C28 H20 D4 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

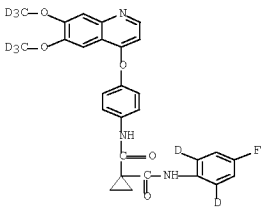


RN 1802168-56-4 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[[6,7-di(methoxy-d)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

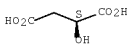
CRN 1802168-49-5
CMF C28 H22 D2 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

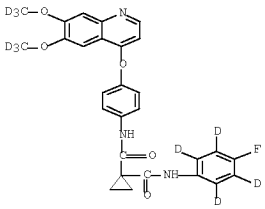
Absolute stereochemistry. Rotation (-).

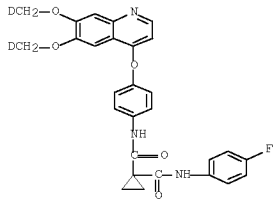


RN 1802168-58-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with
N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

CRN 1802168-51-9
CMF C28 H14 D10 F N3 O5

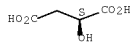




CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



RN 1802168-57-5 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[[6,7-di(methoxy-d3)-4-quinolinyl]oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

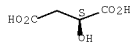
CM 1

CRN 1802168-50-8
CMF C28 H16 D8 F N3 O5

CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

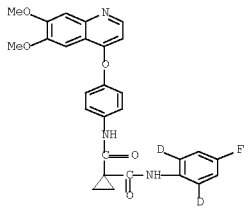


RN 1802168-59-7 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,6-d2)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

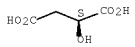
CRN 1802168-52-0
CMF C28 H22 D2 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

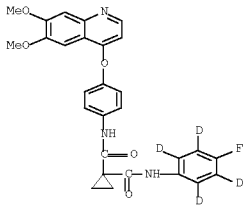


RN 1802168-60-0 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl-2,3,5,6-d4)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

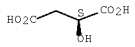
CRN 1802168-53-1
CMF C28 H20 D4 F N3 O5



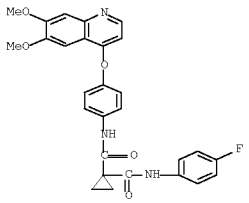
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 220 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1181814 CAPLUS Full-text
DOCUMENT NUMBER: 164:455657
TITLE: Population Pharmacokinetic Model of Cabozantinib in Patients with Medullary Thyroid Carcinoma and Its Application to an Exposure-Response Analysis



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 221 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1173698 CAPLUS Full-text
DOCUMENT NUMBER: 163:302461
TITLE: Compositions and methods for the treatment of intraocular neovascularization and/or leakage using tyrosine kinase inhibitors
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 12pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150196649	A1	20150716	US 2015-14593704	20150109
CA 2936239	A1	20150723	CA 2015-2936239	20150109
WO 2015108787	A2	20150723	WO 2015-US10867	20150109
WO 2015108787	A3	20151112		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

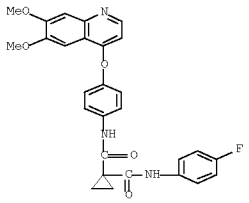
KR 2016126983	A	20161102	KR 2016-7022357	20150109
EP 3094284	A2	20161123	EP 2015-737749	20150109

AUTHOR(S): Miles, Dale; Jumbe, Nelson L.; Lacy, Steven; Nguyen, Linh
CORPORATE SOURCE: Genentech (A member of the Roche Group), South San Francisco, CA, USA
SOURCE: Clinical Pharmacokinetics (2016), 55(1), 93-105
CODEN: CPKNDH; ISSN: 0312-5963
DIGITAL OBJECT ID: 10.1007/s40262-015-0295-x
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background and Objectives: Cabozantinib is a tyrosine kinase inhibitor approved in the USA and EU for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC). The indicated cabozantinib dose is 140 mg/day, with dose modifications allowed for patients who develop adverse events (AEs). The anal. objective was to develop a population pharmacokinetic (PopPK) model in MTC patients and to use the model for exposure-response (ER) anal. of dose modifications. Methods: A PopPK model for cabozantinib was developed using data from three clin. trials (2079 evaluations from 289 patients), including a randomized, double-blind, placebo-controlled phase III study of patients with progressive, metastatic MTC. The PopPK model predictions [model-predicted steady-state area under the plasma concentration-time curve (AUCss,pred)] were used for an ER anal. of the time to first dose modification. Results: The final PopPK model was a one-compartment model with first-order absorption and first-order elimination. Estimated cabozantinib apparent oral clearance (CL/F) and apparent volume of distribution (Vc/F) were 106 L/day [±2.98 % relative standard error (RSE)] (males) and 349 L (±2.73 % RSE), resp. CL/F was reduced by 22 % (to 83 L/day) in females. Sex and body mass index (BMI) were significant covariates that combined contributed 15 % to the variability in cabozantinib CL/F, but did not warrant dose adjustment. Higher cabozantinib AUCss,pred was correlated to an increased risk of early dose modification and a lower average dose through to Day 85. Early cabozantinib dose modification was not associated with a reduction in progression-free survival (PFS). Conclusion: A PopPK model was developed for cabozantinib pharmacokinetics in MTC patients. Higher cabozantinib exposure was associated with earlier first dose modification and a lower average administered dose through to Day 85. Early first dose modification did not appear to impact PFS.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(population pharmacokinetic model of cabozantinib in patients with medullary thyroid carcinoma and its application to exposure)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2017503028	T	20170126	JP 2016-565095		20150109
IN 201617023084	A	20160831	IN 2016-17023084		20160705
MX 2016009312	A	20170106	MX 2016-9312		20160715
PRIORITY APPLN. INFO.:			US 2014-61928061	P	20140116
			US 2014-61969861	P	20140325
			WO 2015-US10867	W	20150109

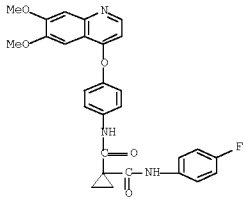
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention provides compns. and methods for the treatment of intraocular neovascularization and/or leakage including wet age-related macular degeneration. The compns. preferably use tyrosine kinase inhibitors with an IC50 for VEGFR2 of 20 nanomolar or less and an IC50 for c-MET of 20 nanomolar or less.
IT 849217-68-1, Cabozantinib 1235470-36-6 1642298-58-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treatment of intraocular neovascularization and/or leakage using tyrosine kinase inhibitors of VEGFR2 and c-MET)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1235470-36-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

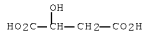
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

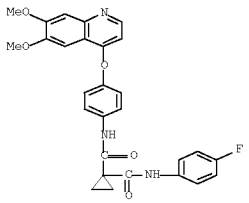
CRN 6915-15-7
CMF C4 H6 O5



RN 1642298-56-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 75-75-2
CMF C H4 O3 S



L4 ANSWER 222 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1169349 CAPLUS Full-text
DOCUMENT NUMBER: 163:218113
TITLE: Preparation of heterocyclic modulators of lipid synthesis for use against cancer and viral infections
INVENTOR(S): Wagman, Allan S.; Johnson, Russell J.; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.; Duke, Greg; Ohol, Yamini; Heuer, Timothy; O'Farrell, Marie
PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

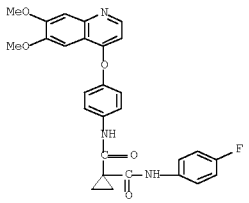
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015105860	A1	20150716	WO 2015-US10459	20150107
WO 2015105860	A9	20160204		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2935767	A1	20150716	CA 2015-2935767	20150107
AU 2015204907	A1	20160721	AU 2015-204907	20150107
IL 246463	A	20160831	IL 2015-246463	20150107
KR 2016105416	A	20160906	KR 2016-7018178	20150107
CN 105980376	A	20160928	CN 2015-80003786	20150107
EP 3092232	A1	20161116	EP 2015-700939	20150107
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

JP 2017502083	T	20170119	JP 2016-562737	20150107
MX 2016008841	A	20161013	MX 2016-8841	20160705
US 20160326141	A1	20161110	US 2016-15110154	20160707
IN 201617024431	A	20160831	IN 2016-17024431	20160718
US 20170119786	A1	20170504	US 2016-15349960	20161111

PRIORITY APPLN. INFO.:

US 2014-61924520	P	20140107
US 2011-61450561	P	20110308
US 2011-61508611	P	20110716
US 2012-61585642	P	20120111
US 2012-13415660	A1	20120308
US 2012-61667894	P	20120703
US 2012-61698511	P	20120907
US 2012-61699819	P	20120911
US 2013-61785933	P	20130314
WO 2013-US48950	A1	20130701
US 2014-14315133	A1	20140625
US 2014-14587908	A3	20141231
WO 2015-US10459	W	20150107
US 2015-14874961	A2	20151005
US 2016-15201824	A2	20160705
US 2016-15110154	A2	20160707

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 163:218113; MARPAT 163:218113
GI



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

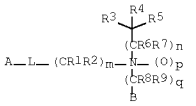
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [LAr = II-IV; Ar = V; R1 = H, CN, halo, etc.; R2 = H, halo, alkyl; R3 = H or F; R21 = H, halo, alkyl, etc.; R22 = H, halo, alkyl; R24 = alkoxy, O(alkylene)alkoxy, cycloalkoxy, etc.; R25 = H, halo, alkyl, etc.; with the provisos], useful for treating conditions characterized by dysregulation of a fatty acid synthase pathway, were prepared E.g., a multi-step synthesis of VI, starting from Me propanoate and Me formate, was described. Exemplified compds. I were evaluated for their FASN inhibition (data given for representative compds. I). Pharmaceutical composition comprising I was disclosed.
IT [illegible], Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of heterocyclic modulators of lipid synthesis for use
against cancer and viral infections)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

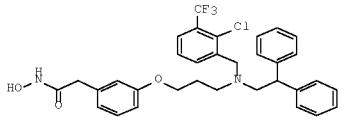
L4 ANSWER 223 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1169171 CAPLUS Full-text
DOCUMENT NUMBER: 163:217976
TITLE: Preparation of tertiary amines and amine oxides as LXR agonists
INVENTOR(S): Martinez, Eduardo J.; Kaiser, Bernd; Tavazoie, Sohail F.; Kurth, Isabel; Gonsalves, Foster Casimir; Darst, David M., Jr.; Tavazoie, Masoud Fakhr
PATENT ASSIGNEE(S): Rgenix, Inc., USA
SOURCE: PCT Int. Appl., 163pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015106164	A1	20150716	WO 2015-US10909	20150109
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2939120	A1	20150716	CA 2015-2939120	20150109
AU 2015204572	A1	20160804	AU 2015-204572	20150109
EP 3091970	A1	20161116	EP 2015-734952	20150109
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

US 20170066791 A1 20170309 US 2016-15110343 20160707
PRIORITY APPLN. INFO.: US 2014-61926150 P 20140110
WO 2015-US10909 W 20150109
OTHER SOURCE(S): CASREACT 163:217976; MARPAT 163:217976
GI



I



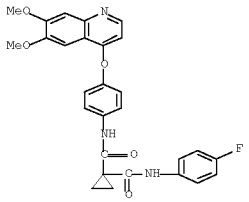
II

AB This invention features compds. of formula I that modulate the activity of liver X receptors, pharmaceutical compns. including the compds. of the invention, and methods of utilizing those compns. for modulating the activity of liver X receptors in the treatment of cancer. Compds. of formula I wherein A is substituted Ph, (un)substituted azacyclyl, and (un)substituted oxobenzopyranyl; L is absent, O, S, amino and CR4R5; m is 2, 3, 4, 5, 6, 7 and 8;, n, p and q are independently 0 and 1; R1, R2, R6, R7, R8 and R9 are independently H, OH, halo, amino, thio, etc.; R3 is H, OH, amino, (un)substituted C1-6 alkyl, etc.; R4 and R6 are independently H, OH, halo, amino, thio, etc.; and pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by reductive amination of 2-chloro-3-trifluoromethylbenzaldehyde with 2,2-diphenethylamine followed by alkylation with 1,3-dibromopropane; the resulting (3-bromopropyl)({[2-chloro-3-(trifluoromethyl)phenyl]methyl})(2,2-diphenylethyl)amine underwent etherification with Me 3-hydroxyphenylacetate to give Me 2-{3-[3-({[2-chloro-3-(trifluoromethyl)phenyl]methyl}-(2,2-diphenylethyl)- amino)-propoxy]phenyl}acetate, which underwent amidation with hydroxylamine hydrochloride to give compound II. The invention compds. were evaluated for their LXR agonistic activity. From the assay it was determine that compound exhibited ApoE induction . 80% at 1 μM and > 40 % at 10 μM, and EC50 value of 1.0 μM.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of tertiary amines and amine oxides as LXR agonists)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

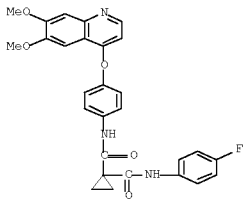
L4 ANSWER 224 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1144766 CAPLUS Full-text
DOCUMENT NUMBER: 164:320926
TITLE: Salvage systemic therapy for advanced urothelial carcinoma: on the cusp of a sea change?
AUTHOR(S): Sonpavde, Guru; Bellmunt, Joaquim
CORPORATE SOURCE: University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, AL, USA
SOURCE: Oncologist (2015), 20(5), 461-463
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2015-0077
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This paper studies about the salvage systemic therapy for advanced urothelial carcinoma.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on salvage systemic therapy for advanced urothelial carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

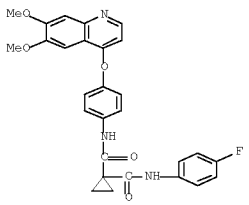
L4 ANSWER 225 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1144752 CAPLUS Full-text
DOCUMENT NUMBER: 163:384755
TITLE: Prospective comprehensive genomic profiling of advanced gastric carcinoma cases reveals frequent clinically relevant genomic alterations and new routes for targeted therapies
AUTHOR(S): Ali, Siraj M.; Sanford, Eric M.; Klempner, Samuel J.; Rubinson, Douglas A.; Wang, Kai; Palma, Norma A.; Chmielecki, Juliann; Yelensky, Roman; Palmer, Gary A.; Morosini, Deborah; Lipson, Doron; Catenacci, Daniel V.; Braiteh, Fadi; Erlich, Rachel; Stephens, Philip J.; Ross, Jeffrey S.; Ou, Sai-Hong Ignatius; Miller, Vincent A.
CORPORATE SOURCE: Foundation Medicine Inc., Cambridge, MA, USA
SOURCE: Oncologist (2015), 20(5), 499-507
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2014-0378
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Gastric cancer (GC) is a major global cancer burden and the second most common cause of global cancer-related deaths. The addition of anti-ERBB2 (HER2) targeted therapy to chemotherapy improves survival for ERBB2-amplified advanced GC patients; however, the majority of GC patients do not harbor this alteration and thus cannot benefit from targeted therapy under current practice paradigms. Materials and Methods: Prospective comprehensive genomic profiling of 116 predominantly locally advanced or metastatic (90.0%) gastric cancer cases was performed to identify genomic alterations (GAs) associated with a potential response to targeted therapies approved by the U.S. Food and Drug Administration or targeted therapy-based clin. trials. Results: Overall, 78% of GC cases harbored one clin. relevant GA or more, with the most frequent alterations being found in TP53 (50%), ARID1A (24%), KRAS (16%), CDH1 (15%), CDKN2A (14%), CCND1 (9.5%), ERBB2 (8.5%), PIK3CA (8.6%), MLL2 (6.9%), FGFR2 (6.0%), and MET (6.0%). Receptor tyrosine kinase genomic alterations were detected in 20.6% of cases, primarily ERBB2, FGFR2, and MET amplification, with ERBB2 alterations evenly split between amplifications and base substitutions. Rare BRAF mutations (2.6%) were also observed One MET-amplified GC patient responded for 5 mo to crizotinib, a multitargeted ALK/ROS1/MET inhibitor. Conclusion: Comprehensive genomic profiling of GC identifies clin. relevant GAs that suggest benefit from targeted therapy including MET-amplified GC and ERBB2 base substitutions.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prospective comprehensive genomic profiling of advanced gastric carcinoma cases reveals frequent clin. relevant genomic alterations and new routes for targeted therapies)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 226 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1128572 CAPLUS Full-text
DOCUMENT NUMBER: 165:127
TITLE: Metabolism and disposition of cabozantinib in healthy male volunteers and pharmacologic characterization of its major metabolites
AUTHOR(S): Lacy, Steven; Hsu, Bih; Miles, Dale; Aftab, Dana; Wang, Ronghua; Nguyen, Linh
CORPORATE SOURCE: Department of Non-Clinical Development, Exelixis, Inc., South San Francisco, CA, USA
SOURCE: Drug Metabolism & Disposition (2015), 43(8), 1190-1207
CODEN: DMDSAI; ISSN: 1521-009X
DIGITAL OBJECT ID: 10.1124/dmd.115.063610
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

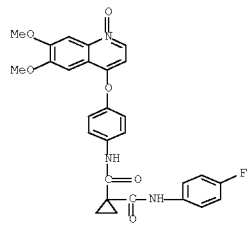
AB Metab. and excretion of cabozantinib, an oral inhibitor of receptor tyrosine kinases, was studied in 8 healthy male volunteers after a single oral dose of 175 mg cabozantinib l-malate containing 14C-cabozantinib (100 μCi/subject). Total mean radioactivity recovery within 48 days was 81.09%; radioactivity was eliminated in feces (53.79%) and urine (27.29%). Cabozantinib was extensively metabolized with 17 individual metabolites identified by liquid chromatog.-tandem mass spectrometry (LC-MS/MS) in plasma, urine, and feces. Relative plasma radioactivity exposures (analyte AUC0-t/total AUC0-t for cabozantinib + major metabolites) were 27.2, 25.2, 32.3, 7, and 6% for cabozantinib and major metabolites monohydroxy sulfate (EXEL-1646), 6-desmethyl amide cleavage product sulfate (EXEL-1644), N-oxide (EXEL-5162), and amide cleavage product (EXEL-5366), resp. Comparable relative plasma exposures determined by LC-MS/MS anal. were 32.4, 13.8, 45.9, 4.9, and 3.1%, resp. These major metabolites each possess in vitro inhibition potencies ≤1/10th of parent cabozantinib against the targeted kinases MET, RET, and VEGFR2/KDR. In an in vitro cytochrome P 450 (CYP) panel, cabozantinib and EXEL-1644 both inhibited most potently CYP2C8 (Kiapp = 4.6 and 1.1 μM, resp.). In an in vitro drug transporter panel, cabozantinib inhibited most potently MATE1 and MATE2-K (IC50 = 5.94 and 3.12 μM, resp.) and was a MRP2 substrate; EXEL-1644 inhibited most potently OAT1, OAT3, OATP1B1, MATE1, and OATP1B3 (IC50 = 4.3, 4.3, 6.1, 16.7, and 20.6 μM, resp.) and was a substrate of MRP2, OAT3, OATP1B1, OATP1B3, and possibly P-gp. Therefore, cabozantinib appears to be the primary pharmacol. active circulating analyte, whereas both cabozantinib and EXEL-1644 may represent potential for drug-drug interactions.

IT 1621681-63-7

RL: BSU (Biological study, unclassified); BIOL (Biological study) (metabolism, disposition and pharmacokinetics of cabozantinib and its biotransformation products in healthy male volunteers and pharmacol. characterization of its major metabolites)

RN 1621681-63-7 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)

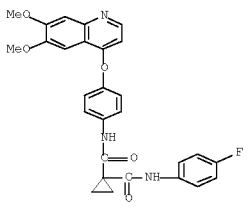


IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (metabolism, disposition and pharmacokinetics of cabozantinib and its biotransformation products in healthy male volunteers and pharmacol. characterization of its major metabolites)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 227 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1127378 CAPLUS Full-text

DOCUMENT NUMBER: 164:142135

TITLE: MET inhibitors for treatment of advanced hepatocellular carcinoma: a review

AUTHOR(S): Qi, Xing-Shun; Guo, Xiao-Zhong; Han, Guo-Hong; Li, Hong-Yu; Chen, Jiang

CORPORATE SOURCE: Department of Gastroenterology, General Hospital of Shenyang Military Area, Shenyang, Liaoning Province, 100840, Peop. Rep. China

SOURCE: World Journal of Gastroenterology (2015), 21(18), 5445-5453
CODEN: WJGAF2; ISSN: 2219-2840

DIGITAL OBJECT ID: 10.3748/wjg.v21.i18.5445

PUBLISHER: Baishideng Publishing Group Inc.

DOCUMENT TYPE: Journal; General Review; (online computer file)

LANGUAGE: English

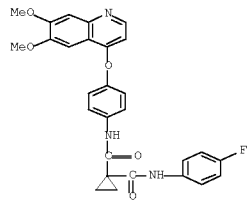
AB The current std. treatment option for advanced hepatocellular carcinoma (HCC) is sorafenib, but its clin. benefit is modest. In spite of many attempts, few drugs can provide any significant improvement of survival as the first- or second-line therapy of choice in phase III randomized controlled trials. Recently, the subgroup anal. of a phase II randomized controlled trial has shown that tivantinib, a selective MET inhibitor, can significantly improve the overall survival in patients with MET-pos. advanced HCC after the failure or intolerance of a prior systemic therapy. These findings enlighten the role of MET inhibitors in the treatment of advanced HCC. In this paper, we review all ongoing and completed clin. trials regarding this topic. As for the first-line therapy of advanced HCC, INC280 and foretinib are being evaluated in 2 phase II single-arm trials; and MSC2156119J and golvatinib plus sorafenib are being compared with sorafenib alone in 2 phase II randomized controlled trials. As for the second-line therapy of advanced HCC, tivantinib and cabozantinib are being compared with placebo in 2 phase II randomized controlled trials.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (phase II and III clin. trials regarding MET inhibitors used for treatment of human advanced hepatocellular carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 228 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:1124138 CAPLUS Full-text

DOCUMENT NUMBER: 163:187706

TITLE: Biomarker for predicting or monitoring efficacy of c-Met inhibitor

INVENTOR(S): Jung, Soo Yeon; Shim, Seon Hui; Song, Yun Jeong; Yoo, Hyeon-Seok

PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea

SOURCE: Eur. Pat. Appl., 147pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2891884	A2	20150708	EP 2015-150360	20150107
EP 2891884	A3	20151014		
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015082121	A	20150715	KR 2015-956	20150106
CN 104762371	A	20150708	CN 2015-10008065	20150107
US 20150192588	A1	20150709	US 2015-14591787	20150107
JP 2015129755	A	20150716	JP 2015-1880	20150107
PRIORITY APPLN. INFO.:			KR 2014-1799	A 20140107
			KR 2015-956	A 20150106

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

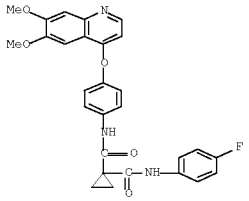
AB A biomarker for predicting and/or monitoring the efficacy of a c-Met inhibitor; a composition for predicting and/or monitoring the efficacy of a c-Met inhibitor, comprising a material detecting the biomarker; a composition for selecting a subject suitable for the application of a c-Met inhibitor, comprising a material detecting the biomarker is presented. In addition a method for predicting and/or monitoring the efficacy of a c-Met inhibitor using the biomarker; a method for selecting a subject suitable for the application of a c-Met inhibitor using the biomarker; and a method for preventing and/or treating cancer comprising administering a c-Met inhibitor to the selected subject is given. One embodiment provides a biomarker for use in predicting and/or monitoring the therapeutic effect of a c-Met inhibitor or selecting a subject suitable for the application of a c-Met inhibitor, wherein the biomarker includes at least one selected from the group consisting of IL-8, BIGH3, or MIF and nucleic acids encoding the proteins. Another embodiment provides a c-Met inhibitor or a pharmaceutical composition including a c-Met inhibitor, for use in inhibiting c-Met and/or treating a cancer in a subject, wherein the subject has a high level of IL-8 or a nucleic acid encoding IL-8 compared to a reference sample in which a c-Met inhibitor is not effective; shows a decreased level of IL-8, BIGH3, MIF, and/or nucleic acids encoding them after administering a c-Met inhibitor; and/or has a mutation of KRAS, BRAF, and/or nucleic acids encoding them. A specific example shows the IL-8 levels in cancer cell-implanted mouse models showing relationship between IL-8 level and responsiveness to an anti-c-Met antibody.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biomarker for predicting or monitoring efficacy of c-Met inhibitor)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

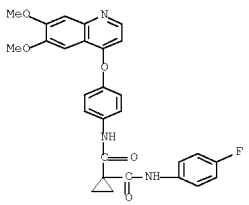


OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

L4 ANSWER 229 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1079985 CAPLUS Full-text
DOCUMENT NUMBER: 163:231592
TITLE: Heteroaromatic compound and its application in medicine for treating proliferative diseases
INVENTOR(S): Liu, Bing; Liu, Jinlei; Zhang, Yingjun; Zhang, Jiancun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 189pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104744446	A	20150701	CN 2014-10835175	20141229
PRIORITY APPLN. INFO.:			CN 2013-10746766 A	20131230
			CN 2014-10108590 A	20140322

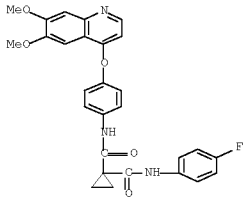
OTHER SOURCE(S): CASREACT 163:231592; MARPAT 163:231592
AB The invention provides a class of heteroarom. compd. or stereisomer, geometrical isomer, tautomer, racemate, oxynitride, hydrate, solvate, metabolite, metabolic precursor and pharmaceutically acceptable salt, or prodrug thereof, used for the treatment of proliferative disease. The invention also discloses the pharmaceutical composition containing such compound and application of the compound of this invention or its pharmaceutical composition in the preparation of medicine for the treatment of proliferative disease.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heteroarom. compound and its application in medicine for treating proliferative diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 231 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1053832 CAPLUS Full-text
DOCUMENT NUMBER: 163:145772
TITLE: Preparation of heterocyclic modulators of lipid synthesis
INVENTOR(S): Heuer, Timothy Sean; Oslob, Johan D.; Mcdowell, Robert S.; Johnson, Russell; Yang, Hanbiao; Evanchik, Marc; Zaharia, Cristiana A.; Cai, Haiying; Hu, Lily W.
PATENT ASSIGNEE(S): 3-V Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 488pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015095767	A1	20150625	WO 2014-US71617	20141219
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR,				



L4 ANSWER 230 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:1073487 CAPLUS Full-text
DOCUMENT NUMBER: 163:480792
TITLE: Response and toxicity of small-molecule tyrosine kinase inhibitors in patients with thyroid carcinoma: a systematic review and meta-analysis
AUTHOR(S): N. Klein Hesselink, E.; Steenvoorden, D.; Kapiteijn, E.; Corssmit, E. P.; van der Horst-Schrivers, A. N. A.; Lefrandt, J. D.; Links, T. P.; Dekkers, O. M.
CORPORATE SOURCE: Department of Endocrinology, Department of Internal Medicine, Division of Vascular Medicine, University Medical Center Groningen, University of Groningen, Groningen, Neth.
SOURCE: European Journal of Endocrinology (2015), 172(5), R215-R225
CODEN: EJOEEP; ISSN: 0804-4643
DIGITAL OBJECT ID: 10.1530/EJE-14-0788
PUBLISHER: BioScientifica Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Context: Many tyrosine kinase inhibitors (TKIs) have been studied in patients with thyroid carcinoma (TC). However, the effect and toxicity of various TKIs in differentiated TC (DTC) and medullary TC (MTC) patients have not been directly compared. The aim of the present systematic review and meta-anal. was to systematically summarize response and toxicity of TKIs in TC patients. Methods: All major databases were systematically searched for publications on TKIs in TC. Primary endpoint was objective response; secondary endpoints were clin. benefit, percentage TKI dose reduction/discontinuation, hand-foot syndrome, diarrhea, and nausea/vomiting. Meta-anal. was performed using an exact likelihood approach and a logistic regression. Pooled percentages and 95% CIs were reported. Results: In total, 22 publications were included. For DTC patients, gefitinib induced no objective responses. Pooled percentage was highest for pazopanib, 49 (95% CI 33-64)%, and was 17 (95% CI 12-24)% for sorafenib. For MTC, gefitinib and imatinib induced no objective responses, whereas sunitinib induced objective response in 43 (95% CI 14-77)%. For vandetanib and cabozantinib, these nos. were 40 (95% CI 34-46)% and 27 (95% CI 22-32)% resp. Clin. benefit was found in 53 (95% CI 48-59)% of DTC patients on sorafenib, and in 84 (95% CI 79-88)% and 55 (95% CI 49-61)% of MTC patients on vandetanib and cabozantinib resp. All TKIs were associated with considerable toxicity. Conclusion: The currently studied TKIs show a modest response, while side effects are not negligible. Therefore, we suggest to solely consider TKIs in TC patients with rapid progressive disease, for whom the benefits of treatment outweigh toxicity.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response and toxicity of small-mol. tyrosine kinase inhibitors in patients with thyroid carcinoma: systematic review and meta-anal.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

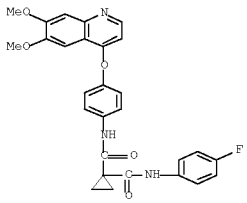
IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2934251	A1	20150625	CA 2014-2934251	20141219
AU 2014368945	A1	20160616	AU 2014-368945	20141219
KR 2016100329	A	20160823	KR 2016-7018773	20141219
CN 106061963	A	20161026	CN 2014-80075661	20141219
EP 3083583	A1	20161026	EP 2014-825066	20141219
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2017505291	T	20170216	JP 2016-541077	20141219
US 20160338998	A1	20161124	US 2016-15106539	20160620
PRIORITY APPLN. INFO.:			US 2013-61919235 P	20131220
			WO 2014-US71617 W	20141219

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 163:145772; MARPAT 163:145772
GI

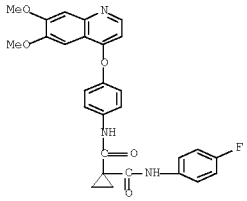
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This invention relates to heterocyclic modulators of lipid synthesis as well as pharmaceutically acceptable salts thereof; to pharmaceutical compns. comprising such compds.; and to methods of treating conditions characterized by dysregulation of a fatty acid synthase pathway by the administration of such compds. and combinations of such compds. and other therapeutic agents. Method of treating a condition characterized by dysregulation of a fatty acid synthase pathway in a subject by administering to the subject a therapeutically effective amount of compound I [LAr = II-IV; Ar = V-IX (wherein Het = 5-6 membered heteroaryl; R1 = H, CN, halo, etc.; R2 = H, halo, alkyl; R3 = H or F; R11 = H or Me); R21 = H, halo, alkyl, etc.; R22 = H, halo, alkyl; R24 = H, CN, alkyl, etc.; R25 = halo, CN, alkyl, etc.], in combination with other therapeutic agent, was claimed. Over three-hundred-eighty compds. I and their heterocyclic analogs were prepared E.g., a multi-step synthesis of X, starting from tert-Bu 4-iodopiperidine-1-carboxylate and 4-bromobenzonitrile, was described. The antiviral activities of the exemplified compds. I were assessed using the HCV1b replicon system (data given).
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of heterocyclic modulators of lipid synthesis useful for treating conditions characterized by dysregulation of a fatty acid synthase pathway)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 232 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:999711 CAPLUS Full-text
DOCUMENT NUMBER: 164:270620
TITLE: Iodide- and glucose-handling gene expression regulated by sorafenib or cabozantinib in papillary thyroid cancer
AUTHOR(S): Ruan, Maomei; Liu, Min; Dong, Qianggang; Chen, Libo
CORPORATE SOURCE: Department of Nuclear Medicine, Sixth People's Hospital, Shanghai Jiao Tong University, Shanghai, 200233, Peop. Rep. China
SOURCE: Journal of Clinical Endocrinology and Metabolism (2015), 100(5), 1771-1779
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2014-3023
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Context: The aberrant silencing of iodide-handling genes accompanied by up-regulation of glucose metabolism presents a major challenge for radioiodine treatment of papillary thyroid cancer (PTC). Objective: This study aimed to evaluate the effect of tyrosine kinase inhibitors on iodide-handling and glucose-handling gene expression in BHP 2-7 cells harboring RET/PTC1 rearrangement. Main Outcome Measures: In this in vitro study, the effects of sorafenib or cabozantinib on cell growth, cycles, and apoptosis were investigated by cell proliferation assay, cell cycle anal., and Annexin V-FITC apoptosis assay, resp. The effect of both agents on signal transduction pathways was evaluated using the Western blot. Quant. real-time PCR, Western blot, immunofluorescence, and radioisotope uptake assays were used to assess iodide-handling and glucose-handling gene expression. Results: Both compds. inhibited cell proliferation in a time-dependent and dose-dependent manner and caused cell cycle arrest in the G0/G1 phase. Sorafenib blocked RET, AKT, and ERK1/2 phosphorylation, whereas cabozantinib blocked RET and AKT phosphorylation. The restoration of iodide-handling gene expression and inhibition of glucose transporter 1 and 3 expression could be induced by either drug. The robust expression of sodium/iodide symporter induced by either agent was confirmed, and 125I uptake was correspondingly enhanced. 18F-fluorodeoxyglucose accumulation was significantly decreased after treatment by either sorafenib or cabozantinib. Conclusions: Sorafenib and cabozantinib had marked effects on cell proliferation, cell cycle arrest, and signal transduction pathways in PTC cells harboring RET/PTC1 rearrangement. Both agents could be potentially used to enhance the expression of iodide-handling genes and inhibit the expression of glucose transporter genes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of tyrosine kinase inhibitors including sorafenib and cabozantinib effect iodide- and glucose-handling gene expression in human papillary thyroid cancer HP 2-7 cells)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

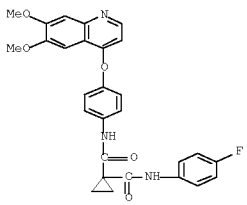
L4 ANSWER 233 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:981422 CAPLUS Full-text
DOCUMENT NUMBER: 163:88178
TITLE: Methods of selecting treatment regimens of cancer with chemotherapy plus VEGF signaling inhibitors using the predictive potential of serum protein and tumor gene expression
INVENTOR(S): Barry, Simon T.; Critchlow, Susan E.; Pommier, Aurelien J.C.
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015082880	A1	20150611	WO 2014-GB53485	20141125

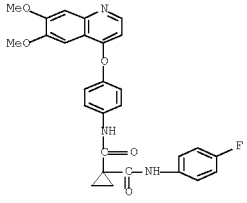
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61910652 P 20131202
AB The present invention is directed to, inter alia, the predictive potential of serum protein and tumor gene expression in patients with metastatic colorectal cancer (mCRC) receiving either chemotherapy plus placebo or chemotherapy plus the VEGF signaling inhibitor cediranib, sunitinib, sorafenib, pazopanib, tivozanib, vandetanib, soraninib, axitinib, cabozantinib, bevacizumab, aflibercept or ramucirumab. The present invention, in addition, provides for patient selection methods, as well as kits, that may be used in determining suitable cancer treatment regimens in subjects with cancer, with particular reference to whether the subject will gain benefit from treatment with VEGF signaling inhibitors.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of selecting treatment regimens of cancer with chemotherapy plus VEGF signaling inhibitors using the predictive potential of serum protein and tumor gene expression)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 234 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:960349 CAPLUS Full-text
DOCUMENT NUMBER: 164:270197
TITLE: Cabozantinib as a new drug for treating metastatic medullary thyroid cancer
AUTHOR(S): Chen, Hui-ling; Zhang, Zhi-ye; Yang, Yan-biao
CORPORATE SOURCE: Department of Pharmacy, Lanzhou City First People's Hospital, Lanzhou, 730050, Peop. Rep. China
SOURCE: Zhongguo Yaofang (2014), 25(29), 2766-2769
CODEN: ZYHAA4; ISSN: 1001-0408
DIGITAL OBJECT ID: 10.6039/j.issn.1001-0408.2014.29.27
PUBLISHER: Zhongguo Yaofang Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 12 refs. is given on the cabozantinib as a new drug for treating metastatic medullary thyroid cancer. The topic discussed include:: (1) clin. pharmacol. research of cabozantinib(action mechanism and pharmacol. effects), (2) clin. research of cabozantinib, (3) adaptation disease and dosage and administration of cabozantinib, (4) drug interactions with cytochrome P 450 and p-glycoprotein, (5) attention and safety evaluation of cabozantinib, (6) administration for special population.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as a new drug for treating metastatic medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



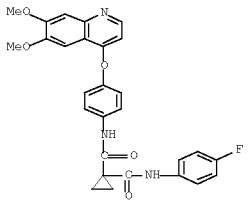
L4 ANSWER 235 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:948166 CAPLUS Full-text
DOCUMENT NUMBER: 164:367374

TITLE: Update on Cardiovascular Safety of Tyrosine Kinase Inhibitors: With a Special Focus on QT Interval, Left Ventricular Dysfunction and Overall Risk/Benefit
AUTHOR(S): Shah, Rashmi R.; Morganroth, Joel
CORPORATE SOURCE: Rashmi Shah Consultancy Ltd, Buckinghamshire, SL9 7JA, UK
SOURCE: Drug Safety (2015), 38(8), 693-710
CODEN: DRSAEA; ISSN: 0114-5916
DIGITAL OBJECT ID: 10.1007/s40264-015-0300-1
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB We previously reviewed the cardiovascular safety of 16 tyrosine kinase inhibitors (TKIs), approved for use in oncol. as of 30 Sept. 2012. Since then, the indications for some of them have been widened and an addnl. nine TKIs have also been approved as of 30 Apr. 2015. Eight of these nine are indicated for use in oncol. and one (nintedanib) for idiopathic pulmonary fibrosis. This report is an update on the cardiovascular safety of those 16 TKIs, including the post-marketing data concerning their pro-arrhythmic effects, and reviews the cardiovascular safety of the nine new TKIs approved since (afatinib, cabozantinib, ceritinib, dabrafenib, ibrutinib, lenvatinib, nintedanib, ponatinib, and trametinib). As before, we focus on specific aspects of cardiovascular safety, namely their potential to induce QT interval prolongation, left ventricular (LV) dysfunction and hypertension but now also summarise the risks of arterial thromboembolic events (ATEs) associated with these agents. Of the newer TKIs, cabozantinib and ceritinib have been shown to induce a mild to moderate degree of QTc interval prolongation while cardiac dysfunction has been reported with the use of afatinib, dabrafenib, lenvatinib, ponatinib and trametinib. The label for axitinib was revised to include a new association with cardiac dysfunction. Hypertension is associated with cabozantinib, lenvatinib, nintedanib, ponatinib and trametinib. Ponatinib, within 10 mo of its approval in Dec. 2012, required voluntary (temporary) suspension of its marketing until significant safety revisions (restricted indication, addnl. warnings and precautions about the risk of arterial occlusion and thromboembolic events and amended dose) were made to its label. Compared with the previous 16 TKIs, more of the recently introduced TKIs are associated with the risk of LV dysfunction, and fewer with QT prolongation. Available data on morbidity and mortality associated with TKIs, together with post-marketing experience with lapatinib and ponatinib, emphasize the need for effective pharmacovigilance and ongoing re-assessment of their risk/benefit after approval of these novel agents. If not adequately managed, these cardiovascular effects significantly decrease the quality of life and increase the morbidity and mortality in a population already at high risk. Evidence accumulated over the last decade suggests that their clin. benefit, although worthwhile, is modest and extends only to progression-free survival and complete response without any effect on overall survival. During uncontrolled use in routine clin. practice, their risk/benefit is likely to be inferior to that perceived from highly controlled clin. trials.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(update on cardiovascular safety of tyrosine kinase inhibitors with special focus on QT interval, left ventricular dysfunction and overall risk/benefit)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



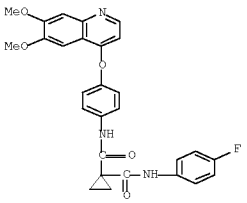
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 236 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:920388 CAPLUS full-text
DOCUMENT NUMBER: 164:271039
TITLE: SnapShot: Kinase Inhibitors II
AUTHOR(S): Wang, Jinhua; Gray, Nathanael S.
CORPORATE SOURCE: Department of Cancer Biology, Dana-Farber Cancer Institute, Boston, MA, 02215, USA
SOURCE: Molecular Cell (2015), 58(4), 710-710.e1
CODEN: MOCEFL; ISSN: 1097-2765
DIGITAL OBJECT ID: 10.1016/j.molcel.2015.05.002
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Selective small-mol. inhibitors of protein kinases can serve as powerful tools to elucidate biol. function. Efforts to develop potential drug candidates have yielded a wealth of kinase inhibitors. However, selecting the optimal kinase inhibitor for a particular application can be challenging. While the optimal inhibitor will be application specific, we have attempted to summarize some of the best reported inhibitors for various kinases.

IT 849217-68-1 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discussion on small-mol. of kinases inhibitors II)

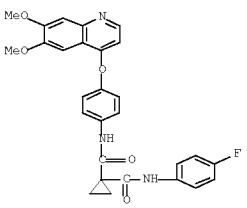
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

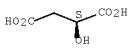
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 237 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:894377 CAPLUS full-text
DOCUMENT NUMBER: 163:1020
TITLE: Compositions and methods for diagnosing, evaluating and treating cancer by means of the DNA methylation status
INVENTOR(S): Clement, Kendell; Getz, Gad; Landau, Dan-Avi; Meissner, Alexander; Wu, Catherine Ju-Ying
PATENT ASSIGNEE(S): The Broad Institute Inc., USA; Dana-Farber Cancer Institute, Inc.; The General Hospital Corporation; President and Fellows of Harvard College
SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

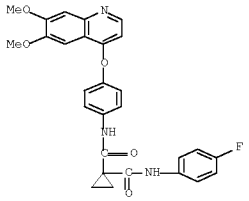
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015077717	A1	20150528	WO 2014-US67146	20141124
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20160326593	A1	20161110	US 2016-15038504	20160523
PRIORITY APPLN. INFO.:			US 2013-61908316 P	20131125
			WO 2014-US67146 W	20141124

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to methods of detg. a cancer treatment prognosis for a subject in need thereof by evaluating epigenetic and genetic changes within a tumor sample from the subject. The present invention further provides methods of treating cancer in a subject by evaluating epigenetic and genetic changes within a tumor sample from the subject, in addition, the present invention provides methods of screening test agents to identify agents that decrease tumor cell plasticity.

IT 849217-68-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for diagnosing, evaluating and treating cancer by means of the DNA methylation status)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 238 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:893490 CAPLUS Full-text
DOCUMENT NUMBER: 163:51687
TITLE: Process for the preparation of cabozantinib salt and its crystal form
INVENTOR(S): Shen, Anxiong; Tang, Dongjun; Kou, Jingping
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 19pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104649969	A	20150527	CN 2014-10676653	20141121

PRIORITY APPLN. INFO.: CN 2013-10596247 A 20131122

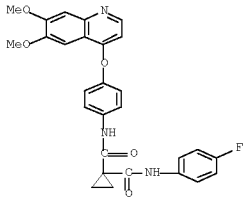
AB The invention relates to the cabozantinib L-malate crystal form A2, which has absorption peaks at 9.33°, 11.75°, 13.44°, 15.16°, 19.72°, 23.14°, and 25.92° determined by X-ray powder diffraction at 2θ. The invention also relates to cabozantinib hydrobromide crystal form I, which has absorption peaks at 8.68°, 13.01°, 7.45°, 19.52°, 20.05°, 21.71°, 23.29°, and 26.28° determined by X-ray powder diffraction at 2θ.

IT 1140909-48-3P 1786398-76-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of cabozantinib salt and its crystal form)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

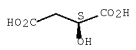
CRN 849217-68-1
CMF C28 H24 F N3 O5



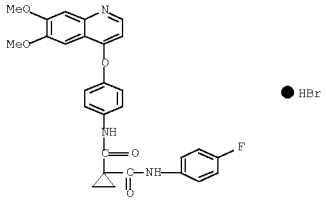
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



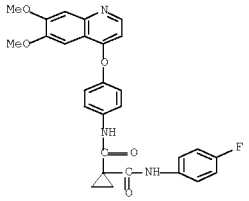
RN 1786398-76-2 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrobromide (1:1) (CA INDEX NAME)



IT 849217-68-1, Cabozantinib

RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of cabozantinib salt and its crystal form)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

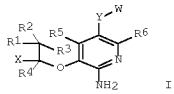


L4 ANSWER 239 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:893241 CAPLUS Full-text
DOCUMENT NUMBER: 163:66113
TITLE: Aminopyridine compounds as protein kinase receptor inhibitors and their preparation, pharmaceutical compositions and use in the treatment of proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Liang; Wang, Tingjin
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 109pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104650049	A	20150527	CN 2014-10429046	20140827

PRIORITY APPLN. INFO.: CN 2013-10383121 A 20130828
CN 2014-10144178 A 20140410

OTHER SOURCE(S): CASREACT 163:66113; MARPAT 163:66113
GI

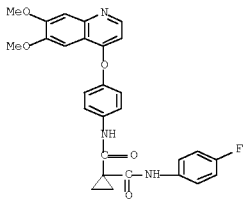


I

AB The invention relates to aminopyridine compds. of formula I, their pharmaceutically acceptable salts, and pharmaceutical formulations, which is used for regulating protein kinase activity, and adjusting signal response within cells or between cells. The invention also relates to compds. I and their stereoisomer, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts or prodrugs which are used in treating mammal, particularly to human hyperproliferative disorders. The pharmaceutical compns. includes the title compds., pharmaceutically acceptable carriers, excipients, diluents, adjuvants, and/or mediums, and other treating agents. The pharmaceutical compns. are used in preparing medicines for preventing, handling, treating or relieving proliferative disorders such as metastatic cancer, colon cancer, gastric adenocarcinoma, bladder cancer, breast cancer, kidney cancer, liver cancer, lung cancer, thyroid cancer, head and neck cancer, prostate cancer, pancreatic cancer, central nervous system cancer, spongioblastoma, bone marrow hyperplasia, atherosclerosis or pulmonary fibrosis. Compds. of formula I wherein R1- R6 are independently H, D or F; X, Y are independently (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl; W is C3-8 cycloalkyl, -(C1-4 alkylene)-(C3-8 cycloalkyl), C3-7 heterocyclyl or -(C1-4 alkylene)-(C3-7 heterocyclyl), etc.; and their stereoisomer, tautomers, nitrogen oxides, solvates, metabolites, pharmaceutically acceptable salts or prodrugs as protein kinase receptor inhibitors useful in the treatment of proliferative disorders thereof, are claimed. Compds. of formula I were prepared by using condensation, reduction, and cross-coupling as the key steps. All the invention compds. were evaluated for their protein kinase inhibitory activity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of aminopyridine compds. as protein kinase receptor inhibitors useful in the treatment of proliferative disorders)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



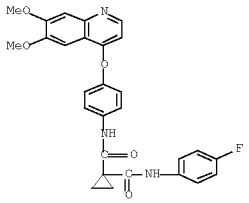
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 240 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:884680 CAPLUS Full-text
DOCUMENT NUMBER: 164:478303
TITLE: Comprehensive transcriptomic analysis of molecularly targeted drugs in cancer for target pathway evaluation
AUTHOR(S): Mashima, Tetsuo; Ushijima, Masaru; Matsuura, Masaaki; Tsukahara, Satomi; Kunimasa, Kazuhiro; Furuno, Aki; Saito, Sakae; Kitamura, Masami; Soma-Nagae, Taeko; Seimiya, Hiroyuki; Dan, Shingo; Yamori, Takao; Tomida, Akihiro
CORPORATE SOURCE: Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo, Japan
SOURCE: Cancer Science (2015), 106(7), 909-920
CODEN: CSACCM; ISSN: 1349-7006
DIGITAL OBJECT ID: 10.1111/cas.12682
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Targeted therapy is a rational and promising strategy for the treatment of advanced cancer. For the development of clin. agents targeting oncogenic signaling pathways, it is important to define the specificity of compds. to the target mol. pathway. Genome-wide transcriptomic anal. is an unbiased approach to evaluate the compound mode of action, but it is still unknown whether the anal. could be widely applicable to classify molecularly targeted anticancer agents. We comprehensively obtained and analyzed 129 transcriptomic datasets of cancer cells treated with 83 anticancer drugs or related agents, covering most clin. used, molecularly targeted drugs alongside promising inhibitors of mol. cancer targets. Hierarchical clustering and principal component anal. revealed that compds. targeting similar target mols. or pathways were clustered together. These results confirmed that the gene signatures of these drugs reflected their modes of action. Of note, inhibitors of oncogenic kinase pathways formed a large unique cluster, showing that these agents affect a shared mol. pathway distinct from classical antitumor agents and other classes of agents. The gene signature anal. further classified kinome-targeting agents depending on their target signaling pathways, and we identified target pathway-selective signature gene sets. The gene expression anal. was also valuable in uncovering unexpected target pathways of some anticancer agents. These results indicate that comprehensive transcriptomic anal. with our database (http://scads.jfcr.or.jp/db/cs/) is a powerful strategy to validate and re-evaluate the target pathways of anticancer compds.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comprehensive transcriptomic anal. of molecularly targeted drugs in cancer for target pathway evaluation)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 241 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:866343 CAPLUS Full-text
DOCUMENT NUMBER: 163:1013
TITLE: mTOR protein kinase inhibitors for enhancing the immune response for treatment of diseases such as cancer
INVENTOR(S): Mannick, Joan; Glass, David Jonathan; Murphy, Leon
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 149pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015073644	A1	20150521	WO 2014-US65408	20141113

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2929181	A1	20150521	CA 2014-2929181	20141113
US 20150140036	A1	20150521	US 2014-14540867	20141113
AU 2014348657	A1	20160519	AU 2014-348657	20141113
KR 2016084438	A	20160713	KR 2016-7015237	20141113
CN 105899232	A	20160824	CN 2014-80072942	20141113
EP 3068435	A1	20160921	EP 2014-815965	20141113

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2016537345	T	20161201	JP 2016-529901	20141113
IN 201617015582	A	20160831	IN 2016-17015582	20160504
MX 2016006316	A	20160726	MX 2016-6316	20160513

PRIORITY APPLN. INFO.:

US 2013-61903636	P	20131113
US 2014-62027121	P	20140721
US 2014-62052629	P	20140919
US 2014-62076142	P	20141106
WO 2014-US65408	W	20141113

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

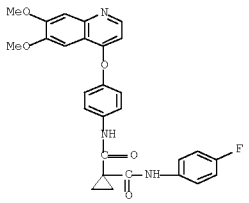
AB The present invention relates, in part, to compns. and methods for enhancement of an immune response by partial mTOR inhibition, e.g., with low, immune enhancing, doses of an mTOR inhibitor, such as RAD001 or rapamycin. In an embodiment, the subject has cancer and the method comprises promoting the subject's immune response to treat cancer.

IT 1140909-48-3, Cabozantinib-S-Malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mTOR protein kinase inhibitors for enhancing the immune response for treatment of diseases such as cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

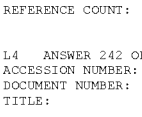
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 242 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:847958 CAPLUS Full-text
DOCUMENT NUMBER: 164:260451
TITLE: Cabozantinib: A MET, RET, and VEGFR2 Tyrosine Kinase Inhibitor
AUTHOR(S): Gruellich, Carsten
CORPORATE SOURCE: Department of Medical Oncology, National Center for Tumor Diseases, Heidelberg University Medical Center, Heidelberg, 69120, Germany
SOURCE: Recent Results in Cancer Research (2014), 201(Small Molecules in Oncology), 207-214
CODEN: RRCRBU; ISSN: 2197-6767
DIGITAL OBJECT ID: 10.1007/978-3-642-54490-3_12
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

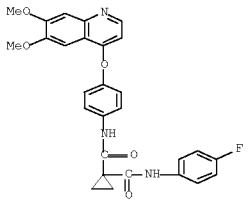
AB A review. Cabozantinib is a receptor tyrosine kinase inhibitor with activity against MET, VEGFR2, FLT3, c-KIT, and RET. Activity of cabozantinib toward a broad range of tumor models could be detected in several preclin. studies. Of note, cabozantinib decreases metastasis potential and tumor invasiveness when compared with placebo or agents that target VEGFR

and have no activity against MET. Clin. phase I and II studies with cabozantinib have been conducted in various malignancies including medullary thyroid cancer (MTC), NSCLC, breast, ovarian, pancreatic, and prostate cancer. In MTC, gain of function mutations of RET are central for tumorigenesis. Hereditary forms of MTC (MEN II) are caused by germline mutations of RET, in sporadic MTC in up to 50 % of cases RET mutations occur. Addnl., activating mol. changes in VEGFR and MET pathways have also been implicated in MTC progression. Clin. responses with cabozantinib in MTC could be observed in early clin. trials, and following confirmation of clin. benefit in a randomized phase III trial, cabozantinib gained FDA approval for first-line treatment of advanced MTC in 2012. In prostate cancer models, MET expression increases with androgen ablation and clin. progression of bone and lymph node metastasis. A phase II trial with cabozantinib also showed very promising response rates in patients with metastatic prostate cancer. Therefore, randomized phase III studies are currently ongoing to validate the efficacy of cabozantinib in heavily pretreated prostate cancer patients.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as MET, RET, and VEGFR2 tyrosine kinase inhibitor)

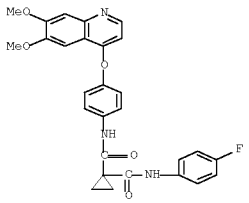
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 243 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:827243 CAPLUS Full-text
DOCUMENT NUMBER: 162:650141
TITLE: Methods using TIE2 kinase inhibitors for the treatment of cancer
INVENTOR(S): Flynn, Daniel L.; Kaufman, Michael D.; Smith, Bryan; Rudoltz, Marc S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 121pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

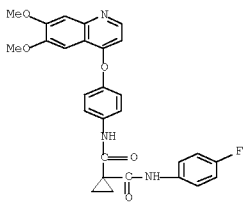
L4 ANSWER 244 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:821056 CAPLUS Full-text
DOCUMENT NUMBER: 164:219602
TITLE: Pharmacological Inhibition of KIT Activates MET Signaling in Gastrointestinal Stromal Tumors
AUTHOR(S): Cohen, Noah A.; Zeng, Shan; Seifert, Adrian M.; Kim, Teresa S.; Sorenson, Eric C.; Greer, Jonathan B.; Beckman, Michael J.; Santamaria-Barria, Juan A.; Crawley, Megan H.; Green, Benjamin L.; Rossi, Ferdinand; Besmer, Peter; Antonescu, Cristina R.; DeMatteo, Ronald P.
CORPORATE SOURCE: Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Cancer Research (2015), 75(10), 2061-2070
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-14-2564
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB These findings offer a preclin. rationale to immediately reposition the MET kinase inhibitor cabozantinib for clin. evaluation in treatment of gastrointestinal stromal tumors that are either sensitive or resistant to imatinib, the kinase inhibitor used to treat this type of sarcoma. Gastrointestinal stromal tumors (GIST) are the most common adult sarcomas and the oncogenic driver is usually a KIT or PDGFRA mutation. Although GISTs are often initially sensitive to imatinib or other tyrosine kinase inhibitors, resistance generally develops, necessitating backup strategies for therapy. In this study, we determined that a subset of human GIST specimens that acquired imatinib resistance acquired expression of activated forms of the MET oncogene. MET activation also developed after imatinib therapy in a mouse model of GIST (KitV558del/+ mice), where it was associated with increased tumor hypoxia. MET activation also occurred in imatinib-sensitive human GIST cell lines after imatinib treatment in vitro. MET inhibition by crizotinib or RNA interference was cytotoxic to an imatinib-resistant human GIST cell population. Moreover, combining crizotinib and imatinib was more effective than imatinib alone in imatinib-sensitive GIST models. Finally, cabozantinib, a dual MET and KIT small-mol. inhibitor, was markedly more effective than imatinib in multiple preclin. models of imatinib-sensitive and imatinib-resistant GIST. Collectively, our findings showed that activation of compensatory MET signaling by KIT inhibition may contribute to tumor resistance. Furthermore, our work offered a preclin. proof of concept for MET inhibition by cabozantinib as an effective strategy for GIST treatment. Cancer Res; 75(10); 2061-70. ©2015 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. inhibition of KIT activates MET signaling in gastrointestinal stromal tumors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 245 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:739043 CAPLUS Full-text
DOCUMENT NUMBER: 162:567725
TITLE: Solid particulate formulations of tyrosine derivatives
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: PCT Int. Appl., 20pp.; Chemical Indexing Equivalent to 162:567667 (US)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015061288	A1	20150430	WO 2014-US61527	20141021

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015069266	A1	20150514	WO 2013-US69005	20131107
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2929715	A1	20150514	CA 2013-2929715	20131107
AU 2013404949	A1	20160526	AU 2013-404949	20131107
KR 2016070188	A	20160617	KR 2016-7014649	20131107
CN 105873440	A	20160817	CN 2013-80081931	20131107
EP 3065549	A1	20160914	EP 2013-896951	20131107
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2017500371	T	20170105	JP 2016-552405	20131107

PRIORITY APPLN. INFO.: WO 2013-US69005 W 20131107

AB The present invention relates to methods using TIE2 kinase inhibitors for the treatment of tumor growth, invasiveness, intravasation, dissemination, metastasis, and immunosuppression. Specifically, the invention relates to methods of using 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea and salts thereof.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods using TIE2 kinase inhibitors for the treatment of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW

US 20150112116	A1	20150423	US 2013-14062194		20131024
US 9585841	B2	20170307			
CA 2927980	A1	20150430	CA 2014-2927980		20141021
AU 2014340263	A1	20160519	AU 2014-340263		20141021
KR 2016072239	A	20160622	KR 2016-7013133		20141021
IL 245173	A	20160630	IL 2014-245173		20141021
EP 3060200	A1	20160831	EP 2014-802529		20141021
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
JP 2016534071	T	20161104	JP 2016-525902		20141021
CN 106232105	A	20161214	CN 2014-80058302		20141021
IN 201617013874	A	20160831	IN 2016-17013874		20160421
MX 2016005166	A	20161214	MX 2016-5166		20160421
PRIORITY APPLN. INFO.:			US 2013-61894279	P	20131022
			US 2013-14062194	A	20131024
			WO 2014-US61527	W	20141021

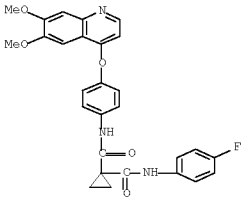
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided are methods comprising providing a tyrosine deriv. such as α-methyltyrosine, and a solid particulate material (and, optionally, melanin) and applying force to said tyrosine derivative and said solid particulate material for a time and under conditions effective to impregnate at least one of said tyrosine derivative and said solid particulate material with the other of said tyrosine derivative and said solid particulate material.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid particulate formulations of tyrosine derivs.)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 246 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:734279 CAPLUS Full-text

DOCUMENT NUMBER: 162:594407

TITLE: High-speed centrifugal mixing devices for uses in pharmaceuticals

INVENTOR(S): Hoffman, Steven

PATENT ASSIGNEE(S): Tyme, Inc., USA

SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015061256	A1	20150430	WO 2014-US61481	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150110735	A1	20150423	US 2013-14059837	20131022
CA 2927979	A1	20150430	CA 2014-2927979	20141021
AU 2014340327	A1	20160519	AU 2014-340327	20141021
KR 2016074580	A	20160628	KR 2016-7013062	20141021
IL 245174	A	20160630	IL 2014-245174	20141021
CN 105848771	A	20160810	CN 2014-80058443	20141021
EP 3060331	A1	20160831	EP 2014-856242	20141021
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR,				

HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2016537187	T	20161201	JP 2016-525925		20141021
IN 201617013876	A	20160831	IN 2016-17013876		20160421
MX 2016005165	A	20161214	MX 2016-5165		20160421
PRIORITY APPLN. INFO.:			US 2013-14059837	A	20131022
			WO 2014-US61481	W	20141021

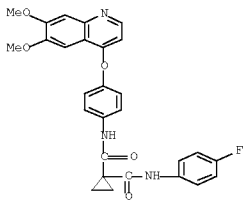
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A centrifugal mixing device can include a shaft assembly that is operably coupled to a motor such that the motor rotates the shaft assembly about a first axis. The devices can further include a turret that is rotatably coupled to the shaft assembly such that the turret rotates about the first axis relative to the shaft assembly. The turret can include a first support, a first canister rotatably coupled to the first support such that the first canister rotates about a second axis, and a second canister rotatably coupled to the first support such that the second canister rotates about a third axis. The turret is configured to rotate about the first axis in a first rotational direction and each of the first and second canisters is configured to rotate about the second and third axes, resp., in a second rotational direction that is opposite the first rotational direction. The centrifugal mixing device consists of the canisters comprising at least 2 different particulate materials. The particulate materials comprises an active pharmaceutical ingredient.

IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-speed centrifugal mixing devices for uses in pharmaceuticals)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinoliny1)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 247 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:721519 CAPLUS Full-text

DOCUMENT NUMBER: 165:87397

TITLE: A new method to determine the new C-Met inhibitor "Cabozantinib" in dosage form and human plasma via micelle-enhanced spectrofluorimetry

AUTHOR(S): Darwish, Hany W.; Abdelhameed, Ali S.; Bakheit, Ahmed H.; Alanazi, Amer M.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh, 11451, Saudi Arabia

SOURCE: RSC Advances (2015), 5(51), 40484-40490
CODEN: RSCACL; ISSN: 2046-2069

DIGITAL OBJECT ID: 10.1039/C5RA04109K

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal; (online computer file)

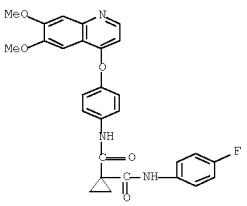
LANGUAGE: English

AB A highly sensitive and simple micelle-enhanced spectrofluorimetric method was developed for the determination of cabozantinib (CBZ) in its pharmaceutical formulation and spiked human plasma without any derivatization. The proposed method is based on the investigation of the fluorescence spectral behavior of CBZ in a Cremophor RH 40 (Cr RH 40) micellar system. In aqueous solution, the fluorescence intensity of CBZ was greatly enhanced (nine fold) in the presence of Cr RH 40. The fluorescence intensity was measured at 343 nm after excitation at 244 nm. The fluorescence-concentration plot was linear over the range 25-800 ng mL-1, with a lower detection limit of 13.34 ng mL-1. The proposed method was successfully applied to the determination of CBZ in laboratory-prepared dosage form and spiked human plasma. Recovery values of CBZ with the current method were 99.68 ± 0.88, 100.53 ± 0.51 and 100.44 ± 3.91% for pure powder, lab-prepared dosage form and spiked human plasma, resp. The results were statistically compared with those obtained by the reported chromatog. method and were found to be in good agreement.

IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); ANST (Analytical study)
(development and validation of simple and rapid micelle-enhanced spectrofluorimetric method for in vitro determination of new C-Met inhibitor,
cabozantinib in dosage form and spiked human plasma)

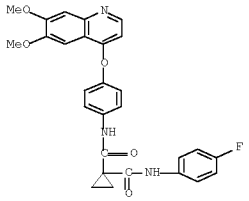
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 248 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:694096 CAPLUS Full-text
DOCUMENT NUMBER: 163:240819
TITLE: New therapies for dedifferentiated papillary thyroid cancer
AUTHOR(S): Fallahi, Poupak; Mazzi, Valeria; Vita, Roberto; Ferrari, Silvia Martina; Materazzi, Gabriele; Galleri, David; Benvenga, Salvatore; Miccoli, Paolo; Antonelli, Alessandro
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, University of Pisa, Pisa, 56126, Italy
SOURCE: International Journal of Molecular Sciences (2015), 16(3), 6153-6182
CODEN: IJMCFK; ISSN: 1422-0067
DIGITAL OBJECT ID: 10.3390/ijms16036153
PUBLISHER: MDPI AG
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB The no. of thyroid cancers is increasing. Std. treatment usually includes primary surgery, TSH suppressive therapy, and ablation of the thyroid remnant with radioactive iodine (RAI). Despite the generally good prognosis of thyroid carcinoma, about 5% of patients will develop metastatic disease, which fails to respond to RAI, exhibiting a more aggressive behavior. The lack of specific, effective and well-tolerated drugs, the scarcity of data about the association of multi-targeting drugs, and the limited role of radioiodine for dedifferentiated thyroid cancer, call for further efforts in the field of new drugs development. Rearranged during transfection (RET)/papillary thyroid carcinoma gene rearrangements, BRAF (B-RAF proto-oncogene, serine/threonine kinase) gene mutations, RAS (rat sarcoma) mutations, and vascular endothelial growth factor receptor 2 angiogenesis pathways are some of the known pathways playing a crucial role in the development of thyroid cancer. Targeted novel compds. have been demonstrated to induce clin. responses and stabilization of disease. Sorafenib has been approved for differentiated thyroid cancer refractory to RAI.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discussion on new therapies for dedifferentiated papillary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

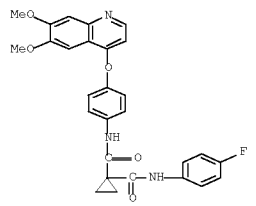


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 178 THERE ARE 178 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 249 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:691735 CAPLUS Full-text
DOCUMENT NUMBER: 162:567753
TITLE: High-speed centrifugal mixing devices for uses in pharmaceuticals
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 15pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150110735	A1	20150423	US 2013-14059837	20131022
CA 2927979	A1	20150430	CA 2014-2927979	20141021
WO 2015061256	A1	20150430	WO 2014-US61481	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014340327	A1	20160519	AU 2014-340327	20141021
KR 2016074580	A	20160628	KR 2016-7013062	20141021
IL 245174	A	20160630	IL 2014-245174	20141021
CN 105848771	A	20160810	CN 2014-80058443	20141021
EP 3060331	A1	20160831	EP 2014-856242	20141021
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2016537187	T	20161201	JP 2016-525925	20141021
IN 201617013876	A	20160831	IN 2016-17013876	20160421
MX 2016005165	A	20161214	MX 2016-5165	20160421
ZA 2016002769	A	20170426	ZA 2016-2769	20160421

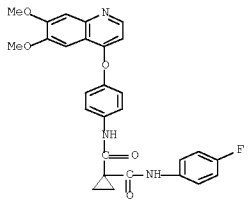
PRIORITY APPLN. INFO.: US 2013-14059837 A 20131022
WO 2014-US61481 W 20141021
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A centrifugal mixing device can include a shaft assembly that is operably coupled to a motor such that the motor rotates the shaft assembly about a first axis. The devices can further include a turret that is rotatably coupled to the shaft assembly such that the turret rotates about the first axis relative to the shaft assembly. The turret can include a first support, a first canister rotatably coupled to the first support such that the first canister rotates about a second axis, and a second canister rotatably coupled to the first support such that the second canister rotates about a third axis. The turret is configured to rotate about the first axis in a first rotational direction and each of the first and second canisters is configured to rotate about the second and third axes, resp., in a second rotational direction that is opposite the first rotational direction. The centrifugal mixing device consists of the canisters comprising at least 2 different particulate materials. The particulate materials comprises an active pharmaceutical ingredient.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-speed centrifugal mixing devices for uses in pharmaceuticals)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 250 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:691420 CAPLUS Full-text
DOCUMENT NUMBER: 162:567667
TITLE: Solid particulate formulations of tyrosine derivatives
INVENTOR(S): Hoffman, Steven
PATENT ASSIGNEE(S): Tyme, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 6pp.; Chemical Indexing Equivalent to 162:567725 (WO)
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150112116	A1	20150423	US 2013-14062194	20131024
US 9585841	B2	20170307		
CA 2927980	A1	20150430	CA 2014-2927980	20141021
WO 2015061288	A1	20150430	WO 2014-US61527	20141021
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014340263	A1	20160519	AU 2014-340263	20141021
KR 2016072239	A	20160622	KR 2016-7013133	20141021
IL 245173	A	20160630	IL 2014-245173	20141021
EP 3060200	A1	20160831	EP 2014-802529	20141021
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2016534071	T	20161104	JP 2016-525902	20141021
CN 106232105	A	20161214	CN 2014-80058302	20141021
MX 2016005166	A	20161214	MX 2016-5166	20160421
ZA 2016002770	A	20170426	ZA 2016-2770	20160421
US 20170080093	A1	20170323	US 2016-15365120	20161130

PRIORITY APPLN. INFO.: US 2013-61894279 P 20131022
US 2013-14062194 A 20131024
WO 2014-US61527 W 20141021
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Provided are methods comprising providing a tyrosine deriv. such as α-methyltyrosine, and a solid particulate material (and, optionally, melanin) and applying force to said tyrosine derivative and said solid particulate material for a time and under conditions effective to impregnate at least one of said tyrosine derivative and said solid particulate material with the other of said tyrosine derivative and said solid particulate material.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid particulate formulations of tyrosine derivs.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 251 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:656704 CAPLUS Full-text
DOCUMENT NUMBER: 162:487306
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Institut de Recerca Biomedica (IRB Barcelona), Spain; Institucio Catalana de Recerca i Estudis Avancats
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015052583	A2	20150416	WO 2014-IB2675	20141007
WO 2015052583	A3	20150723		

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2926894	A1	20150416	CA 2014-2926894	20141007
AU 2014333513	A1	20160428	AU 2014-333513	20141007
KR 2016061424	A	20160531	KR 2016-7011949	20141007
EP 3055429	A2	20160817	EP 2014-824529	20141007

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

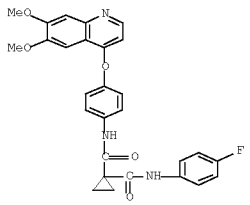
CN 105980576	A	20160928	CN 2014-80064111	20141007
JP 2016539625	T	20161222	JP 2016-521355	20141007
US 20170101683	A1	20170413	US 2016-15027946	20160407
MX 2016004557	A	20160722	MX 2016-4557	20160408

PRIORITY APPLN. INFO.: US 2013-61888984 P 20131009
WO 2014-IB2675 W 20141007

AB The present invention relates to a method for the prognosis of bone metastasis in HER2+ breast cancer, which comprises determining if the MAF gene is amplified in a primary tumor sample. Likewise, the present invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the MAF gene expression level, amplification or translocation. The present invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The present invention also relates to a c-Maf inhibitor as therapeutic agent for use in the treatment of HER2+ breast cancer metastasis. The present invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the present invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for determining prognosis of bone metastasis in HER2+ breast cancer and use of c-Maf inhibitor as therapeutic agent)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

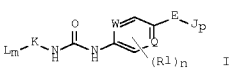


L4 ANSWER 252 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:639512 CAPLUS Full-text
DOCUMENT NUMBER: 162:590248
TITLE: Preparation of substituted urea derivatives for treating FLT3 kinase mediated or induced diseases
INVENTOR(S): Zheng, Changchun; Liu, Bing; Zhang, Weihong; Zhang, Yingjun; Long, Bohua
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 69pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

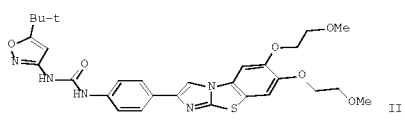
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104513257	A	20150415	CN 2014-10498232	20140925
CN 104513257	B	20170215		
CN 104513258	A	20150415	CN 2014-10498181	20140925

PRIORITY APPLN. INFO.: CN 2013-10445435 A 20130926
CN 2014-10108087 A 20140322

OTHER SOURCE(S): CASREACT 162:590248; MARPAT 162:590248
GI



I

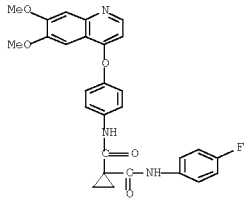


II

AB This invention provides substituted urea derivs. I [wherein K = 5- or 6-membered heteroaryl; Q and W = independently CH or N; L = independently NH2, NO2, alkylthio, alkyl, etc.; R1 = independently H, F, Cl, Br, I, etc.; E = bicyclic or tricyclic heteroaryl; J = G-(CH2)q-R; G = independently O, S, SO, SO2, CO, etc.; R = independently H, alkoxy, alkyl, alkenyl, etc.; m = 1-4; n = 0-4; p = 2-4; q = 1-4], stereoisomers, geometrical isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, esters, pharmaceutically acceptable salts, or prodrugs for treating FLT3 kinase mediated or induced diseases, such as autoimmune diseases, inflammatory diseases and proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 6.0 nM against FLT3 kinase.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. for treating FLT3 kinase mediated or induced diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 253 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:613471 CAPLUS Full-text
DOCUMENT NUMBER: 162:532738
TITLE: High drug loading system to co-deliver anticancer drugs and nucleic acids for cancer therapy
INVENTOR(S): Cheng, Gang; Tang, Qiong; Cao, Bin
PATENT ASSIGNEE(S): The University of Akron, USA
SOURCE: U.S. Pat. Appl. Publ., 10pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150099005	A1	20150409	US 2014-14510442	20141009

PRIORITY APPLN. INFO.: US 2013-61888709 P 20131009
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

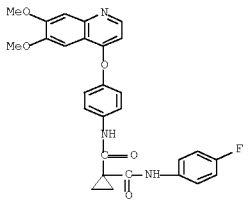
AB A high drug loading system is described comprising of at least one anticancer drug; at least one peptide; and at least one nucleic acid.

IT 1140909-48-3, Cabozantinib-S-malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high drug loading system to co-deliver anticancer drugs and nucleic acids for cancer therapy)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

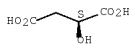
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



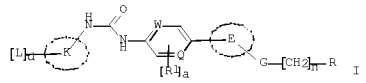
L4 ANSWER 254 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:560353 CAPLUS Full-text
DOCUMENT NUMBER: 162:488682
TITLE: Preparation of substituted urea derivatives for modulating the FLT3 kinase activity and inhibiting FLT3-ITD
INVENTOR(S): Cheng, Changchung; Liu, Bing; Zhang, Yingjun; Long, Bohua; Zhang, Weihong
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015043492	A1	20150402	WO 2014-CN87469	20140925

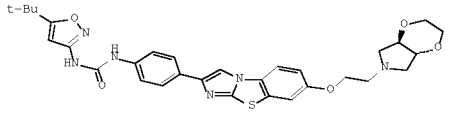
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CN 104513259	A	20150415	CN 2014-10498216	20140925
CN 104513252	A	20150415	CN 2014-10499464	20140925

PRIORITY APPLN. INFO.: CN 2013-10445605 A 20130926
CN 2014-10107854 A 20140322
OTHER SOURCE(S): CASREACT 162:488682; MARPAT 162:488682
GI

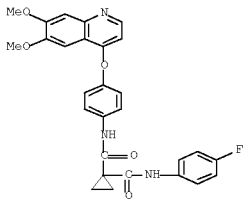


I



II

AB The title compds. I [each of Q and W = (independently) CH or N; G = O, S, C(O), etc.; R = alkoxy, alkyl, (un)substituted amino, etc.; ring K = 5-6 membered heteroaryl group, of which at least two ring members are heteroatoms independently selected from O, S, NR4 and N; each L = (independently) amino, nitro, alkylthio, etc.; ring E = bicyclic or tricyclic heteroarylene; R1 = H, halo, haloalkyl, etc.; R4 = H, alkyl, cycloalkyl, etc.; a = 0-4; d, n = 1-4; with the provisos] which are useful in modulating the FLT3 kinase activity, inhibiting FLT3-ITD, and treating the diseases mediated by FLT3 kinase or caused by FLT3-ITD, were prepared and claimed. E.g., a multi-step synthesis of II, starting from (4aS,7aS)-hexahydro-2H-[1,4]dioxino[2,3-c]pyrrole and 2-chloroethanol, was described. Exemplified compds. I were tested for FLT3 kinase inhibition (data given for representative compds. I). Pharmaceutical compns. comprising compound I, alone or in combination with other therapeutic agents, were disclosed.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted urea derivs. for modulating the FLT3 kinase activity and inhibiting FLT3-ITD)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

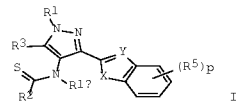


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

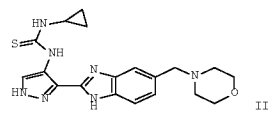
L4 ANSWER 255 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:527604 CAPLUS Full-text
DOCUMENT NUMBER: 162:475187
TITLE: Preparation of pyrazole derivatives as protein kinase over expression inhibitors
INVENTOR(S): Zhang, Jiancun; Liu, Bing; Zhang, Yingjun; Nie, Linlin; Yang, Xueqi
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 80pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104447701	A	20150325	CN 2014-10471458	20140916

PRIORITY APPLN. INFO.: CN 2013-10426478 A 20130917
CN 2014-10109414 A 20140321
OTHER SOURCE(S): MARPAT 162:475187
GI

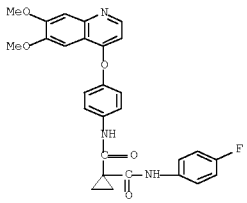


I

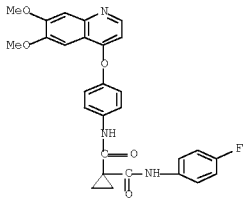


II

AB The title compds. with general formula I [wherein R1 and R1a are independently H or C1-4 alkyl; R2 is alkyl amino, aryl, heteroaryl, etc.; X is CR4aR4 or NR6; Y is CR4a or N; R3 is H, F, Cl, etc.; R3 is H, F, Cl, Br, etc.; R5 is H, alkyl, alkenyl, alkynyl, etc.; p = 1 -4] or isomers, N-oxide, hydrates, solvates, metabolites, esters, prodrugs, or pharmaceutically acceptable salts there of were prepared as protein kinase over expression inhibitors. For example, compound II was prepared in a multi-step synthesis. The title substituted pyrazole derivative for inhibiting protein kinase over expression, or stereoisomer, geometric isomer, tautomer, oxynitride, solvate, hydrate, metabolite, ester, pharmaceutically acceptable salt or prodrug thereof, pharmaceutical compns. containing these compds. as active ingredients, and the application of these compds. or pharmaceutical compns. in preparing the drugs for preventing, treating of reducing cell growth disorders. (assay data given).
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of pyrazolylaminopyrimidine derivs. as aurora kinase
inhibitor useful in the treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 256 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:494404 CAPLUS Full-text
DOCUMENT NUMBER: 162:570128
TITLE: Dermatologic adverse events in pediatric patients receiving targeted anticancer therapies: A pooled analysis
AUTHOR(S): Belum, Viswanath Reddy; Washington, Courtney; Pratilas, Christine A.; Sibaud, Vincent; Boralevi, Franck; Lacouture, Mario E.
CORPORATE SOURCE: Department of Dermatology, Memorial Sloan Kettering Cancer Center, New York, NY, USA
SOURCE: Pediatric Blood & Cancer (2015), 62(5), 798-806
CODEN: PBCEAQ; ISSN: 1545-5017
DIGITAL OBJECT ID: 10.1002/pbc.25429
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background : The dermatol. adverse events (AEs) of various molecularly targeted therapies are well-described in adult cancer patients. Little has been reported on the incidence and clin. presentation of such AEs in pediatric patients with cancer. To address this gap, we analyzed the dermatol. AEs reported across clin. trials of targeted anticancer therapies in pediatric patients. Procedures : We conducted an electronic literature search (PubMed, American Society of Clin. Oncol. annual meetings' abstrs., , NCI's Pediatric Oncol. Branch webpage) to identify clin. trials involving targeted anticancer therapies that reported dermatol. AEs in their safety data. Studies were limited to the pediatric population, monotherapy trials (oncol.), and English language publications. Results : Pooled data from 19 clin. studies investigating 11 targeted anticancer agents (alemtuzumab, rituximab, imatinib, dasatinib, erlotinib, vandetanib, sorafenib, cabozantinib, pazopanib, everolimus, and temsirolimus) were analyzed. The most frequently encountered dermatol. AEs were rash (127/660; 19%), xerosis (18/100; 18%), mucositis (68/402; 17%), and pruritus (12/169; 7%). Other AEs included pigmentary abnormalities of the skin/hair (13%), hair disorders (trichomegaly, hypertrichosis, alopecia, and madarosis; 14%), urticaria (7%), palmoplantar erythrodysesthesia (7%), erythema, acne, purpura, skin fissures, other 'unknown skin changes', exanthem, infection, flushing, telangiectasia, and photosensitivity. Conclusion : This study describes the dermatol. manifestations of targeted anticancer therapy-related AEs in the pediatric population. Since these AEs are often associated with significant morbidity, it is imperative that pediatric oncologists be familiar with their recognition and management, to avoid unnecessary dose modifications and/or termination, and to prevent impairments in patients' quality of life. Pediatr Blood Cancer 2015;62:798-806. © 2015 Wiley Periodicals, Inc.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dermatol. adverse events in pediatric patients receiving targeted anticancer therapies)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

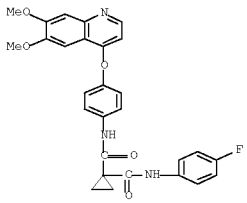


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 257 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:460229 CAPLUS Full-text
DOCUMENT NUMBER: 162:398722
TITLE: Anti-human angiopoietin 2 antibody for enhancing efficacy of antitumor agent and for combination cancer therapy
INVENTOR(S): Kim, Kyung Eun; Han, Sang Yeul; Koh, Gou Young; Lee, Hyo Seon; Kim, Chan
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd, S. Korea; Korea Advanced Institute of Science and Technology
SOURCE: Eur. Pat. Appl., 66pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2848631	A1	20150318	EP 2014-178842	20140729
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015032075	A	20150325	KR 2013-112089	20130917
US 20150079112	A1	20150319	US 2014-14446199	20140729
US 9505841	B2	20161129		
PRIORITY APPLN. INFO.:			KR 2013-112089 A	20130917

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method of preventing or treating cancer using an anti-Ang2 antibody or an antigen-binding fragment thereof that specifically binds to an angiogenesis-inducing factor Angiopoietin-2 (Ang2) and complexes to a Tie2 receptor while bound with Ang2.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human angiopoietin 2 antibody for enhancing efficacy of antitumor agent and for combination cancer therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

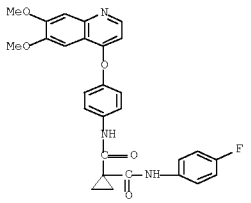


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 258 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:458209 CAPLUS Full-text
DOCUMENT NUMBER: 162:447668
TITLE: Anti-human VSTM5 antibodies, fragments and conjugates for therapy and diagnosis of cancer, infection and immune disease
INVENTOR(S): Levine, Zurit; Rotman, Galit; Dassa, Liat; Levy, Ofer; Cojocaru, Gad S.; Toporik, Amir; Kliger, Yossef; Pow, Andrew; Liang, Spencer
PATENT ASSIGNEE(S): Compugen Ltd., Israel
SOURCE: PCT Int. Appl., 490pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015037005	A1	20150319	WO 2014-IL50814	20140911
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2922805	A1	20150319	CA 2014-2922805	20140911
AU 2014319921	A1	20160317	AU 2014-319921	20140911
IL 244576	A	20160421	IL 2014-244576	20140911
EP 3043819	A1	20160720	EP 2014-844096	20140911
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160272707	A1	20160922	US 2016-15021239	20160310
PRIORITY APPLN. INFO.:			US 2013-61876324 P	20130911
			WO 2014-IL50814 W	20140911

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention relates to VSTM5-specific antibodies, antibody fragments, and VSTM5 polypeptides, conjugates and compns. comprising same, for modulating (antagonizing or agonizing) one or more of the effects of VSTM5 expression on immunity. More specifically, the present invention relates to VSTM5-specific antibodies, antibody fragments, and VSTM5 polypeptides, conjugates and compns. comprising same for treating and aiding in the diagnosis of cancer, infectious diseases and immune related diseases, e.g., those associated with aberrant (higher or lower than normal) VSTM5 expression by diseased and/or immune cells and/or aberrant (increased or reduced) VSTM5-mediated effects on immunity.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-human VSTM5 antibodies, fragments and conjugates for therapy and diagnosis of cancer, infection and immune disease)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

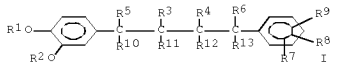


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

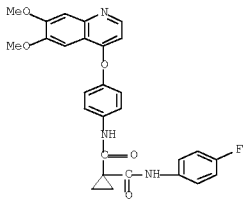
L4 ANSWER 259 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:423197 CAPLUS Full-text
DOCUMENT NUMBER: 162:419539
TITLE: Cancer therapy using dual kinase inhibitors such as catecholic butanes
INVENTOR(S): White, Thomas F.; Hoth, Daniel
PATENT ASSIGNEE(S): Triact Therapeutic, Inc., USA
SOURCE: PCT Int. Appl., 76pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015035410	A1	20150312	WO 2014-US54832	20140909
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2923667	A1	20150312	CA 2014-2923667	20140909
US 20150071919	A1	20150312	US 2014-14481837	20140909
US 9381246	B2	20160705		
EP 3044593	A1	20160720	EP 2014-842383	20140909
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				

PRIORITY APPLN. INFO.: US 2013-61875502 P 20130909
WO 2014-US54832 W 20140909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 162:419539
GI



AB The application relates to methods for treating a proliferative disorder by administering to a subject a pharmaceutical composition of a dual kinase inhibitor e.g. catecholic butanes of formula I [R1, R2 = independently H, lower alkyl, lower acyl; R3 - R6, R10 - R13 = independently H, lower alkyl; R7 - R9 = independently H, OH, lower alkoxy, lower acyloxy]. Patients to be treated include those that have been treated with Tarceva or other therapeutic compds. and relapsed or are resistant to treatment. The compds. described herein may exhibit a synergistic effect when administered with another agent.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer therapy using a dual kinase inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

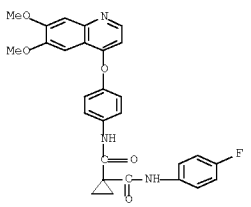


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 260 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:422447 CAPLUS Full-text
DOCUMENT NUMBER: 162:371151
TITLE: Combination therapy for the treatment of cancer using c-met inhibitor and c-myc inhibitor
INVENTOR(S): Lee, Ji Min; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 83pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150071932	A1	20150312	US 2014-14481509	20140909
US 9457043	B2	20161004		
KR 2015029175	A	20150318	KR 2013-107995	20130909

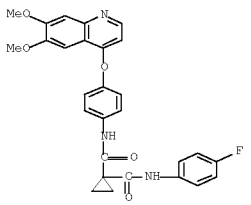
PRIORITY APPLN. INFO.: KR 2013-107995 A 20130909
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 162:371151
AB The invention relates to a method of preventing and/or treating a cancer including co-administering a c-Met inhibitor and a c-Myc Inhibitor to a subject in need thereof. The invention relates to a pharmaceutical composition comprising a c-Met inhibitor and a c-Myc inhibitor. The inhibitor comprises at least one selected from the group consisting of an antibody, an antigen-binding fragment thereof, aptamers, siRNA, shRNA, microRNA, or a small mol. The invention relates to a kit comprising a pharmaceutically effective amount of a c-Met inhibitor as an active ingredient, and a second pharmaceutical composition comprising a pharmaceutically effective amount of a c-Myc inhibitor as an active ingredient, packaged together.
IT 849217-68-1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for the treatment of cancer using c-met inhibitor and c-myc inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 261 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:422412 CAPLUS Full-text
DOCUMENT NUMBER: 162:423721
TITLE: Combination cancer therapy using c-met inhibitor and β-catenin inhibitor
INVENTOR(S): Lee, Ji Min; Kim, Kyung Ah
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 98pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150071930	A1	20150312	US 2014-14480174	20140908
US 9457081	B2	20161004		
KR 2015028652	A	20150316	KR 2013-107568	20130906

PRIORITY APPLN. INFO.: KR 2013-107568 A 20130906
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose a method of preventing and/or treating cancer. The method comprises the administration of a c-Met inhibitor and a β-catenin inhibitor. In several examples, an anti-MET receptor antibody in combination with a β-catenin inhibitor are shown to be effective in inhibiting the proliferation of breast, colon, and renal cancer cells.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy using MET inhibitor and β-catenin inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 262 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:414572 CAPLUS Full-text

DOCUMENT NUMBER: 162:425170
TITLE: Preparation of substituted pyridine compounds as tyrosine kinase inhibitors for treating proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Liang; Wang, Tingjin
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 142pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015034729	A1	20150312	WO 2014-US53017	20140827

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61873963 P 20130905
OTHER SOURCE(S): CASREACT 162:425170; MARPAT 162:425170
GI

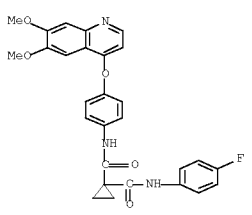
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridine compds. of general formula I (wherein each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; each of X and Y is independently C6-10aryl or 5-10 membered heteroaryl, both optionally substituted; W is C3-8cycloalkyl, -(C1-4-alkylene)(C3-8cycloalkyl), C3-7heterocyclyl or -(C1-4-alkylene)-C3-7heterocyclyl, each optionally substituted), pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 4-step synthesis that involved reaction of intermediate tert-Bu 4-(5-bromopyridin-2-yl)piperazine-1-carboxylate with III, and deprotecting the intermediate formed. The stability of the example compds. in human and rat liver microsomes, their pharmacokinetic profile in rats, and their ALK kinase and c-met kinase inhibitory activities were measured.
IT 849217-68-1, Cabozantinib

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CN 105659085 A 20160608 CN 2014-80057475 20140828
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R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

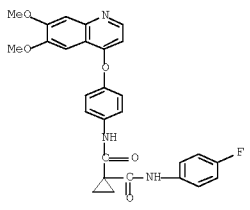
JP 2016528914 T 20160923 JP 2016-537848 20140828
US 20160208328 A1 20160721 US 2016-14915121 20160226
PRIORITY APPLN. INFO.: WO 2013-CN82487 A 20130828
WO 2014-US53142 W 20140828
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Gene expression signature predictive of cancer patient response to multi-kinase inhibitor is disclosed. Also disclosed are methods predicting the efficacy of the multi-kinase inhibitor for treating cancer in a patient. Also disclosed are methods for distinguishing responders from non-responders to a multi-kinase inhibitor in treating cancer. Also disclosed are methods for treating a cancer patient with a multi-kinase inhibitor.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene expression signature predictive of subject response to a multi-kinase inhibitor)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 264 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:359181 CAPLUS Full-text
DOCUMENT NUMBER: 163:714261
TITLE: Patient-Derived Xenografts from Non-Small Cell Lung Cancer Brain Metastases Are Valuable Translational Platforms for the Development of Personalized Targeted Therapy
AUTHOR(S): Lee, Hye Won; Lee, Jung-il; Lee, Se Jeong; Cho, Hyun Jung; Song, Hye Jin; Jeong, Da Eun; Seo, Yun Jee; Shin, Sang; Joung, Je-Gun; Kwon, Yong-Jun; Choi, Yoon-La; Park, Woong-Yang; Lee, Hyun Moo; Seol, Ho Jun; Shim, Young Mog; Joo, Kyeung Min; Nam, Do-Hyun
CORPORATE SOURCE: Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, S. Korea
SOURCE: Clinical Cancer Research (2015), 21(5), 1172-1182
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-14-1589
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: The increasing prevalence of distant metastases from non-small cell lung cancer (NSCLC) indicates an urgent need for novel therapeutic modalities. Brain metastasis is particularly common in NSCLC, with severe adverse effects on clin. prognosis. Although the mol. heterogeneity of NSCLC and availability of various targeted agents suggest personalized therapeutic approaches for such brain metastases, further development of appropriate preclin. models is needed to validate the strategies. Exptl. Design: We established patient-derived xenografts (PDX) using NSCLC brain metastasis surgical samples and elucidated their possible preclin. and clin. implications for personalized treatment. Results: NSCLC brain metastases (n = 34) showed a significantly higher successful PDX establishment rate than primary specimens (n = 64; 74% vs. 23%). PDXs derived from NSCLC brain metastases recapitulated the pathol., genetic, and functional properties of corresponding parental tumors. Furthermore, tumor spheres established in vitro from the xenografts under serum-free conditions maintained their in vivo brain metastatic potential. Differential phenotypic and mol. responses to 20 targeted agents could subsequently be screened in vitro using these NSCLC PDXs derived from brain metastases. Although PDX establishment from primary NSCLCs was significantly influenced by histol. subtype, clin. aggressiveness, and genetic alteration status, the brain metastases exhibited consistently adequate in vivo tumor take rate and in vitro tumor sphere formation capacity, regardless of clin. and mol. conditions. Conclusions: Therefore, PDXs from NSCLC brain metastases may better represent the heterogeneous advanced NSCLC population and could be utilized as preclin. models to meet unmet clin. needs such as drug screening for personalized treatments. Clin Cancer Res; 21(5); 1172-82. ©2014 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(patient-derived xenografts from non-small cell lung cancer brain metastases are valuable translational platforms for the development of personalized targeted therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyridine compds. as tyrosine kinase inhibitors for treating proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

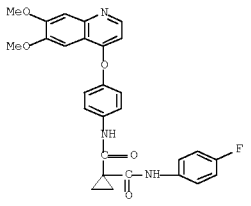


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 263 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:383707 CAPLUS Full-text
DOCUMENT NUMBER: 162:337080
TITLE: Gene expression signatures predictive of subject response to a multi-kinase inhibitor and methods of using the same
INVENTOR(S): Guo, Sheng; Chen, Dawei; Zhang, Juan; Cai, Jie; Li, Henry Qixiang
PATENT ASSIGNEE(S): Crown Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015031604	A1	20150305	WO 2014-US53142	20140828

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

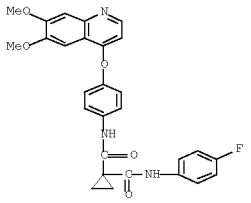


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

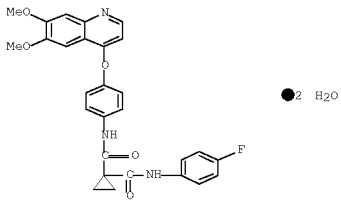
L4 ANSWER 265 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:316867 CAPLUS Full-text
DOCUMENT NUMBER: 162:399931
TITLE: Novel crystal form of quinoline compound and preparation method thereof
INVENTOR(S): Tang, Dongjun; Liu, Yanping; Kou, Jingping
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 15pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104370811	A	20150225	CN 2014-10399795	20140814
PRIORITY APPLN. INFO.:			CN 2013-10356174 A	20130815

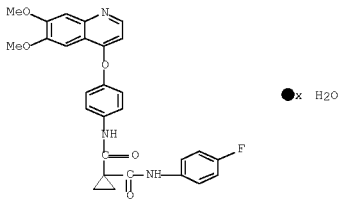
AB The present invention relates to a novel crystal form of quinoline compd. N-(4-{[6,7-dimethoxyquinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarbonamide and preparation method thereof, and belongs to medicinal chemical field. The crystal form is basically pure crystal form I or crystal form II. In the X-ray powder diffraction pattern of crystal form I, there are peaks at 2θ angles of about 11.9, 12.9, 14.4, 16.0, 22.1 and 26.0 degrees. In the X-ray powder diffraction pattern of crystal form II, there are peaks at 2θ angles of about 11.6, 14.1, 18.5, 21.1, 22.2, 23.2, 24.1 and 29.0 degrees. The novel crystal form possesses good stability and mobility, which is conducive to operate in storage, transfer and production, and the novel crystal form can be used for preparing pharmaceutically acceptable salt thereof for application in pharmaceutics.
IT [illegible]
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal forms of quinoline compound by using three-component coupling and/or condensation as the key steps)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1669412-61-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrate (1:2) (CA INDEX NAME)

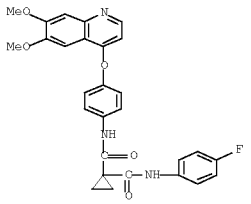


RN 1669412-63-8 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, hydrate (1:?) (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

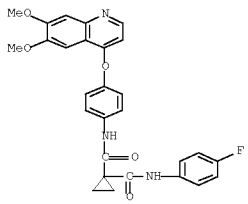
L4 ANSWER 266 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:312826 CAPLUS Full-text
DOCUMENT NUMBER: 163:407215
TITLE: Treating medullary thyroid cancer in the age of targeted therapy
AUTHOR(S): Cabanillas, Maria E.; Hu, Mimi I.; Jimenez, Camilo; Grubbs, Elizabeth G.; Cote, Gilbert J.
CORPORATE SOURCE: Department of Endocrine Neoplasia & Hormonal Disorders, Unit 1461, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX, 77030, USA
SOURCE: International Journal of Endocrine Oncology (2014), 1(2), 203-216
CODEN: IJEOBC; ISSN: 2045-0869
DIGITAL OBJECT ID: 10.2217/ije.14.26
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor deriving from the thyroid parafollicular cell. Thyroidectomy continues to serve as the primary initial treatment for this cancer. Because standard cytotoxic chemotherapy has proven ineffective, reoperation and external beam radiation therapy had been the only tools to treat recurrences or distant disease. The discovery that aberrant activation of RET, a receptor tyrosine kinase, is a primary driver of MTC tumorigenesis led to clin. trials using RET-targeting tyrosine kinase inhibitors. The successes of those trials led to the approval of vandetanib and cabozantinib for treating patients with progressive or symptomatic MTC. The availability of these drugs, along with addnl. targeted therapies in development, requires a thoughtful reconsideration of the approach to treating patients with unresectable locally advanced and/or metastatic progressive MTC.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating medullary thyroid cancer in age of targeted therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 267 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:312823 CAPLUS Full-text
DOCUMENT NUMBER: 163:437839
TITLE: Protein kinase inhibitor therapy in advanced thyroid cancer: ethical challenges and potential solutions
AUTHOR(S): Bible, Keith C.; Ain, Kenneth B.; Rosenthal, M. Sara
CORPORATE SOURCE: Mayo Clinic, Division of Medical Oncology, Rochester, MN, USA
SOURCE: International Journal of Endocrine Oncology (2014), 1(2), 145-151
CODEN: IJEOBC; ISSN: 2045-0869
DIGITAL OBJECT ID: 10.2217/ije.14.24
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Protein kinase inhibitors (PKIs) have emerged as highly promising therapies in progressive metastatic radioiodine-refractory differentiated thyroid cancer and in medullary thyroid cancer; two were recently approved in the USA for use in medullary thyroid cancer (vandetanib, cabozantinib), and another for use in progressive metastatic radioiodine-refractory differentiated thyroid cancer (sorafenib). Although more than 90% of thyroid cancer patients fare well in response to conventional treatment, PKI therapy has the potential to provide benefit. Nonetheless, PKIs produce numerous side effects, may worsen quality of life, may hasten mortality (by 1-2%), require discerning clin. acumen, are not yet proven to improve thyroid cancer survival and are very costly. This raises questions about who should prescribe PKIs, and about whether their use in thyroid cancer is truly beneficent and ethically justified. Restraint should be exercised in their use in thyroid cancer, with potential risks and benefits carefully weighed and solns. devised to help ameliorate many of the problems associated with their use.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(protein kinase inhibitor therapy in advanced thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



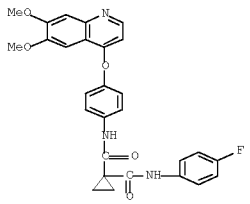
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 268 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:293134 CAPLUS Full-text
DOCUMENT NUMBER: 162:337073
TITLE: 1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy
INVENTOR(S): Jefford, Charles William; Hoessli, Daniel
PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 69pp.; Chemical Indexing Equivalent to 162:337069 (GB)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015022497	A1	20150219	WO 2014-GB52392	20140805
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
GB 2517199	A	20150218	GB 2013-14639	20130815
EP 3033078	A1	20160622	EP 2014-750606	20140805
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US 20160158193	A1	20160609	US 2016-15041198	20160211

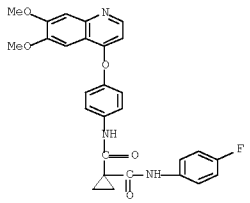
PRIORITY APPLN. INFO.: GB 2013-14639 A 20130815
WO 2014-GB52392 W 20140805

OTHER SOURCE(S): MARPAT 162:337073
AB The invention provides 1,2,4-trioxane compds. or pharmaceutically acceptable salts, esters, solvates, tautomers, stereoisomers thereof, for use as adjuvants for tyrosine kinase inhibitors in the treatment of cancer. Preferably the tyrosine kinase inhibitor is selected from imatinib, gefitinib, erlotinib, lapatinib, canertinib, vatalanib, sorafenib or genistein. The cancer may be selected from lymphoma, breast cancer, leukemia, gastrointestinal tumors, nonsmall cell lung cancer, melanoma, renal carcinoma, multiple myeloma, kidney cancer, colon cancer, pancreatic cancer, lung cancer, ovarian cancer and prostate cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 269 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:283370 CAPLUS Full-text
DOCUMENT NUMBER: 163:438161
TITLE: Is there an antiandrogen withdrawal syndrome with enzalutamide?
AUTHOR(S): Rodriguez-Vida, Alejo; Bianchini, Diletta; Van Hemelrijck, Mieke; Hughes, Simon; Malik, Zafar; Powles, Thomas; Bahl, Amit; Rudman, Sarah; Payne, Heather; de Bono, Johann; Chowdhury, Simon
CORPORATE SOURCE: Great Maze Pond, Guy's and St Thomas' NHS Foundation Trust, London, UK
SOURCE: BJU International (2015), 115(3), 373-380
CODEN: BJINFO; ISSN: 1464-410X
DIGITAL OBJECT ID: 10.1111/bju.12826
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Objective : To examine prostate-specific antigen (PSA) levels after enzalutamide discontinuation to assess whether an antiandrogen withdrawal syndrome (AAWS) exists with enzalutamide. Methods : We retrospectively identified 30 consecutive patients with metastatic prostate cancer who were treated with enzalutamide after docetaxel. Post-discontinuation PSA results were available for all patients and were determined at 2-weekly intervals until starting further anticancer systemic therapy. PSA withdrawal response was defined as a PSA decline by ≥50% from the last on-treatment PSA, with a confirmed decrease ≥3 wk later. Patient characteristics were evaluated in relation to the AAWS using univariate logistic regression anal. Results : The median (range) patient age was 70.5 (56-86) years and the median (range) follow-up was 9.0 (0.5-16) months. The most common metastatic sites were the bone (86.7%) and lymph nodes (66.7%). Most patients (70%) had previously received abiraterone and 12 patients (40%) had also received cabazitaxel. The median (range) treatment duration with enzalutamide was 3.68 (1.12-21.39) months. PSA levels after enzalutamide withdrawal were monitored for a median (range) time of 35 (10-120) days. Only one patient (3.3%) had a confirmed PSA response ≥50% after enzalutamide discontinuation. One patient (3.3%) had a confirmed PSA response of between 30 and 50% and another patient (3.3%) had an unconfirmed PSA response of between 30 and 50%. The median overall survival was 15.5 mo (95% CI 8.1-24.7). None of the factors analyzed in the univariate anal. were significant predictors of PSA decline after enzalutamide discontinuation. Conclusions : This retrospective study provides the first evidence that enzalutamide may have an AAWS in a minority of patients with metastatic castration-resistant prostate cancer. Further studies are needed to confirm the existence of an enzalutamide AAWS and to assess its relevance in prostate cancer management.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiandrogen withdrawal syndrome with enzalutamide)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

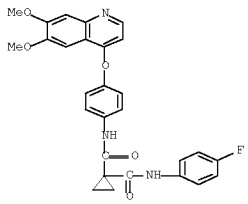
L4 ANSWER 270 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:283246 CAPLUS Full-text
DOCUMENT NUMBER: 163:418637
TITLE: Cabozantinib reverses multidrug resistance of human hepatoma HepG2/adr cells by modulating the function of P-glycoprotein
AUTHOR(S): Xiang, Qing-feng; Zhang, Dong-mei; Wang, Jing-nan; Zhang, Hong-wu; Zheng, Zhe-yu; Yu, Da-cheng; Li, Ying-jie; Xu, Jun; Chen, Ya-jin; Shang, Chang-zhen
CORPORATE SOURCE: Department of Hepatopancreatobiliary Surgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Peop. Rep. China
SOURCE: Liver International (2015), 35(3), 1010-1023
CODEN: LIINCM; ISSN: 1478-3223
DIGITAL OBJECT ID: 10.1111/liv.12524
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background & Aims : Cabozantinib, a small-mol. multitargeted tyrosine kinase inhibitor, has entered into a phase III clin. trial for the treatment of hepatocellular carcinoma (HCC). This study assessed the mechanistic effect of cabozantinib on the reversal of P-glycoprotein (P-gp)-mediated multidrug resistance (MDR). Methods : CCK-8 assays and tumor xenografts were used to investigate the reversal of MDR in vitro and in vivo resp. Substrate retention assays were evaluated by fluorescence microscope and flow cytometry. Western blotting was used to detect protein expression levels. mRNA expression was determined by qPCR. The ATPase activity of P-gp was investigated using Pgp-Glo® assay systems. The binding mechanism of cabozantinib to P-gp at the mol. level was evaluated using docking anal. Results : Cabozantinib enhanced the cytotoxicity of P-gp substrate drugs in HepG2/adr and HEK293-MDR1 cells but had no effect on non-P-gp substrates. In addition, cabozantinib increased the accumulation of P-gp substrates in HepG2/adr cells but had no effect in HepG2 cells. Furthermore, cabozantinib did not alter the expression of P-gp mRNA or protein but did stimulate the activity of P-gp ATPase. The docking study indicated that cabozantinib and

verapamil may partially share a binding site on P-gp. The reversal concns. of cabozantinib did not affect the expression of MET, AKT and ERK1/2. Significantly, cabozantinib increased the inhibitory efficacy of doxorubicin in P-gp-overexpressing HepG2/adr cell xenografts in nude mice. Conclusion : Cabozantinib reverses P-gp-mediated MDR by directly inhibiting the efflux function of P-gp, indicating that cabozantinib may help to reverse P-gp-mediated MDR in HCC and other cancer chemotherapy.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on cabozantinib reverses multidrug resistance of human hepatoma HepG2/adr cells by modulating function of P-glycoprotein)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 271 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:281739 CAPLUS Full-text

DOCUMENT NUMBER: 162:337069

TITLE: 1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy

INVENTOR(S): Jefford, Charles William; Hoessli, Daniel Christian

PATENT ASSIGNEE(S): Switz.

SOURCE: Brit. UK Pat. Appl., 66pp.; Chemical Indexing Equivalent to 162:337073 (WO)
CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2517199	A	20150218	GB 2013-14639	20130815
WO 2015022497	A1	20150219	WO 2014-GB52392	20140805
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 3033078	A1	20160622	EP 2014-750606	20140805
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160158193	A1	20160609	US 2016-15041198	20160211

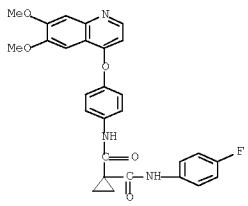
PRIORITY APPLN. INFO.: GB 2013-14639 A 20130815
WO 2014-GB52392 W 20140805

AB The invention provides 1,2,4-trioxane compds. or pharmaceutically acceptable salts, esters, solvates, tautomers, stereoisomers thereof, for use as adjuvants for tyrosine kinase inhibitors in the treatment of cancer. Preferably the tyrosine kinase inhibitor is selected from imatinib, gefitinib, erlotinib, lapatinib, canertinib, vatalanib, sorafenib or genistein. The cancer may be selected from lymphoma, breast cancer, leukemia, gastrointestinal tumors, nonsmall cell lung cancer, melanoma, renal carcinoma, multiple myeloma, kidney cancer, colon cancer, pancreatic cancer, lung cancer, ovarian cancer and prostate cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,2,4-trioxanes as adjuvants for tyrosine kinase inhibitors in anti-cancer chemotherapy)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 272 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:258957 CAPLUS Full-text

DOCUMENT NUMBER: 162:370540

TITLE: Design and Optimization of a Series of 1-Sulfonylpyrazolo[4,3-b]pyridines as Selective c-Met Inhibitors

AUTHOR(S): Ma, Yuchi; Sun, Guangqiang; Chen, Danqi; Peng, Xia; Chen, Yue-Lei; Su, Yi; Ji, Yinchun; Liang, Jin; Wang, Xin; Chen, Lin; Ding, Jian; Xiong, Bing; Ai, Jing; Ieng, Meiyu; Shen, Jingkang

CORPORATE SOURCE: Department of Medicinal Chemistry, State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 201203, Peop. Rep. China

SOURCE: Journal of Medicinal Chemistry (2015), 58(5), 2513-2529
CODEN: JMCMAR; ISSN: 0022-2623

DIGITAL OBJECT ID: 10.1021/jm502018y

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

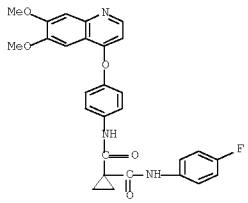
OTHER SOURCE(S): CASREACT 162:370540

AB C-Met has emerged as an attractive target for targeted cancer therapy because of its abnormal activation in many cancer cells. To identify high potent and selective c-Met inhibitors, we started with profiling the potency and in vitro metabolic stability of a reported hit 7. By rational design, a novel sulfonylpyrazolo[4,3-b]pyridine 9 with improved DMPK properties was discovered. Further elaboration of π-π stacking interactions and solvent accessible polar moieties led to a series of highly potent and selective type I c-Met inhibitors. On the basis of in vitro and in vivo pharmacol. and pharmacokinetics studies, compound 46 was selected as a preclin. candidate for further anticancer drug development.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design and optimization of a series of 1-sulfonylpyrazolo[4,3-b]pyridines as selective c-Met inhibitors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 273 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:232900 CAPLUS Full-text

DOCUMENT NUMBER: 163:340057

TITLE: Potent antitumor activity of cabozantinib, a c-MET and VEGFR2 inhibitor, in a colorectal cancer patient-derived tumor explant model

AUTHOR(S): Song, Eun-Kee; Tai, W. M.; Messersmith, Wells A.; Bagby, Stacey; Purkey, Alicia; Quackenbush, Kevin S.; Pitts, Todd M.; Wang, Guoliang; Blatchford, Patrick; Yahn, Rachel; Kaplan, Jeffrey; Tan, Aik Choon; Atreya, Chloe E.; Eckhardt, Gail; Kelley, Robin K.; Venook, Alan; Kwak, Eunice L.; Ryan, David; Arcaroli, John J.

CORPORATE SOURCE: Division of Medical Oncology, University of Colorado Denver and University of Colorado Cancer Center, Aurora, CO, USA

SOURCE: International Journal of Cancer (2015), 136(8), 1967-1975
CODEN: IJCNAW; ISSN: 0020-7136

DIGITAL OBJECT ID: 10.1002/ijc.29225

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

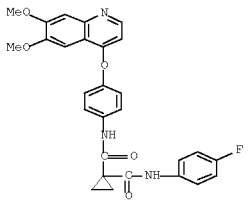
AB Antiangiogenic therapy is commonly used for the treatment of colorectal cancer (CRC). Although patients derive some clin. benefit, treatment resistance inevitably occurs. The MET signaling pathway has been proposed to be a major contributor of resistance to antiangiogenic therapy. MET is upregulated in response to vascular endothelial growth factor pathway inhibition and plays an essential role in tumorigenesis and progression of tumors. In this study, we set out to determine the efficacy of cabozantinib in a preclin. CRC patient-derived tumor xenograft model. We demonstrate potent inhibitory effects on tumor growth in 80% of tumors treated. The greatest antitumor effects were observed in tumors that possess a mutation in the PIK3CA gene. The underlying antitumor mechanisms of cabozantinib consisted of inhibition of angiogenesis and Akt activation and significantly decreased expression of genes involved in the PI3K pathway. These findings

support further evaluation of cabozantinib in patients with CRC. PIK3CA mutation as a predictive biomarker of sensitivity is intriguing and warrants further elucidation. A clin. trial of cabozantinib in refractory metastatic CRC is being activated.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VEGFR2 and c-Met inhibitor, cabozantinib show antitumor activity in xenograft mouse model of colorectal cancer especially with PIK3CA mutation via inhibiting angiogenesis, Akt activation and lowering expression of PI3K pathway genes)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 274 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:226654 CAPLUS Full-text

DOCUMENT NUMBER: 163:214328

TITLE: Dual effects of a targeted small-molecule inhibitor (cabozantinib) on immune-mediated killing of tumor cells and immune tumor microenvironment permissiveness when combined with a cancer vaccine

AUTHOR(S): Kwilas, Anna R.; Ardiani, Andressa; Donahue, Renee N.; Aftab, Dana T.; Hodge, James W.

CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: Journal of Translational Medicine (2014), 12, 294/1-294/15, 15 pp.
CODEN: JTMOBV; ISSN: 1479-5876

DIGITAL OBJECT ID: 10.1186/s12967-014-0294-y

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)

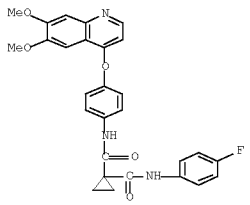
LANGUAGE: English

AB Background: Growing awareness of the complexity of carcinogenesis has made multimodal therapies for cancer increasingly compelling and relevant. In recent years, immunotherapy has gained acceptance as an active therapeutic approach to cancer treatment, even though cancer is widely considered an immunosuppressive disease. Combining immunotherapy with targeted agents that have immunomodulatory capabilities could significantly improve its efficacy. Methods: We evaluated the ability of cabozantinib, a receptor tyrosine kinase inhibitor, to modulate the immune system in vivo as well as alter the phenotype of tumor cells in vitro in order to determine if this inhibitor could act synergistically with a cancer vaccine. Results: Our studies indicated that cabozantinib altered the phenotype of MC38-CEA murine tumor cells, rendering them more sensitive to immune-mediated killing. Cabozantinib also altered the frequency of immune sub-populations in the periphery as well as in the tumor microenvironment, which generated a more permissive immune environment. When cabozantinib was combined with a poxviral-based cancer vaccine targeting a self-antigen, the combination significantly reduced the function of regulatory T cells and increased cytokine production from effector T cells in response to the antigen. These alterations to the immune landscape, along with direct modification of tumor cells, led to markedly improved antitumor efficacy. Conclusions: These studies support the clin. combination of cabozantinib with immunotherapy for the treatment of cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual role of targeted small mol. inhibitor cabozantinib combined with cancer vaccine on immune mediated killing of tumor cells and immune tumor microenvironment permissiveness)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 275 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:213358 CAPLUS Full-text

DOCUMENT NUMBER: 162:245319

TITLE: Preparation of pyrazolone compounds that are protein tyrosine kinase activity modulators useful in treatment of proliferative and other diseases

INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC

SOURCE: U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

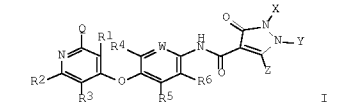
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20150037280	A1	20150205	US 2013-13945924	20130719
US 8975282	B2	20150310		
US 20150050239	A1	20150219	US 2013-13945925	20130719
US 8969388	B2	20150303		
US 20150141463	A1	20150521	US 2015-14601207	20150120
US 9326975	B2	20160503		

PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
US 2013-13945924 A3 20130719

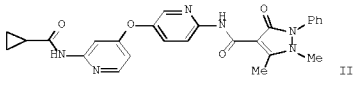
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 162:245319; MARPAT 162:245319

GI



I



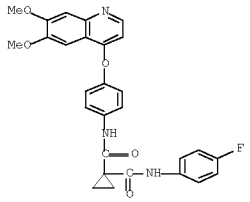
II

AB The invention provides novel substituted pyrazolone compds. of formula I [each of R1-R7 is independently H, F, Cl, (C1-C6)alkyl, (C1-C6)haloalkyl, etc.; each of X, Y and Z is independently H, (C1-C6)alkyl, (C6-C10)aryl, etc.; W is CR7 or N; Q as defined in the disclosure], pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The example compound II was prepared in two-step synthesis (procedure shown) was tested in multiple bioassay for activity in modulation of protein tyrosine kinase, pharmacokinetics and metabolic stability, as well as for antiproliferative activity. The invention also provides pharmaceutically acceptable comps. comprising such compds. and methods of using the comps. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyrazolone compds. that are protein tyrosine kinase activity modulators useful in treatment of proliferative and other diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 276 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:210763 CAPLUS Full-text

DOCUMENT NUMBER: 162:283487

TITLE: Dielectrophoresis methods for determining a property of a plurality of cancer cells to determine drug efficacy and/or resistance

INVENTOR(S): Schmelz, Eva M.; Elvington, Elizabeth S.; Salmanzadeh, Alireza; Sano, Mike; Roberts, Paul C.; Davalos, Rafael V.

PATENT ASSIGNEE(S): Virginia Tech Intellectual Properties, Inc., USA

SOURCE: PCT Int. Appl., 82pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015017729	A1	20150205	WO 2014-US49296	20140731

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR,

IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20100224493	A1	20100909	US 2010-720406	20100309
US 8968542	B2	20150303		
US 20120085649	A1	20120412	US 2011-13269286	20111007

PRIORITY APPLN. INFO.:
US 2010-720406 A2 20100309
US 2011-13269286 A2 20111007
US 2013-61860309 P 20130731
US 2009-61158553 P 20090309
US 2009-61252942 P 20091019
US 2010-61390748 P 20101007

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided are dielectrophoresis (DEP) devices and methods that allow cell sorting to identify, isolate, and/or sep. cells of interest based on elec. and phys. properties of the cells. Particularly, provided are systems and methods for manipulating particles suspended in a fluid, e.g., cells, micro- or nano-particles, using their elec. signatures. Such methods can be performed using DEP, iDEP, and/or cDEP (contactless dielectrophoresis, where direct contact between the electrodes and the sample is avoided). Typically, an elec. field is induced in a sample comprising the target particles and/or cells, such as cancer cells, and the spatial distribution of cells is measured to identify one or more characteristics or properties of the cancer cells. The identified characteristics of the sorted cells can be used to determine drug efficacy and/or resistance with respect to the cells.

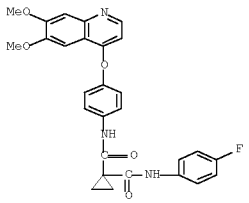
IT 1140909-48-3, Cabozantinib-S-Malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dielectrophoresis methods for determining a property of a plurality of cancer cells to determine drug efficacy and/or resistance)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

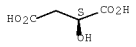
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 277 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER:	2015:203193 CAPLUS Full-text
DOCUMENT NUMBER:	162:294277
TITLE:	Methods of treating a cancer through targeted disruption of alpha connexin 43-zonula occludens-1 (zo-1) interaction
INVENTOR(S):	Gourdie, Robert G.; Sheng, Zhi
PATENT ASSIGNEE(S):	USA
SOURCE:	PCT Int. Appl., 152pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2015017034	A1	20150205	WO 2014-US42528	20140616

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG,

SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20160166637	A1	20160616	US 2016-14909674	20160202

PRIORITY APPLN. INFO.:
US 2013-61861686 P 20130802
WO 2014-US42528 W 20140616

AB The present disclosure describes methods of treating a cancer based on the targeted disruption of alpha connexin 43-zonula occludens-1 (ZO-1) interaction. The methods may include administering to a subject an effective amount of a composition comprising a peptide with a contiguous sequence of amino acids representing a portion of the C-terminus of an alpha connexin protein or conservative variant thereof, wherein said C-terminus includes the sequence up to the transmembrane domain, optionally in combination with administration of a chemotherapeutic agent. In embodiments, the cancer is glioma and the chemotherapeutic agent is temozolomide. The methods may also include administration of vectors encoding the peptide or host cells comprising the vectors. Also described are compns. for treating a cancer comprising one or more peptides, nucleic acids, vectors, and/or host cells, optionally in combination with a chemotherapeutic agent such as temozolomide.

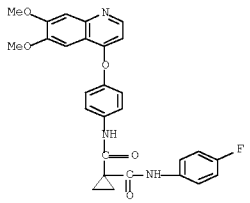
IT 1140909-48-3, Cabozantinib-s-malate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of treating cancer through targeted disruption of alpha connexin 43-zonula occludens-1 interaction)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

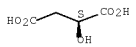
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

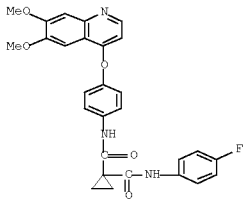
L4 ANSWER 278 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER:	2015:173876 CAPLUS Full-text
DOCUMENT NUMBER:	162:320090
TITLE:	An LC-MS/MS method for the quantitation of cabozantinib in rat plasma: Application to a pharmacokinetic study
AUTHOR(S):	Su, Qinghong; Li, Jian; Ji, Xiwei; Li, Jingyun; Zhou, Tianyan; Lu, Wei; Li, Liang
CORPORATE SOURCE:	Department of Pharmaceutics, School of Pharmaceutical Sciences, Peking University Health Science Center, Beijing, 100191, Peop. Rep. China
SOURCE:	Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences (2015), 985, 119-123 CODEN: JCBAAI; ISSN: 1570-0232
DIGITAL OBJECT ID:	10.1016/j.jchromb.2015.01.024
PUBLISHER:	Elsevier B.V.
DOCUMENT TYPE:	Journal; (online computer file)
LANGUAGE:	English

AB A simple, rapid and sensitive high-performance liq. chromatog. tandem mass-spectrometric method (LC-MS/MS) for the novel multiple tyrosine kinase inhibitor (TKI) cabozantinib was developed and validated using erlotinib as internal standard (IS). Plasma samples were pre-treated by liquid-liquid extraction with Et acetate. Separation was achieved on a reversed phase C18 column (50 × 2 mm, 5 μm) at ambient temperature using isocratic elution with acetonitrile-water (45:55, volume/volume) containing 5 mM ammonium formate buffer (finally adjusted to apparent pH* = 5.0 with formic acid) at a flow rate of 0.4 mL/min. The analytes were monitored by a triple quadrupole tandem mass spectrometer with electrospray ionization source in the pos. ion mode. Calibration curve was linear (r > 0.99) in a concentration range of 0.5-1000 ng/mL with the lower limit of quantification (LLOQ) of 0.5 ng/mL. Intra- and inter-day accuracy and precision were validated by relative error values (RE) and relative standard deviation values (RSD), resp., which were both lower than the limit of 15%. This method was successfully applied to a pharmacokinetic study of cabozantinib in rats.

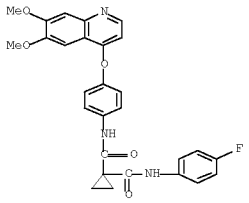
IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL

(Biological study); USES (Uses)
(LC-MS/MS method for the quantitation of cabozantinib in rat plasma with application to a pharmacokinetic study)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



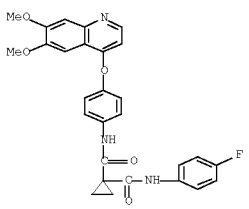
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 279 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:159139 CAPLUS Full-text
DOCUMENT NUMBER: 162:560084
TITLE: Progress in Discovery of KIF5B-RET Kinase Inhibitors for the Treatment of Non-Small-Cell Lung Cancer
AUTHOR(S): Song, Minsoo
CORPORATE SOURCE: New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Taegu, 701 310, S. Korea
SOURCE: Journal of Medicinal Chemistry (2015), 58(9), 3672-3681
CODEN: JMCMAR; ISSN: 0022-2623
DIGITAL OBJECT ID: 10.1021/jm501464c
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. A new chimeric fusion transcript of KIF5B (the kinesin family 5B gene) and the RET (Rearranged during Transcription) oncogene, KIF5B-RET, was found in 1-2% of lung adenocarcinomas (LADCs) in late 2011. Several related clin. trials for non-small-cell lung cancer (NSCLC) with KIF5B-RET rearrangements using existing RET inhibitors, such as lenvatinib, vandetanib, sunitinib, ponatinib, cabozantinib, and AUY922, have been swiftly initiated by the discovery of the KIF5B-RET fusion gene. Anti-RET activity and the status of clin. development of these known RET tyrosine kinase inhibitors (TKIs) for KIF5B-RET fusion-pos. NSCLC are discussed. A kinase inhibitor that can target a driver mutation specifically may lead to a superior clin. benefit compared with broad-spectrum kinase inhibitors. In this regard, an anal. of the structure of RET kinase and its complex with known RET inhibitors are also briefly discussed.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progress in discovery of KIF5B-RET kinase inhibitors for the treatment of nonsmall cell lung cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



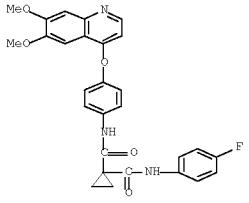
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 280 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:152289 CAPLUS Full-text
DOCUMENT NUMBER: 162:320143
TITLE: Pharmacokinetics and tissue distribution model of cabozantinib in rat determined by UPLC-MS/MS
AUTHOR(S): Wang, Xianqin; Wang, Shuanghu; Lin, Feiyan; Zhang, Qingwei; Chen, HuiLing; Wang, Xianchuan; Wen, Congcong; Ma, Jianshe; Hu, Lufeng
CORPORATE SOURCE: Analytical and Testing Center, Wenzhou Medical University, Wenzhou, 325035, Peop. Rep. China
SOURCE: Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences (2015), 983-984, 125-131
CODEN: JCBAAI; ISSN: 1570-0232
DIGITAL OBJECT ID: 10.1016/j.jchromb.2015.01.020
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib (XL184) is a novel small mol. inhibitor of receptor tyrosine kinases (RTKs) targeted at mesenchymal-epithelial transition factor (MET). To study the pharmacokinetics and tissue distribution in rat, a specific ultra-performance liquid chromatog.-tandem mass spectrometry (UPLC-MS/MS) method was developed with midazolam as internal standard The calibration curves in plasma and tissues were linear in the range of 5-5000 ng/mL (R2 > 0.99). The recoveries were better than 80.4% and matrix effects ranged from 96.9% to 105.1%. Then, the developed UPLC-MS/MS method was applied to determine the concentration of XL184 in blood and tissues. The pharmacokinetics of four different dosages (iv 5, 10 mg/kg and ig 15, 30 mg/kg) revealed that XL184 was eliminated slowly, the t1/2 was longer than 10 h and the absolute bioavailability was 25.6±8.3%. The concentration distribution of XL184 in tissues was liver > lung > kidney > spleen > heart. Based on the concentration-time of XL184 in tissues, a BP-ANN distribution model was developed with good performance, and can be used to predict the concentration of XL184 in tissues.
IT 849217-68-1, Cabozantinib
RL: ANT (Analyte); PKT (Pharmacokinetics); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(XL184; pharmacokinetics and tissue distribution model of cabozantinib in rat determined by UPLC-MS/MS)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 281 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:142298 CAPLUS Full-text
DOCUMENT NUMBER: 163:360237
TITLE: QTc interval prolongation with vascular endothelial growth factor receptor tyrosine kinase inhibitors
AUTHOR(S): Ghatalia, P.; Je, Y.; Kaymakcalan, M. D.; Sonpavde, G.; Choueiri, T. K.
CORPORATE SOURCE: Department of Internal Medicine, University of Alabama at Birmingham (UAB), Birmingham, AL, USA
SOURCE: British Journal of Cancer (2015), 112(2), 296-305
CODEN: BJCAAI; ISSN: 0007-0920
DIGITAL OBJECT ID: 10.1038/bjc.2014.564
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Multi-targeted vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) are known to cause cardiac toxicity, but the relative risk (RR) of QTc interval prolongation and serious arrhythmias associated with them are not reported. Methods: We conducted a trial-level meta-anal. of randomized phase II and III trials comparing arms with and without a US Food and Drug Administration-approved VEGFR TKI (sunitinib, sorafenib, pazopanib, axitinib, vandetanib, cabozantinib, ponatinib and regorafenib). A total of 6548 patients from 18 trials were selected. Statistical analyses were conducted to calculate the summary incidence, RR and 95% CIs. Results: The RR for all-grade and high-grade QTc prolongation for the TKI vs no TKI arms was 8.66 (95% CI 4.92-15.2, P<0.001) and 2.69 (95% CI 1.33-5.44, P=0.006), resp., with most of the events being asymptomatic QTc prolongation. Resp., 4.4% and 0.83% of patients exposed to VEGFR TKI had all-grade and high-grade QTc prolongation. On subgroup anal., only sunitinib and vandetanib were associated with a statistically significant risk of QTc prolongation, with higher doses of vandetanib associated with a greater risk. The rate of serious arrhythmias including torsades de pointes did not seem to be higher with high-grade QTc prolongation. The risk of QTc prolongation was independent of the duration of therapy. Conclusions: In the largest study to date, we show that VEGFR TKI can be associated with QTc prolongation. Although most cases were of low clin. significance, it is unclear whether the same applies to patients treated off clin. trials.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on QTc interval prolongation with vascular endothelial growth factor receptor tyrosine kinase inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



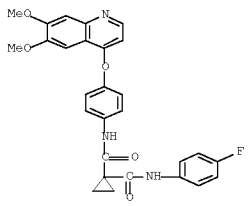
OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 282 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:138904 CAPLUS Full-text
DOCUMENT NUMBER: 163:511501
TITLE: Current role of cabozantinib in metastatic castration-resistant prostate cancer
AUTHOR(S): Fay, Andre P.; Albiges, Laurence; Bellmunt, Joaquim
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02215, USA
SOURCE: Expert Review of Anticancer Therapy (2015), 15(2), 151-156
CODEN: ERATBJ; ISSN: 1473-7140
DIGITAL OBJECT ID: 10.1586/14737140.2015.1003047
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB Over 80% of men with castration-resistant prostate cancer have bone metastases. This condition can dramatically impact quality of life and is associated with short-term survival. Consequently, the development of bone-targeted therapies is a relevant topic on prostate cancer management. Hepatocyte growth factor receptor and vascular endothelial growth factor signaling pathways have been identified to play a role in prostate cancer progression and bone metastasis and are potential targets for therapeutic intervention. Early-phase studies have shown encouraging responses in bone metastases and pain control with cabozantinib, a multi-tyrosine kinase inhibitor targeting hepatocyte growth factor receptor and vascular endothelial growth factor receptor. Despite striking responses seen in some patients, preliminary results from a pivotal Phase III study have failed to produce survival benefit. This review encompasses preclin. and clin. data of cabozantinib in metastatic castration-resistant prostate cancer highlighting future research options for this agent.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(current role of cabozantinib in metastatic castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

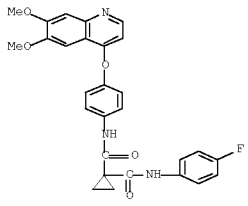


OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 283 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:104550 CAPLUS Full-text
DOCUMENT NUMBER: 162:265265
TITLE: Thyroid carcinoma, version 2.2014: featured updates to the NCCN guidelines
AUTHOR(S): Tutele, R. Michael; Haddad, Robert I.; Ball, Douglas W.; Byrd, David; Dickson, Paxton; Duh, Quan-Yang; Ehya, Hormoz; Haymart, Megan; Hoh, Carl; Hunt, Jason P.; Iagaru, Andrei; Kandeel, Fouad; Kopp, Peter; Lamonica, Dominick M.; Lydiatt, William M.; McCaffrey, Judith; Moley, Jeffrey F.; Parks, Lee; Raeburn, Christopher D.; Ridge, John A.; Ringel, Matthew D.; Scheri, Randall P.; Shah, Jatin P.; Sherman, Steven I.; Sturgeon, Cord; Waguespack, Steven G.; Wang, Thomas N.; Wirth, Lori J.; Hoffmann, Karin G.; Hughes, Miranda
CORPORATE SOURCE: Memorial Sloan Kettering Cancer Center, USA
SOURCE: Journal of the National Comprehensive Cancer Network (2014), 12(12), 1671-1680
CODEN: JNCCA4; ISSN: 1540-1405
PUBLISHER: Harborside Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. These NCCN Guidelines Insights focus on some of the major updates to the 2014 NCCN Guidelines for Thyroid Carcinoma. Kinase inhibitor therapy may be used to treat thyroid carcinoma that is symptomatic and/or progressive and not amenable to treatment with radioactive iodine. Sorafenib may be considered for select patients with metastatic differentiated thyroid carcinoma, whereas vandetanib or cabozantinib may be recommended for select patients with metastatic medullary thyroid carcinoma. Other kinase inhibitors may be considered for select patients with either type of thyroid carcinoma. A new section on "Principles of Kinase Inhibitor Therapy in Advanced Thyroid Cancer" was added to the NCCN Guidelines to assist with using these novel targeted agents.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(featured updates to the NCCN guidelines for thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

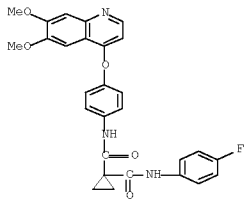


REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 284 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:100945 CAPLUS Full-text
DOCUMENT NUMBER: 163:480691
TITLE: Targeting Angiogenesis in Thyroid Cancer
AUTHOR(S): Lkhoyaali, S.; Benhmida, S.; Aitelhaj, M.; Layachi, M.; Abahssain, H.; Ismaili, H. N.; Errihani, H.
CORPORATE SOURCE: Department of Medical Oncology, Mohammed VI University Hospital, Marrakech, Morocco
SOURCE: Current Angiogenesis (2014), 3(2), 107-112
CODEN: CAUNBS; ISSN: 2211-5528
DIGITAL OBJECT ID: 10.2174/22115528026661407161705 21
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Thyroid cancers are characterized by a good prognosis but 10 to 15% of patients progress and become refractory to current therapies. Systemic treatment based on chemotherapy in these settings has shown limited efficacy, with response rates not exceeding 25%. At progression, differentiated thyroid cancer is characterized by a high level of expression of vascular endothelial growth factor (VEGF). This high expression of VEGF is associated with an aggressive tumor behavior and a poor clin. outcome.; We will review the recent advances in targeting angiogenesis in the treatment of recurrent and metastatic thyroid carcinoma.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting Angiogenesis in Thyroid Cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 285 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2015:100878 CAPLUS Full-text
DOCUMENT NUMBER: 163:292268
TITLE: Should the Incorporation of Structural Alerts be Restricted in Drug Design? An Analysis of Structure-Toxicity Trends with Aniline-Based Drugs
AUTHOR(S): Kalgutkar, A. S.
CORPORATE SOURCE: Pharmacokinetics, Dynamics and Metabolism Department-New Chemical Entities, Pfizer Worldwide Research and Development, Cambridge, MA, 02139, USA
SOURCE: Current Medicinal Chemistry (2015), 22(4), 438-464
CODEN: CMCHE7; ISSN: 0929-8673
DIGITAL OBJECT ID: 10.2174/0929867321666141112122118
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

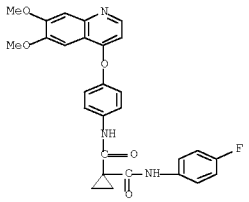
AB Certain idiosyncratic adverse drug reactions (IADRs) can be triggered by electrophilic protein-reactive metabolites that are formed in the process of drug metabolism While methodologies (e.g., structural alert concept in drug design, glutathione (GSH) trapping, and protein covalent binding) for examining reactive metabolite (RM) formation are available, predicting the IADR potential applying these parameters remains a significant challenge. The present work examines toxicity trends associated with the aniline structural alert in the top 200 prescribed drugs of 2011 and recently approved (2009-2013) small mol. drugs, in relation with 30 aniline-based drugs withdrawn from com. use or associated with a black box warning for IADRs. The aniline sub-structure was found in several drugs from the toxic, mostprescribed, and recently approved category. RMs resulting from the bioactivation of the aniline alert was also noted in the three categories chosen for comparison. A major discriminator between the toxic drugs and the majority of drugs in the most-prescribed list, however, was the daily dose - drugs most frequented associated with IADRs were the ones with higher daily doses (exceeding hundreds of milligrams). A greater tolerance for IADRs was also noted with certain drugs intended to treat rare, unmet medical needs (e.g., cancer). Overall, the anal. suggests that optimization of pharmacol. potency and pharmacokinetics that would lead to a lower daily

dose, and therefore, a lower body burden of parent drug/metabolites, should be taken into consideration in drug discovery.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anal. of structure-toxicity trends with aniline-based drugs)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 286 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:28803 CAPLUS Full-text

DOCUMENT NUMBER: 162:393504

TITLE: Development of therapeutic drug for castration-resistant prostate cancer

AUTHOR(S): Zhou, Xiang-jun; Zhang, Jie

CORPORATE SOURCE: Department of Urology, Renmin Hospital of Wuhan University, Wuhan, 430060, Peop. Rep. China

SOURCE: Shijie Linchuang Yaowu (2014), 35(2), 74-79
CODEN: SLYHAA; ISSN: 1672-9188

PUBLISHER: Shijie Linchuang Yaowu Bianjibu

DOCUMENT TYPE: Journal; General Review

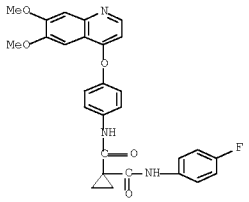
LANGUAGE: Chinese

AB A review with 28 ref. is given on development of therapeutic drug for castration-resistant prostate cancer. The treatment of castration-resistant prostate cancer (CRPC) is still a challenge, as there are few effective therapies to lengthen life of patients. Many novel approaches with extended survival benefit currently in development yielded promising results for patients. This review describes the therapeutic drug for CRPC. The therapeutic drug comprises antiandrogen drug such as abiraterone, enzalutamide, orteronel, galeterone; cytotoxic chemotherapy such as docetaxel, cabazitaxel; immunotherapy such as sipuleucel-T, rilimogene galvacirepvec, ipilimumab; targeting therapy including endothelin-A receptor antagonist such as atrasentan, zibotentan, tyrosine kinase inhibitor such as dasatinib and sorafenib, cabozantinib, anti-angiogenesis agent such as bevacizumab, aflibercept, tasquinimod, clusterin inhibitor such as custirsen, and radium chloride.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of therapeutic drug for castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 287 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:26950 CAPLUS Full-text

DOCUMENT NUMBER: 163:325796

TITLE: Cabozantinib Overcomes Crizotinib Resistance in ROS1 Fusion-Positive Cancer

AUTHOR(S): Katayama, Ryohei; Kobayashi, Yuka; Friboulet, Luc; Lockerman, Elizabeth L.; Koike, Sumie; Shaw, Alice T.; Engelman, Jeffrey A.; Fujita, Naoya

CORPORATE SOURCE: Division of Experimental Chemotherapy, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo, Japan

SOURCE: Clinical Cancer Research (2015), 21(1), 166-174
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-14-1385

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

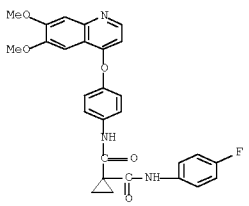
LANGUAGE: English

AB Purpose: ROS1 rearrangement leads to constitutive ROS1 activation with potent transforming activity. In an ongoing phase I trial, the ALK tyrosine kinase inhibitor (TKI) crizotinib shows remarkable initial responses in patients with non-small cell lung cancer (NSCLC) harboring ROS1 fusions; however, cancers eventually develop crizotinib resistance due to acquired mutations such as G2032R in ROS1. Thus, understanding the crizotinib-resistance mechanisms in ROS1-rearranged NSCLC and identification of therapeutic strategies to overcome the resistance are required. Exptl. Design: The sensitivity of CD74-ROS1-transformed Ba/F3 cells to multiple ALK inhibitors was examined Acquired ROS1 inhibitor-resistant mutations in CD74-ROS1 fusion were screened by N-ethyl-N-nitrosourea mutagenesis with Ba/F3 cells. To overcome the resistance mutation, we performed high-throughput drug screening with small-mol. inhibitors and anticancer drugs used in clin. practice or being currently tested in clin. trials. The effect of the identified drug was assessed in the CD74-ROS1-mutant Ba/F3 cells and crizotinib-resistant patient-derived cancer cells (MGH047) harboring G2032R-mutated CD74-ROS1. Results: We identified multiple novel crizotinib-resistance mutations in the ROS1 kinase domain, including the G2032R mutation. As the result of high-throughput drug screening, we found that the cMET/RET/VEGFR inhibitor cabozantinib (XL184) effectively inhibited the survival of CD74-ROS1 wild-type (WT) and resistant mutants harboring Ba/F3 and MGH047 cells. Furthermore, cabozantinib could overcome all the resistance by all newly identified secondary mutations. Conclusions: We developed a comprehensive model of acquired resistance to ROS1 inhibitors in NSCLC with ROS1 rearrangement and identified cabozantinib as a therapeutic strategy to overcome the resistance. Clin Cancer Res; 21(1); 166-74. cpr2014 AACR.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib overcoming crizotinib resistance in ROS1 fusion-pos. cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

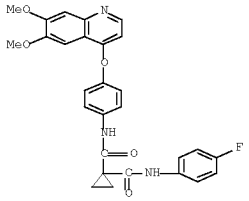


RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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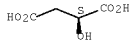
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

L4 ANSWER 288 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2015:21816 CAPLUS Full-text

DOCUMENT NUMBER: 162:172165

TITLE: A Novel Multiple Tyrosine-kinase Targeted Agent to Explore the Future Perspectives of Anti-Angiogenic Therapy for the Treatment of Multiple Solid Tumors: Cabozantinib

AUTHOR(S): Roy, Subhajit; Narang, Bawneet K.; Rastogi, Shiva K.; Rawal, Ravindra K.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Indo-Soviet Friendship College of Pharmacy, Punjab, 142 001, India

SOURCE: Anti-Cancer Agents in Medicinal Chemistry (2015), 15(1), 37-47
CODEN: AAMCE4; ISSN: 1871-5206

DIGITAL OBJECT ID: 10.2174/1871520614666140902153840

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

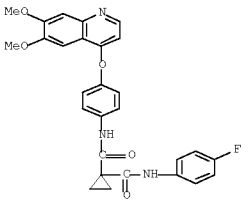
LANGUAGE: English

AB A review. The process of angiogenesis involves the formation of new blood vessels from pre-existing vasculature by the over expression of certain factors leading to the growth and development of all solid tumor types. Hepatocyte growth factor receptor abbreviated as c-Met and vascular

endothelial growth factor abbreviated as VEGF are some of the factors responsible for the induction in tumor growth and development. Recently a number of analogs associated with these receptors are under study. US FDA on Nov. 29, 2012 approved a drug named cabozantinib formerly known as XL184 which is being marketed under the trade name of Cometriq for the treatment of Medullary Thyroid Cancer (MTC). Designing of the drug has been done in such a fashion that it can inhibit both VEGFR2 and c-Met simultaneously without over expressing any of the factors leading to the inhibition of angiogenesis. The drug is still under study for the evaluation of its efficacy in cases of many other solid tumor types including breast cancer, castration resistant prostate cancer (CRPC), renal cell carcinoma (RCC), hepatocellular carcinoma (HCC), gastric or gastroesophageal junction cancer, melanoma, small cell lung cancer (SCLC), ovarian cancer and primary peritoneal or fallopian tube carcinoma. This review article consists of preclin. and clin. data of cabozantinib and its efficacy and safety towards various types of solid tumors.

IT 849217-68-1, Cabozantinib 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel multiple tyrosine-kinase targeted agent, cabozantinib to explore future perspectives of anti-angiogenic therapy for treatment of human multiple solid tumors and in mouse models)

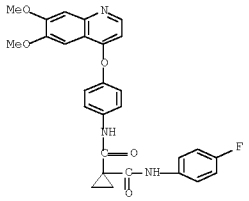
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

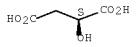
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



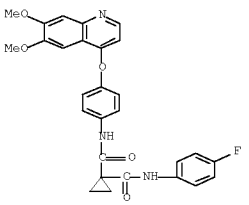
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 289 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2163755 CAPLUS Full-text
DOCUMENT NUMBER: 162:309823
TITLE: Antiangiogenic drugs for castration-resistant prostate cancer: Recent findings
AUTHOR(S): Huang, Dao-guang; Gan, Wei-dong
CORPORATE SOURCE: Department of Urology, Nanjing Drum Tower Hospital, the Affiliated Hospital, School of Medicine, Nanjing University, Nanjing, Jiangsu Province, 210008, Peop. Rep. China
SOURCE: Zhonghua Nankexue Zazhi (2014), 20(10), 932-937
CODEN: ZNZHB5
DIGITAL OBJECT ID: 10.13263/j.cnki.nja.2014.10.014
PUBLISHER: Zhonghua Nankexue Zazhi Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review. In the recent years, treatment options for castration-resistant prostate cancer had evolved from conventional antiandrogens and chemotherapy to novel androgen receptor signaling inhibitors, a new generation of taxanes, and immunotherapy. Randomized clin. trials had shown that docetaxel, cabazitaxel, enzalutamide, abiraterone acetate, radium-223, and sipuleucel-T could improve the overall survival of the patients with androgen-independent prostate cancer. However, drug resistance was inevitable and androgen-independent prostate cancer remained a major clin. burden, which urgently called for novel therapeutic options for the improvement of the patients' survival and quality of life. Angiogenesis played a central role in the formation and progression of prostate cancer, and the anti angiogenic targeted therapy was shown in many clin. trials to be an effective therapeutic supplement for advanced prostate cancer beyond surgery and endocrine treatment. The recent findings of antiangiogenic mugs for castration-resistant prostate cancer was reviewed.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiangiogenic drugs for castration-resistant prostate cancer: Recent findings)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

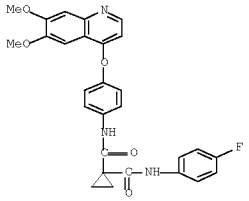


L4 ANSWER 290 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2157654 CAPLUS Full-text
DOCUMENT NUMBER: 162:99756
TITLE: New drug cabozantinib malate for medullary thyroid cancer treatment
AUTHOR(S): Lu, Juanli; Liu, Yang; Sun, Huiping
CORPORATE SOURCE: Department of Pharmacy, General Hospital of Armed Police Forces, Beijing, 100039, Peop. Rep. China
SOURCE: Zhongguo Linchuang Yaoxue Zazhi (2014), 23(1), 58-62
CODEN: ZLYZA5; ISSN: 1007-4406
PUBLISHER: Zhongguo Linchuang Yaoxue Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review with 21 refs. to introduce the new drug cabozantinib malate for medullary thyroid cancer treatment, including its basic properties, action mechanism, pharmacokinetic parameters, clin. trial, drug interactions, adverse reactions, and comparison on therapeutic effect with vandetanib.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new drug cabozantinib malate for medullary thyroid cancer treatment)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



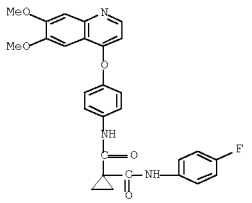
L4 ANSWER 291 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2146461 CAPLUS Full-text
DOCUMENT NUMBER: 162:114047
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 12pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
US 20140378401	A1	20141225	US 2013-14132822	20131218
WO 2014204791	A1	20141224	WO 2014-US42221	20140613

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-13924189 A2 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The ophthalmic drug delivery vehicles provide comfort and compliance; drug solubility, residence time and permeability; and reduce side effects. In addition, the delivery vehicle can be slightly modified to provide an artificial tear formulation. The ophthalmic drug delivery vehicles include 2-12% nonionic surfactant, one or more non-Newtonian high blend viscosity enhancing, non-gelling agents and 0.1-0.90% sodium chloride. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.
IT 849217-68-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



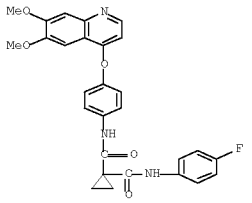
L4 ANSWER 292 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2146420 CAPLUS Full-text
DOCUMENT NUMBER: 162:144424
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 924,189.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140378401	A1	20141225	US 2013-14132822	20131218
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
WO 2014204791	A1	20141224	WO 2014-US42221	20140613

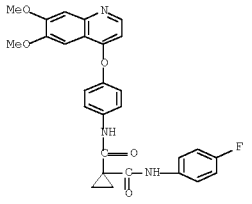
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-13924189 A2 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The ophthalmic drug delivery vehicles provide comfort and compliance; drug solubility, residence time and permeability; and reduce side effects. In addition, the delivery vehicle can be slightly modified to provide an artificial tear formulation. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 293 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2145974 CAPLUS Full-text
DOCUMENT NUMBER: 163:58679
TITLE: Cabozantinib in chemotherapy-pretreated metastatic castration-resistant prostate cancer: results of a phase II nonrandomized expansion study
AUTHOR(S): Smith, Matthew R.; Sweeney, Christopher J.; Corn, Paul G.; Rathkopf, Dana E.; Smith, David C.; Hussain, Maha; George, Daniel J.; Higano, Celestia S.; Harzstark, Andrea L.; Sartor, A. Oliver; Vogelzang, Nicholas J.; Gordon, Michael S.; de Bono, Johann S.; Haas, Naomi B.; Logothetis, Christopher J.; Elfiky, Aymen; Scheffold, Christian; Laird, A. Douglas; Schimmoller, Frauke; Basch, Ethan M.; Scher, Howard I.
CORPORATE SOURCE: USA
SOURCE: Journal of Clinical Oncology (2014), 32(30), 3391-3399
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2013.54.5954
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose Cabozantinib (XL184), an oral inhibitor of multiple receptor tyrosine kinases such as MET and VEGFR2, was evaluated in a phase II nonrandomized expansion study in castration-resistant prostate cancer (CRPC). Patients and Methods Patients received open-label cabozantinib at daily starting doses of 100 mg or 40 mg until disease progression or unacceptable toxicity. The primary end point was bone scan response, defined as ≥ 30% reduction in bone scan lesion area. Other efficacy end points included overall survival, pain, analgesic use, and biomarkers. Results One hundred forty-four patients sequentially enrolled in either a 100-mg (n = 93) or 40-mg (n = 51) study cohort. Ninety-one patients (63%) had a bone scan response, often by week 6. Treatment resulted in clin. meaningful pain relief (57% of patients) and reduction or discontinuation of narcotic analgesics (55% of patients), as well as improvements in measurable soft tissue disease, circulating tumor cells, and bone biomarkers. Improvements in each of these outcomes were observed in both cohorts: bone scan response in 73% and 45%, resp.; redns. in measurable soft tissue disease in 80% and 79%, resp. Median overall survival was 10.8 mo for the entire population. Most common grade 3 or 4 adverse events were fatigue (22%) and hypertension (14%). Fewer dose redns. because of toxicity were required in the 40-mg group. Conclusion The evidence suggests that cabozantinib has clin. meaningful activity in CRPC. Cabozantinib resulted in improvements in bone scans, pain, analgesic use, measurable soft tissue disease, circulating tumor cells, and bone biomarkers. Taken together, these phase II observations warrant further development of cabozantinib in prostate cancer.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of cabozantinib in chemotherapy-pretreated metastatic castration-resistant prostate cancer patients in phase II nonrandomized expansion study)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 294 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2128221 CAPLUS Full-text
DOCUMENT NUMBER: 162:127174
TITLE: Ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations
INVENTOR(S): Horn, Gerald
PATENT ASSIGNEE(S): GNT, LLC, USA
SOURCE: PCT Int. Appl., 57pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014204791	A1	20141224	WO 2014-US42221	20140613

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

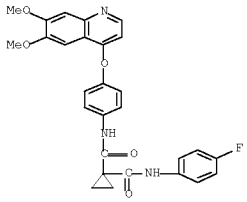
US 20140378391	A1	20141225	US 2013-13924189	20130621
US 8999938	B2	20150407		
US 20140378401	A1	20141225	US 2013-14132822	20131218

PRIORITY APPLN. INFO.: US 2013-13924189 A 20130621
US 2013-14132822 A 20131218
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The ophthalmic drug delivery vehicles include 1-15% nonionic surfactant, one or more non-Newtonian high blend viscosity enhancing, non-gelling agents and 0.025-0.90% sodium chloride. Particularly, formulations that have the non-Newtonian characteristics at 37° of creating a viscosity increase in ratio of 3:1 within 1-2 s at the low shear force between blinks and drops within the fraction of a second to the high shear force of each blink, which on dilution maintain a viscosity of ≥10 cPs during each blink and which do not cause excessive stinging or discomfort, are disclosed. Thus, a formulation comprised dexmedetomidine 0.09, CM-cellulose 0.75, Poloxamer-407 5.50, NaCl 0.25, an benzalkonium chloride 0.02%.

IT 849217-68-1 1642298-56-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic lipophilic and hydrophilic drug delivery vehicle formulations)

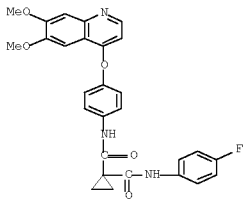
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1642298-56-3 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 75-75-2
CMF C H4 O3 S



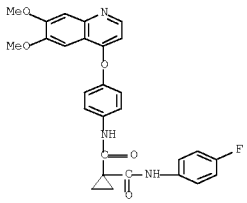
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 295 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2126341 CAPLUS Full-text
DOCUMENT NUMBER: 162:148367
TITLE: Medullary thyroid cancer in the era of tyrosine kinase inhibitors: to treat or not to treat-and with which drug-those are the questions
AUTHOR(S): Cabanillas, Maria E.; Hu, Mimi I.; Jimenez, Camilo
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2014), 99(12), 4390-4396
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2014-2811
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Context: Medullary thyroid cancer (MTC) is a rare form of thyroid cancer comprising approx. 4% of all thyroid cancers. The majority of patients have a relatively good prognosis; however, a subgroup of patients will require systemic therapy. Large phase III randomized trials led to the approval of two drugs-vandetanib and cabozantinib-for progressive or symptomatic MTC. The decision regarding which drug to initiate first is not entirely clear and is a common concern amongst treating physicians. Evidence Acquisition and Synthesis: A review of the literature in English was conducted, and data were summarized and integrated into a decision matrix. Conclusions: The decision regarding which drug to initiate first for progressive MTC should be based on a careful review of the medical history, phys. examination findings, medication list, ECG, laboratory results, and tumor characteristics. It is necessary to consider the relative contraindications when choosing which drug to initiate first.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medullary thyroid cancer in era of tyrosine kinase inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

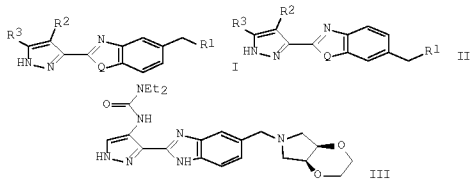


OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 296 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2105568 CAPLUS Full-text
DOCUMENT NUMBER: 162:137867
TITLE: Substituted pyrazole-type deriv. as aurora kinase inhibitor useful in treatment of various diseases and its preparation
INVENTOR(S): Liu, Bing; Zhang, Yingjun; Zhang, Jiquan; Li, Yanping; Yang, Xueqi; Zhang, Jiancun; Zheng, Changchun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 96pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104211692	A	20141217	CN 2014-10245663	20140604
PRIORITY APPLN. INFO.:			CN 2013-10217864	A 20130604
			CN 2014-10109643	A 20140321

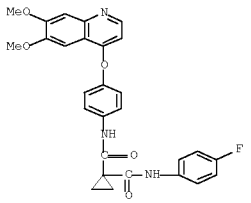
OTHER SOURCE(S): MARPAT 162:137867
GI



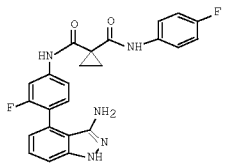
AB The invention relates to substituted pyrazole-type deriv. of formula I and II as aurora kinase inhibitor useful in treatment of various diseases and their preparation Compds. I and II, wherein Q is NH or O; R1 is one of morpholinyl, C5-12 bridged bicyclic group, etc.; R2 is R4R4aN-CO-NH, R5R5aCHCONH, or R6OCONH; and R3 is H or C1-6 alkyl; R4 is H, C1-6 alkyl, C3-6 cycloalkyl, etc.; R4a is C1-6 alkyl, C3-6 cycloalkyl, C6-10 aryl, etc.; R5 and R5a are independently H, C3-6 cycloalkyl, etc.; R6 is C1-6 alkyl or C6-10 aryl; their stereoisomer, geometric isomer, tautomer, nitrogen oxide, hydrate, solvate, metabolite, ester, pharmaceutically acceptable salt or prodrug are claimed. Compound III was prepared by multi-step procedure (procedure given). The invention compds. were evaluated for their aurora kinase inhibitor activity. From assay, it was determined that III exhibited the IC50 value of 2.16 nM against aurora A kinase .

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted pyrazole-type derivative as aurora kinase inhibitor useful in treatment of various diseases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

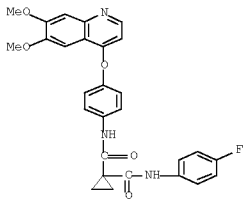


L4 ANSWER 297 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2087478 CAPLUS Full-text
DOCUMENT NUMBER: 162:183726
TITLE: Discovery and SAR study of c-Met kinase inhibitors bearing an 3-amino-benzo[d]isoxazole or 3-aminoindazole scaffold
AUTHOR(S): Jiang, Xiaolong; Liu, Hongyan; Song, Zilan; Peng, Xia; Ji, Yinchun; Yao, Qizheng; Geng, Meiyu; Ai, Jing; Zhang, Ao
CORPORATE SOURCE: Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry (2015), 23(3), 564-578
CODEN: BMECEP; ISSN: 0968-0896
DIGITAL OBJECT ID: 10.1016/j.bmc.2014.12.002
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 162:183726
GI



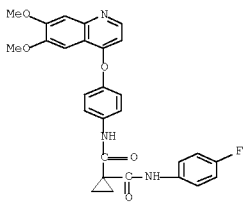
I

AB A series of 3-amino-benzo[d]isoxazole-/3-aminoindazole-based compds. were designed, synthesized and pharmacol. evaluated as tyrosine kinase c-Met inhibitors. The SAR study was conducted leading to identification of nine compds. with IC50s less than 10 nM against c-Met. Compound I stood out as the most potent c-Met inhibitor displaying potent inhibitory effects both at enzymic (IC50 = 1.8 nM) and cellular (IC50 = 0.18 μM on EBC-1 cells) levels. In addition, I had a relatively good selectivity compared to a panel of the inhouse 14 RTKs.
IT 849217-68-1
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery and SAR study of c-Met kinase inhibitors bearing an 3-amino-benzo[d]isoxazole or 3-aminoindazole scaffold)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



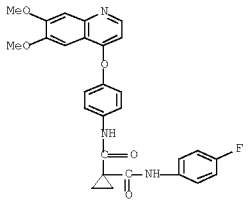
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 298 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2072471 CAPLUS Full-text
DOCUMENT NUMBER: 163:156450
TITLE: Adaptive Responses to Dasatinib-Treated Lung Squamous Cell Cancer Cells Harboring DDR2 Mutations
AUTHOR(S): Bai, Yun; Kim, Jae-Young; Watters, January M.; Fang, Bin; Kinose, Fumi; Song, Lanxi; Koomen, John M.; Teer, Jamie K.; Fisher, Kate; Chen, Yian Ann; Rix, Uwe; Haura, Eric B.
CORPORATE SOURCE: Department of Thoracic Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA
SOURCE: Cancer Research (2014), 74(24), 7217-7228
CODEN: CNREA8; ISSN: 0008-5472
DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-14-0505
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study of cancer cell signaling perturbed by the tyrosine kinase inhibitor dasatinib suggests rational combinations to improve the efficacy of this drug in the subset of lung cancers where it is used. DDR2 mutations occur in approx. 4% of lung squamous cell cancer (SCC) where the tyrosine kinase inhibitor dasatinib has emerged as a new therapeutic option. We found that ERK and AKT phosphorylation was weakly inhibited by dasatinib in DDR2-mutant lung SCC cells, suggesting that dasatinib inhibits survival signals distinct from other oncogenic receptor tyrosine kinases (RTK) and/or compensatory signals exist that dampen dasatinib activity. To gain better insight into dasatinib's action in these cells, we assessed altered global tyrosine phosphorylation (pY) after dasatinib exposure using a mass spectrometry-based quant. phosphoproteomics approach. Overlaying protein-protein interaction relationships upon this dasatinib-regulated pY network revealed decreased phosphorylation of Src family kinases and their targets. Conversely, dasatinib enhanced tyrosine phosphorylation in a panel of RTK and their signaling adaptor complexes, including EGFR, MET/GAB1, and IGF1R/IRS2, implicating a RTK-driven adaptive response associated with dasatinib. To address the significance of this observation, these results were further integrated with results from a small-mol. chemical library screen. We found that dasatinib combined with MET and insulin-like growth factor receptor (IGF1R) inhibitors had a synergistic effect, and ligand stimulation of EGFR and MET rescued DDR2-mutant lung SCC cells from dasatinib-induced loss of cell viability. Importantly, we observed high levels of tyrosine-phosphorylated EGFR and MET in a panel of human lung SCC tissues harboring DDR2 mutations. Our results highlight potential RTK-driven adaptive-resistant mechanisms upon DDR2 targeting, and they suggest new, rationale cotargeting strategies for DDR2-mutant lung SCC. Cancer Res; 74(24); 7217-28. cpr2014 AACR.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adaptive responses to dasatinib-treated lung squamous cell cancer cells harboring DDR2 mutations)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 299 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2068289 CAPLUS Full-text
DOCUMENT NUMBER: 162:228992
TITLE: Anti-angiogenic agents in metastatic NSCLC
AUTHOR(S): Das, Millie; Wakelee, Heather
CORPORATE SOURCE: VA Palo Alto Heath Care System, Palo Alto, CA, USA
SOURCE: Lung Cancer (4th Edition) (2014), 527-540. Editor(s): Roth, Jack A.; Hong, Waun Ki; Komaki, Ritsuko U. Wiley-Blackwell: Hoboken, N. J.
CODEN: 69THV4; ISBN: 978-1-118-46874-6
DIGITAL OBJECT ID: 10.1002/9781118468791.ch34
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB This review highlights the role of anti-angiogenic agents in metastatic non-small cell lung cancer (NSCLC). Anti-angiogenic agents being studied in NSCLC include monoclonal antibodies against VEGF, tyrosine kinase inhibitors directed at VEGF receptors, as well as vascular disrupting agents which do not involve inhibition of VEGF.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discussion on role of anti-angiogenic agents in metastatic non-small cell lung cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 300 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:2037552 CAPLUS Full-text
DOCUMENT NUMBER: 163:187272
TITLE: RET-Rearranged Lung Adenocarcinomas with Lymphangitic

Spread, Psammoma Bodies, and Clinical Responses to Cabozantinib

AUTHOR(S): Mukhopadhyay, Sanjay; Pennell, Nathan A.; Ali, Siraj M.; Ross, Jeffrey S.; Ma, Patrick C.; Velcheti, Vamsidhar

CORPORATE SOURCE: Solid Tumor Oncology, and Translational Hematology and Oncology Research, Cleveland Clinic, Cleveland, OH, 9500, USA

SOURCE: Journal of Thoracic Oncology (2014), 9(11), 1714-1719
CODEN: JTOOB7; ISSN: 1556-0864

DIGITAL OBJECT ID: 10.1097/JTO.0000000000000323

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; (online computer file)

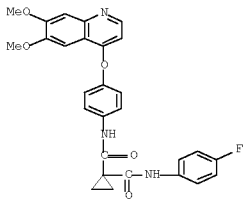
LANGUAGE: English

AB Oncogenic rearrangements of the RET gene have recently been described in 1% to 2% of lung adenocarcinomas. We report five cases of RET-rearranged lung adenocarcinoma with an unusual constellation of clin. and histol. features that has not previously been described in tumors with this genomic alteration. The age at diagnosis of the five patients (4F, 1M) ranged from 44 to 77 years. All were never-smokers. Radiol., four tumors showed lymphangitic spread within the lungs at presentation; three of these had multiple bilateral lung nodules. Histol. showed psammoma bodies within the tumor in four of five cases. Mol. testing for activating EGFR mutations by standard genotyping and ALK expression by immunohistochem. was neg. in all cases. Addnl. mol. anal. was prompted by the clin. profile in that all five patients were never-smokers with metastatic, relapsed, and/or refractory disease; and also by unusual histol. findings in two cases. Comprehensive genomic profiling performed by means of a clin. grade cancer gene panel next-generation sequencing assay demonstrated a KIF5B-RET fusion in three; and fluorescence in-situ hybridization documented a RET rearrangement in two. Three of the patients were treated with the RET inhibitor cabozantinib. By Response Evaluation Criteria In Solid Tumors (RECIST) criteria, two had a confirmed partial response (at 6 wk and 4 wk) and one had stable disease. Our findings suggest that the combination of lymphangitic spread and psammoma bodies may be characteristic of a subset of advanced stage RET-rearranged lung adenocarcinomas. These findings should prompt addnl. mol. testing for RET translocations, particularly in never-smokers with EGFR- and ALK-neg. lung adenocarcinoma.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on RET-rearranged lung adenocarcinomas with lymphangitic spread, psammoma bodies, and clin. responses to cabozantinib)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 301 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:2015786 CAPLUS Full-text

DOCUMENT NUMBER: 162:37339

TITLE: Preparation of alkenyl-pyrrolo[2,3-b]pyridine compounds as protein tyrosine kinase modulators useful for treatment of proliferative disorders

INVENTOR(S): Xi, Ning; Li, Xiaobo

PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.

SOURCE: PCT Int. Appl., 117pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014193647	A2	20141204	WO 2014-US37856	20140513
WO 2014193647	A3	20150129		

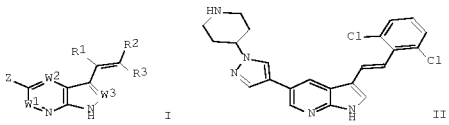
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61827599 P 20130526

OTHER SOURCE(S): CASREACT 162:37339; MARPAT 162:37339

GI



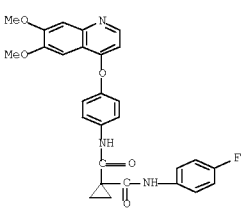
I II

AB The invention provides substituted alkenyl pyrrolo[2,3-b]pyridine compds. of formula I, pharmaceutical acceptable salts and formulations thereof as protein tyrosine kinase modulators capable of modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion and, thus useful for the treatment of proliferative disorders. I [wherein W1, W2, and W3 are independently N or (un)substituted C; R1, R2, and R3 are independently H, CN, (hetero)aryl, etc.; Z is (un)substituted 5- to 6-membered heteroaryl] or a stereoisomer, geometric isomer, tautomer, N-oxide, hydrate, solvate, metabolite, prodrug, or pharmaceutically acceptable salt thereof is claimed. (E)-II was prepared in a multistep process (preparation given). I were evaluated for kinase inhibitor activity using radiochem. anal. and [γ33P-ATP]. From this assay it was determined that (E)-II demonstrated IC50 values of 44 nM and 8 nM for ALK kinase and c-Met kinase, resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of alkenyl-pyrrolo[2,3-b]pyridine compds. as protein tyrosine kinase modulators useful for treatment of proliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 302 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1955485 CAPLUS Full-text

DOCUMENT NUMBER: 164:33863

TITLE: Novel therapies for thyroid cancer

AUTHOR(S): Krajewska, Jolanta; Jarzab, Barbara

CORPORATE SOURCE: Nuclear Medicine and Endocrine Oncology Department, Gliwice Branch, M.Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Pol.

SOURCE: Expert Opinion on Pharmacotherapy (2014), 15(18), 2641-2652
CODEN: EOPHF7; ISSN: 1465-6566

DIGITAL OBJECT ID: 10.1517/14656566.2014.969240

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal; General Review; (online computer file)

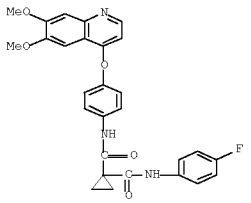
LANGUAGE: English

AB Introduction: New therapeutic options for both differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC) have opened up during the past few years, as the key role of tyrosine kinases in the pathogenesis of thyroid carcinoma has been proved. Recently, two tyrosine kinase inhibitors (TKIs) targeting VEGFR vandetanib (Caprelsa) and cabozantinib (Cometriq) have been approved for advanced MTC, whereas, sorafenib (Nexavar) has been accepted to treat late-stage of DTC. Their efficacy was demonstrated in Phase III studies, compared to placebo; each of them significantly prolonged the progression-free survival. Areas covered: Common adverse reactions related to VEGFR blockade are hypertension, proteinuria, impaired wound healing, hemorrhage and thrombosis, and congestive heart failure. Fatigue, different gastrointestinal disturbances with diarrhea, appetite decrease and weight loss are observed in the majority of patients. Another frequent TKI side effect is TSH increase secondary to inhibition of MCT8-dependent T3 and T4 uptake in pituitary. Expert opinion: So far, no direct comparison of both treatment outcomes and toxicity between particular drugs has been carried out. The evidence-based medicine guidelines are necessary to precisely indicate what drug to use: more effective or less toxic and when to start the treatment.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(discussion on novel therapies for thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



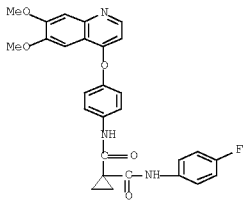
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 303 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1943046 CAPLUS Full-text
DOCUMENT NUMBER: 161:714155
TITLE: Method for the prognosis and treatment of renal cell carcinoma metastasis
INVENTOR(S): Gomis, Roger; Lacey, David L.
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 92pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014184679	A2	20141120	WO 2014-IB1715	20140313
WO 2014184679	A3	20150319		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20160032399	A1	20160204	US 2015-14776390	20150914

PRIORITY APPLN. INFO.: US 2013-61801642 P 20130315
WO 2014-IB1715 W 20140313

AB The present invention relates to a method for the prognosis of bone metastasis in renal cell carcinoma which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering renal cell carcinoma. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of renal cell carcinoma metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering renal cell carcinoma and for classifying a subject from renal cell carcinoma into a cohort.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MAF gene as marker for prognosis and treatment of renal cell carcinoma metastasis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



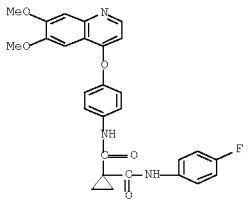
L4 ANSWER 304 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1940485 CAPLUS Full-text
DOCUMENT NUMBER: 161:765704
TITLE: Short-chain phosphatidylcholine lipids and their use in therapy
INVENTOR(S): Van Hell, Albert; Verheij, Marcel; Marrink, Siewert Jan; Koning, Gerben
PATENT ASSIGNEE(S): Stichting Het Nederlands Kanker Instituut - Antoni Van Leeuwenhoek Ziekenhuis, Neth.; Erasmus University Medical Centre; Rijksuniversiteit Groningen
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014184726	A2	20141120	WO 2014-IB61379	20140512
WO 2014184726	A3	20150219		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: GB 2013-8753 A 20130515
OTHER SOURCE(S): MARPAT 161:765704
AB The invention pertains generally to the field of therapy and medical treatment, and more specifically to certain compds. of the following formula (for convenience, collectively referred to herein as "short-chain phosphatidylcholine lipids" and "SCPC lipids"), which, inter alia, are useful in methods of improving drug delivery, bioavailability, and efficacy. The invention also pertains to pharmaceutical formulations, and more specifically to co-formulations of known drugs (e.g., amphiphilic drugs) (e.g., anthracyclines) (e.g., doxorubicin) with these SCPC lipids, and their use in therapy, such as cancer treatment.
IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(short-chain phosphatidylcholine lipids co-formulations and use for treatment of diseases such as cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

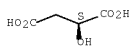
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



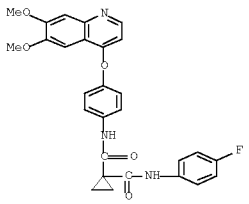
L4 ANSWER 305 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1921290 CAPLUS Full-text
DOCUMENT NUMBER: 163:87631
TITLE: Axitinib and crizotinib combination therapy inhibits bone loss in a mouse model of castration resistant prostate cancer
AUTHOR(S): Eswaraka, Jeetendra; Giddabasappa, Anand; Han, Guangzhou; Lalwani, Kush; Eisele, Koleen; Feng, Zheng; Affolter, Timothy; Christensen, James; Li, Gang
CORPORATE SOURCE: Global Science and Technology (WCM), Pfizer Global Research and Development, San Diego, CA, 92121, USA
SOURCE: BMC Cancer (2014), 14, 742/1-742/10
CODEN: BCMACL; ISSN: 1471-2407
DIGITAL OBJECT ID: 10.1186/1471-2407-14-742
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Castration resistant prostate cancer (CRPC) is a leading cause of cancer-related deaths in men. The primary cause of mortality and morbidity in patients is bone metastases and remodeling resulting in osteoblastic and osteolytic lesions. Recently, cabozantinib, a multi-kinase inhibitor (VEGFR2 and c-MET inhibitor), was shown to have efficacy on bone lesions in patients. In this study we tested multi-kinase inhibitors: axitinib (VEGFR inhibitor) and crizotinib (c-MET inhibitor) in a combination trial in mice models. Methods: VCaP-Luc cells were grown as

s.c. implants in intact and castrated NOD-SCID-gamma (NSG) mice to confirm the androgen dependency. For bone metastasis model two cohorts of NSG mice (castrated and intact) received orthotopic injection of VCaP-Luc cells into the bone marrow cavity of left tibia. Mice were monitored weekly for tumor growth using bioluminescence imaging. Animals were randomized into 4 groups based on the tumor bioluminescence signal: vehicle, crizotinib alone, axitinib alone, crizotinib and axitinib in combination. Animals were imaged weekly by in vivo 2-D X-ray imaging to monitor bone remodeling. At the end of the study animals were euthanized and both tibias were extracted for ex vivo high-resolution 3-D micro-computed tomog. (μCT) imaging. Results: S.c. model showed that androgen stimulation may be helpful but not essential for the growth of VCaP-Luc cells. VCaP-Luc cells grown intra-tibially in intact animals caused extensive remodeling of bone with mixed osteoblastic (bone formation) and osteolytic (bone matrix dissoln.) lesions. The osteoblastic lesions were predominant and at times extended beyond the tibial shaft into the surrounding tissue. In contrast, only osteolytic lesions were prominent throughout the study in castrated animals. Treatment with crizotinib alone reduced the osteolytic lesions in castrated animals. Axitinib alone reduced the osteoblastic lesions in the intact animals. Combination therapy with axitinib and crizotinib remarkably inhibited the tibial remodeling by VCaP-Luc cells which resulted in a significant reduction of both osteoblastic and osteolytic lesions. Conclusion: Our data show that combined inhibition of c-MET and VEGFR can be beneficial for treatment of metastatic bone disease in CRPC and that the drugs act on two different stages of the disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(axitinib and crizotinib combination therapy inhibits bone loss in mouse model of castration resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 306 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1853168 CAPLUS Full-text

DOCUMENT NUMBER: 162:33543

TITLE: Significances of RET fusion gene in non-small cell lung cancer

AUTHOR(S): Liu, Jingjing; Bi, Minghong

CORPORATE SOURCE: Department of Medical Oncology, First Affiliated Hospital of Bengbu Medical College, Bengbu, 233004, Peop. Rep. China

SOURCE: Zhongguo Feiai Zazhi (2013), 16(11), 615-620
CODEN: ZFZHAG; ISSN: 1009-3419

DIGITAL OBJECT ID: 10.3779/j.issn.1009-3419.2013.11.11

PUBLISHER: Zhongguo Feiai Zazhi Bianji Weiyuanhui

DOCUMENT TYPE: Journal; General Review

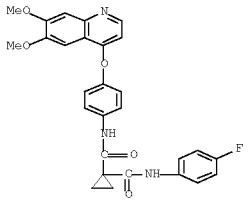
LANGUAGE: Chinese

AB A review with 33 refs. Lung cancer is the leading cause of cancer-related death worldwide, mol. target therapy has become a hot research direction of non-small cell lung cancer(NSCLC) treatment. RET fusion gene with an identifiable clin. pathol. features, is present in some subsets of lung cancer, and its treatment is effective by RET inhibitor, suggesting that RET fusion gene may be a new target for individualized treatment to the subgroup of NSCLC. This article reviews the structural characteristics of RET fusion gene and expression model in clin. samples, and treatment of NSCLC.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(significances of RET fusion gene in non-small cell lung cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 307 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1827672 CAPLUS Full-text

DOCUMENT NUMBER: 161:690410

TITLE: Pharmaceutical combinations of a protein kinase C (PKC) inhibitor and a c-MET receptor tyrosine kinase inhibitor for treatment of proliferative diseases

INVENTOR(S): Porter, Dale; Emery, Caroline; Tan, Lujian

PATENT ASSIGNEE(S): Novartis AG, Switz.

SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014174478	A1	20141030	WO 2014-IB60976	20140424

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

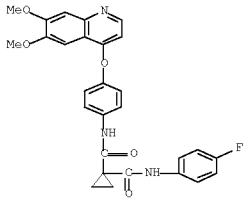
PRIORITY APPLN. INFO.: US 2013-61816266 P 20130426

AB A pharmaceutical combination comprising (a) a protein kinase C (PKC) inhibitor, or a pharmaceutically acceptable salt thereof, and (b) at least one c-MET receptor tyrosine kinase inhibitor, or a pharmaceutically acceptable salt, and optionally a pharmaceutically acceptable carrier, for simultaneous, sep. or sequential administration; the uses of such combination in the treatment of proliferative diseases; and methods of treating a subject suffering from a proliferative disease comprising administering a therapeutically effective amount of such combination.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combinations of a protein kinase C (PKC) inhibitor and a c-MET receptor tyrosine kinase inhibitor for treatment of proliferative diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 308 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1821658 CAPLUS Full-text

DOCUMENT NUMBER: 161:715766

TITLE: Preparation of quinazolineamine derivatives for treating proliferative diseases

INVENTOR(S): Zhang, Yingjun; Liu, Bing; Liu, Jinlei; Zhang, Jiancun; Zheng, Changchun

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 147pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104119350	A	20141029	CN 2014-10175636	20140428
CN 104119350	B	20170412		
WO 2014177038	A1	20141106	WO 2014-CN76377	20140428

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20160039838	A1	20160211	US 2015-14774702	20150911
US 9556191	B2	20170131		

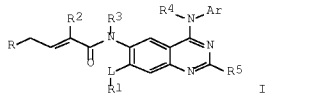
PRIORITY APPLN. INFO.:

CN 2013-10156470	A	20130428
CN 2014-10108773	A	20140323
WO 2014-CN76377	W	20140428

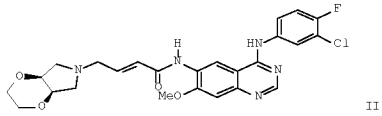
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 161:715766; MARPAT 161:715766

GI



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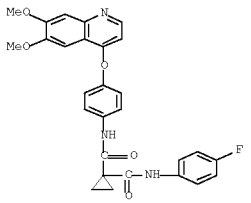
II

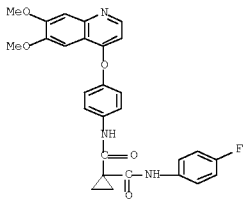
AB The present invention provides quinazolineamine derivs. I [wherein R = bicyclic heterocyclyl; R1 = H, D, F, Cl, Br, I, etc.; R2 = H, F, Cl, Br, I, NH2, etc.; R3 and R4 = independently H, D, or alkyl; R5 = H, D, F, Cl, Br, I, alkyl, etc.; Ar = (un)substituted Ph or indazole-5-yl] stereoisomers, geometric isomers, tautomers, N-oxides, hydrates, solvates, metabolites, pharmaceutically acceptable salts, or prodrugs thereof for prevention, treatment, or relieving proliferative diseases. For example, II was prepared in a multi-step synthesis, which showed inhibitory activity with IC50 of 3.2, 14, and 8.3 nM against EGFR, HER-2, and EGFR T790M kinases, resp. Pharmaceutical compns. comprising the title compound were also described.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of quinazolineamine derivs. for treating proliferative diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)





OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 310 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1791911 CAPLUS Full-text

DOCUMENT NUMBER: 161:680644

TITLE: Cancer-associated chimeric genes arising from translocations and their use in diagnosis, prognosis, and therapy of cancer

INVENTOR(S): Rhodes, Daniel; Sadis, Seth; Wyngaard, Peter; Khazanov, Nikolay; Bandla, Santhoshi; Tomilo, Mark; Eddy, Sean; Bowden, Emma

PATENT ASSIGNEE(S): Life Technologies Corporation, USA

SOURCE: PCT Int. Appl., 272pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014172046	A2	20141023	WO 2014-US29592	20140314
WO 2014172046	A3	20150618		
WO 2014172046	A9	20160225		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

AU 2014254394	A1	20151203	AU 2014-254394	20140314
AU 2014254394	A9	20160317		
EP 2986736	A2	20160224	EP 2014-721666	20140314

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

CN 105378110	A	20160302	CN 2014-80034585	20140314
JP 2016518123	T	20160623	JP 2016-508941	20140314

PRIORITY APPLN. INFO.:

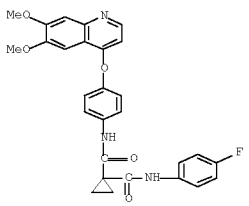
US 2013-61813182	P	20130417
US 2013-61813465	P	20130418
US 2013-61824253	P	20130516
US 2013-61860115	P	20130730
US 2013-61907939	P	20131122
US 2013-61915392	P	20131212
US 2014-61935650	P	20140204
US 2014-61940226	P	20140214
WO 2014-US29592	W	20140314

AB Chimeric genes arising from chromosomal translocations that play a role in the etiol. of cancer are identified for use in diagnosis, prognosis, and selection and monitoring of therapies. These chimeric genes were identified by a large-scale survey of 19 cancers in 4,225 patients.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selection for cancer therapy; cancer-associated chimeric genes arising from translocations and their use in diagnosis, prognosis, and therapy of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 311 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1790149 CAPLUS Full-text

DOCUMENT NUMBER: 161:686526

TITLE: Cabozantinib malate and its preparation method

INVENTOR(S): Meng, Qingyi; Zhang, Aiming; Xu, Wenwei; Zhang, Xiquan

PATENT ASSIGNEE(S): Lianyungang Runzhong Pharmaceutical Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 7pp.
CODEN: CNXXEV

L4 ANSWER 309 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1792793 CAPLUS Full-text

DOCUMENT NUMBER: 162:498601

TITLE: Enrichment of c-Met+ tumorigenic stromal cells of giant cell tumor of bone and targeting by cabozantinib

AUTHOR(S): Liu, L.; Aleksandrowicz, E.; Fan, P.; Schoensiegel, F.; Zhang, Y.; Saehr, H.; Gladkich, J.; Mattern, J.; Depeweg, D.; Lehner, B.; Fellenberg, J.; Herr, I.

CORPORATE SOURCE: Department of Molecular OncoSurgery, General, Visceral and Transplantation Surgery, University of Heidelberg and German Cancer Research Center (DKFZ), Heidelberg, Germany

SOURCE: Cell Death & Disease (2014), 5(10), e1471
CODEN: CDDEA4; ISSN: 2041-4889

DIGITAL OBJECT ID: 10.1038/cddis.2014.440

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Giant cell tumor of bone (GCTB) is a very rare tumor entity, which is little examined owing to the lack of established cell lines and mouse models and the restriction of available primary cell lines. The stromal cells of GCTB have been made responsible for the aggressive growth and metastasis, emphasizing the presence of a cancer stem cell population. To identify and target such tumor-initiating cells, stromal cells were isolated from eight freshly resected GCTB tissues. Tumorigenic properties were examined by colony and spheroid formation, differentiation, migration, MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay, immunohistochem., antibody protein array, Alu in situ hybridization, FACS anal. and xenotransplantation into fertilized chicken eggs and mice. A sub-population of the neoplastic stromal cells formed spheroids and colonies, differentiated to osteoblasts, migrated to wounded regions and expressed the metastasis marker CXC-chemokine receptor type 4, indicating self-renewal, invasion and differentiation potential. Compared with adherent-growing cells, markers for pluripotency, stemness and cancer progression, including the CSC surface marker c-Met, were enhanced in spheroidal cells. This c-Met-enriched sub-population formed xenograft tumors in fertilized chicken eggs and mice. Cabozantinib, an inhibitor of c-Met in phase II trials, eliminated CSC features with a higher therapeutic effect than standard chemotherapy. This study identifies a c-Met+ tumorigenic sub-population within stromal GCTB cells and suggests the c-Met inhibitor cabozantinib as a new therapeutic option for targeted elimination of unresectable or recurrent GCTB.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-Met-enriched tumorigenic human stromal cells of giant cell tumor of bone formed xenograft tumors in fertilized chicken eggs and mouse where cabozantinib strongly inhibited self-renewal potential and in vivo growth of stromal cell)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104109128	A	20141022	CN 2013-10164410	20130419
CN 104109128	B	20161005		

PRIORITY APPLN. INFO.: CN 2013-10164410 20130419

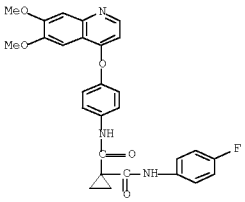
AB The present invention relates to cabozantinib malate and its prepn. method, and specifically, the present invention relates to cabozantinib·n malate, its preparation method, and a pharmaceutical composition comprising the same. The inventive cabozantinib·n malate has excellent stability, and can be used for preparing medicines for the treatment of tumors, especially in preparation of medicine for the treatment of medullary thyroid cancer. The preparation method of cabozantinib·n malate includes: (a) adding cabozantinib to an organic solvent, (b) adding malic acid n times molar amount of cabozantinib to mixture of step (a), and (c) precipitating to obtain cabozantinib·n malate, wherein, n is selected from 0.4-0.6, preferably 0.5.

IT 1140909-48-3 1365530-43-3 1634653-27-2
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cabozantinib malate and preparation method)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

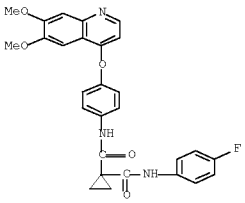
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CRN 849217-68-1
CMF C28 H24 F N3 O5



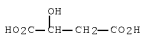
CM 2

CRN 97-67-6
CMF C4 H6 O5



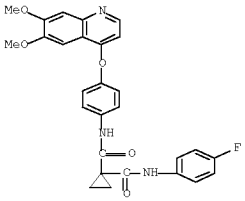
CM 2

CRN 6915-15-7
CMF C4 H6 O5

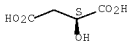


IT 849217-68-1, Cabozantinib
RL: RCT (Reactant); RACT (Reactant or reagent)
(cabozantinib malate and preparation method)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



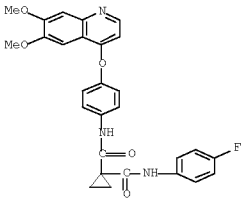
Absolute stereochemistry. Rotation (-).



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

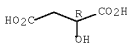
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



RN 1634653-27-2 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

L4 ANSWER 312 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1782124 CAPLUS Full-text
DOCUMENT NUMBER: 161:705479
TITLE: Crystal of cabozantinib· 0.5 malate
INVENTOR(S): Meng, Qingyi; Zhang, Aiming; Xu, Wenwei; Zhang, Xiquan
PATENT ASSIGNEE(S): Chia Tai Tianqing Pharmaceutical Group Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104109124	A	20141022	CN 2013-10138216	20130419
CN 104109124	B	20160831		

PRIORITY APPLN. INFO.: CN 2013-10138216 20130419

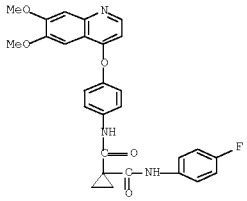
AB The invention relates to crystal of cabozantinib·0.5malate, a crystal composition and a pharmaceutical composition of the crystal, preparing method thereof, and application thereof in manufacture of drugs treating tumor-related diseases. In the x-ray powder diffraction spectrum of the crystal using Cu-Kα radiation, there are diffraction peaks at 2θ of 5.48°, 10.88°, 15.24°, 21.97° and 24.56°.

IT 1635373-15-7
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(0.5 malate; crystal of cabozantinib·0.5malate)

RN 1635373-15-7 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:2) (CA INDEX NAME)

CM 1

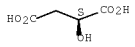
CRN 849217-68-1
CMF C28 H24 F N3 O5



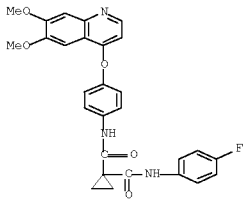
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal of cabozantinib·0.5malate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



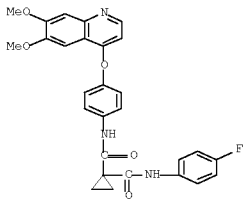
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)

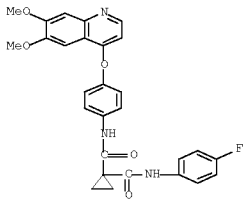
L4 ANSWER 313 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1754957 CAPLUS Full-text
DOCUMENT NUMBER: 161:635758
TITLE: Platform for targeted delivery to stem cells and tumor cells and methods thereof
INVENTOR(S): Carvalho Da Fonseca, Nuno Andre; Gomes Da Silva, Ligia Catarina; Dantas Nunes Caldeira De Moura, Vera Lucia; De Magalhaes Simoes, Sergio Paulo; Sereno De Almeida Moreira, Joao Nuno
PATENT ASSIGNEE(S): Universidade de Coimbra, Port.
SOURCE: PCT Int. Appl., 59pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014167126	A2	20141016	WO 2014-EP57446	20140411
WO 2014167126	A3	20150108		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
AU 2014253040	A1	20151105	AU 2014-253040	20140411
EP 2983720	A2	20160217	EP 2014-721226	20140411
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160058886	A1	20160303	US 2015-14784247	20151013

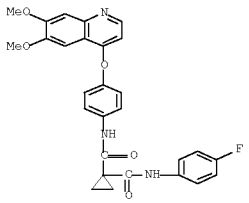
PRIORITY APPLN. INFO.: WO 2014-EP57446 W 20140411
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention involves therapy and diagnostics using nanoparticles that provide targeted delivery of agents to cancer cells and stem cells, including cancer stem cells, the nanoparticles being pH sensitive and incorporating cytotoxic ceramides.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(platform for targeted delivery to stem cells and tumor cells and methods thereof)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 314 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1754784 CAPLUS Full-text
DOCUMENT NUMBER: 163:225877
TITLE: Sequencing of lung cancer genomes and its translation to the therapy
AUTHOR(S): Iwakawa-Kawabata, Reika; Kohno, Takashi
CORPORATE SOURCE: Div. of Genome Biology, National Cancer Center, Japan
SOURCE: Jikken Igaku (2014), 32(12), 1865-1870
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review discussing the sequencing of lung cancer genomes and its translation to the therapy.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequencing of lung cancer genomes and its translation to the therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 315 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1742452 CAPLUS Full-text
DOCUMENT NUMBER: 163:438125
TITLE: A Phase I Study of Cabozantinib (XL184) in Patients with Differentiated Thyroid Cancer
AUTHOR(S): Cabanillas, Maria E.; Brose, Marcia S.; Holland, Jaymes; Ferguson, Kimberly C.; Sherman, Steven I.
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Thyroid (2014), 24(10), 1508-1514
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2014.0125
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Cabozantinib targets tyrosine kinases including MET, vascular endothelial growth factor (VEGF) receptor 2, and rearranged during transfection (RET). Differentiated thyroid cancer (DTC) is a tumor type that may be sensitive to cabozantinib. Therefore, we evaluated cabozantinib in a cohort of heavily pretreated patients with metastatic DTC. .Methods: This single-arm open-label phase I trial assessed the safety, tolerability, and antitumor activity of cabozantinib in DTC patients taking part in a drug-drug interaction study. Adult patients with histol. confirmed metastatic or surgically unresectable DTC (including papillary, follicular, or Huerthle cell) were enrolled. Patients received daily oral dosing of 140 mg cabozantinib. Safety was assessed by evaluation of adverse events (AEs), vital signs, electrocardiograms, laboratory tests, and concomitant medications. Tumor response by magnetic resonance imaging or computed tomog. scan was investigator assessed using Response Evaluation Criteria In Solid Tumors (RECIST) v1.0. Results: The study enrolled 15 patients who had failed standard radioactive iodine therapy. Patients had received a median of two prior systemic agents, and 11 patients (73%) had previously received at least one VEGF pathway inhibiting therapy. Common AEs included diarrhea, nausea, fatigue, and decreased appetite. Partial response was reported in eight patients (53%). Median progression-free survival and median overall survival were not reached. Conclusions: Cabozantinib demonstrates a safety profile similar to other multitargeted VEGFR inhibitors in advanced DTC patients. The antitumor activity observed in this study warrants further investigation of cabozantinib in patients with advanced DTC.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase I Study of Cabozantinib (XL184) in Patients with Differentiated Thyroid Cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

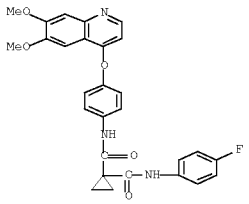


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 316 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1716754 CAPLUS Full-text
DOCUMENT NUMBER: 161:582215
TITLE: Preparation of cabozantinib and dosage forms for treatment of cancer
INVENTOR(S): Decillis, Arthur
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165786	A1	20141009	WO 2014-US33016	20140404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2981263	A1	20160210	EP 2014-724909	20140404
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160022662	A1	20160128	US 2015-14782537	20151005
PRIORITY APPLN. INFO.:			US 2013-61808511 P	20130404

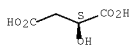
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

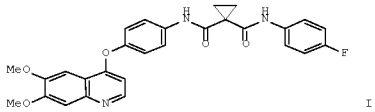


RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

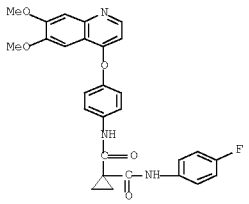
CRN 849217-68-1
CMF C28 H24 F N3 O5

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:582215
GI



I

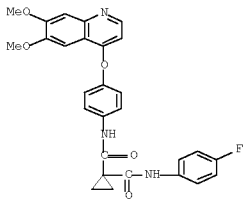
AB This invention relates to a dosage form of cabozantinib (I) and a method of employing the dosage form to treat cancer. I was prepared starting with 6,7-dimethoxy-4-quinolinol through a number of steps. I S-maleate was also prepared and tablets containing I were prepared
IT 849217-68-1, Cabozantinib 1140909-48-3, Cabozantinib S-malate 1365530-43-3
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cabozantinib and dosage forms for treatment of cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

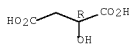
CRN 849217-68-1



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 317 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1715795 CAPLUS Full-text
DOCUMENT NUMBER: 161:577833
TITLE: Methods and compositions for treating cancers having acquired resistance to chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): Tactical Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 23pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165412	A2	20141009	WO 2014-US32253	20140328
WO 2014165412	A3	20150129		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR,				

IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140294806	A1	20141002	US 2013-13986103		20130401
US 9089570	B2	20150728			
CA 2902144	A1	20141009	CA 2014-2902144		20140328
AU 2014248377	A1	20150903	AU 2014-248377		20140328
IL 241827	A	20151130	IL 2014-241827		20140328
CN 105120663	A	20151202	CN 2014-80019712		20140328
EP 2981169	A2	20160210	EP 2014-779684		20140328
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
KR 2016026824	A	20160309	KR 2015-7022953		20140328
JP 2016515619	T	20160530	JP 2016-506341		20140328
IN 2015DN07750	A	20160122	IN 2015-DN7750		20150828
PRIORITY APPLN. INFO.:			US 2013-13986103	A	20130401
			WO 2014-US32253	W	20140328

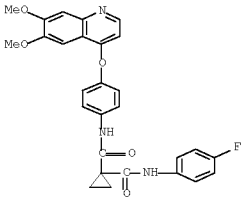
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 318 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1710486 CAPLUS Full-text

DOCUMENT NUMBER: 161:577829

TITLE: Drug combinations to treat cancer

INVENTOR(S): Sweeney, Christopher J.; Kantoff, Philip W.

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 78pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

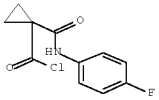
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014165779	A1	20141009	WO 2014-US33008	20140404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2908815	A1	20141009	CA 2014-2908815	20140404
AU 2014248001	A1	20151119	AU 2014-248001	20140404
IL 241868	A	20151130	IL 2014-241868	20140404
KR 2015138268	A	20151209	KR 2015-7030445	20140404
EP 2983639	A1	20160217	EP 2014-724594	20140404
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2016515628	T	20160530	JP 2016-506653	20140404
US 20160082019	A1	20160324	US 2015-14782493	20151005
MX 2015014046	A	20160516	MX 2015-14046	20151005
IN 2015KN03651	A	20160318	IN 2015-KN3651	20151103
PRIORITY APPLN. INFO.:			US 2013-61808516	P 20130404
			WO 2014-US33008	W 20140404

OTHER SOURCE(S): CASREACT 161:577829; MARPAT 161:577829

GI

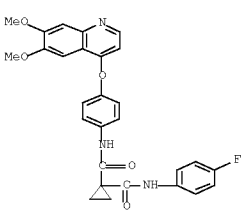


AB This invention relates to the combination of cabozantinib and abiraterone to treat cancer, particularly castration resistant prostate cancer.

IT 849217-68-1P, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug combinations to treat cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P

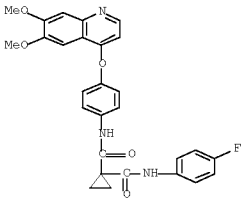
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug combinations to treat cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

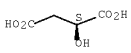
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 319 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1689164 CAPLUS Full-text

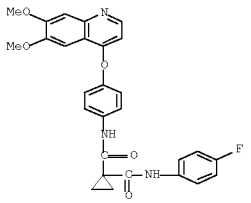
DOCUMENT NUMBER: 162:58578

TITLE: Cabozantinib inhibits growth of androgen-sensitive and castration-resistant prostate cancer and affects bone remodeling [Erratum to document cited in CA160:363229]

AUTHOR(S): Nguyen, Holly M.; Ruppender, Nazanin; Zhang, Xiaotun; Brown, Lisha G.; Gross, Ted S.; Morrissey, Colm; Gulati, Roman; Vessella, Robert L.; Schimmoller, Frauke; Aftab, Dana T.; Corey, Eva

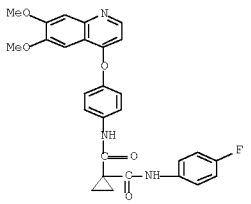
CORPORATE SOURCE: Department of Urology, University of Washington, Seattle, WA, USA

SOURCE: PLoS One (2014), 9(8), e106797/1, 1 pp.
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0106797
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB On page 1, the funding information was incomplete; the cor. funding statement is given.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET, VEGFR2, RET expressions were found higher while cabozantinib by inhibiting these targets it safely, effectively inhibited tumor growth, improved bone remodeling in androgen-sensitive, metastatic CRPC tumor xenografted mouse (Erratum))
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



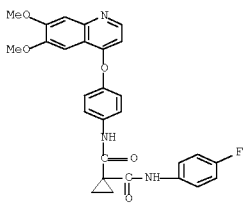
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 320 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1684883 CAPLUS Full-text
DOCUMENT NUMBER: 161:588524
TITLE: Emerging molecular targets in oncology: clinical potential of MET/hepatocyte growth-factor inhibitors
AUTHOR(S): Smyth, Elizabeth C.; Sclafani, Francesco; Cunningham, David
CORPORATE SOURCE: Department of Gastrointestinal Oncology, Royal Marsden Hospital, Sutton, UK
SOURCE: OncoTargets and Therapy (2014), 7, 1001-1014, 14 pp.
CODEN: OTNHAZ; ISSN: 1178-6930
DIGITAL OBJECT ID: 10.2147/OTT.S44941
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The MET/hepatocyte growth-factor (HGF) signaling pathway plays a key role in the processes of embryogenesis, wound healing, and organ regeneration. Aberrant activation of MET/HGF occurs through multiple mechanisms including gene amplification, mutation, protein overexpression, and abnormal gene splicing interrupting autocrine and paracrine regulatory feedback mechanisms. In many cancers including non-small-cell lung cancer, colorectal, gastric, renal, and hepatocellular cancer, dysregulation of MET may lead to a more aggressive cancer phenotype and may be a neg. prognostic indicator. Successful therapeutic targeting of the MET/HGF pathway has been achieved using monoclonal antibodies against the MET receptor and its ligand HGF in addition to MET-specific and multitargeted small-mol. tyrosine-kinase inhibitors with several drugs in late-phase clin. trials including onartuzumab, rilotumumab, tivantinib, and cabozantinib. MET frequently interacts with other key oncogenic tyrosine kinases including epidermal growth-factor receptor (EGFR) and HER-3 and these interactions may be responsible for resistance to anti-EGFR therapies. Similarly, resistance to MET inhibition may be mediated through EGFR activation, or alternatively by increasing levels of MET amplification or acquisition of novel "gatekeeper" mutations. In order to optimize development of effective inhibitors of the MET/HGF pathway clin. trials must be enriched for patients with demonstrable MET-pathway dysregulation for which robustly standardized and validated assays are required.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. targets in oncol. and clin. potential of MeT/hepatocyte growth-factor inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 140 THERE ARE 140 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 321 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1684761 CAPLUS Full-text
DOCUMENT NUMBER: 161:588517
TITLE: Cabozantinib for progressive metastatic medullary thyroid cancer: a review
AUTHOR(S): Colombo, Joshua R.; Wein, Richard O.
CORPORATE SOURCE: Department of Otolaryngology, Head and Neck Surgery, Tufts Medical Center, Boston, MA, USA
SOURCE: Therapeutics and Clinical Risk Management (2014), 10, 395-404, 10 pp.
CODEN: TCRMA6; ISSN: 1178-203X
DIGITAL OBJECT ID: 10.2147/TCRM.S46041
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Medullary thyroid cancer is uncommon and patients typically present with advanced disease. Treatment options for patients with progressive, metastatic medullary thyroid cancer had been limited until recently. Tyrosine kinase inhibitors have garnered increasing interest in this subset of patients. The US Food and Drug Administration recently approved cabozantinib, a tyrosine kinase inhibitor, after promising results were shown in a large Phase III clin. trial. This review summarizes the clin. pharmacol., clin. trials, and safety data for cabozantinib and concludes with a discussion of possible future directions for the treatment of medullary thyroid cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for progressive metastatic medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



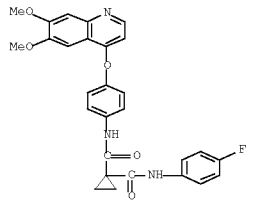
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 322 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1660666 CAPLUS Full-text
DOCUMENT NUMBER: 161:546938
TITLE: Methods and compositions for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate
INVENTOR(S): Karmali, Rashida A.
PATENT ASSIGNEE(S): Tactical Therapeutics Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140294806	A1	20141002	US 2013-13986103	20130401
US 9089570	B2	20150728		
CA 2902144	A1	20141009	CA 2014-2902144	20140328
WO 2014165412	A2	20141009	WO 2014-US32253	20140328
WO 2014165412	A3	20150129		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014248377	A1	20150903	AU 2014-248377	20140328
IL 241827	A	20151130	IL 2014-241827	20140328
CN 105120663	A	20151202	CN 2014-80019712	20140328
EP 2981169	A2	20160210	EP 2014-779684	20140328
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2016026824	A	20160309	KR 2015-7022953	20140328
JP 2016515619	T	20160530	JP 2016-506341	20140328
IN 2015DN07750	A	20160122	IN 2015-DN7750	20150828

PRIORITY APPLN. INFO.: US 2013-13986103 A 20130401
WO 2014-US32253 W 20140328
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB This invention provides methods and compns. useful for treating early and late stage metastatic cancer to prevent or treat acquired resistance due to gene amplification or mutation in response to chemotherapeutic and/or targeted drugs. In particular, the methods and compns. include carboxyamidotriazole orotate (CTO) alone or in combination with specific regimens of chemotherapeutic and/or targeted drugs designed to overcome the genomic resistance raised to prior therapy.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treating cancers having acquired resistance to prior chemotherapeutic and targeted drugs using carboxyamidotriazole orotate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-

quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



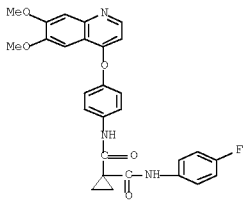
L4 ANSWER 323 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1657302 CAPLUS Full-text
DOCUMENT NUMBER: 161:559304
TITLE: Methods of treating proliferative diseases such as cancer using natural compounds and/or ketogenic diet
INVENTOR(S): Reynolds, Brent; Deleyrolle, Loic
PATENT ASSIGNEE(S): University of Florida Research Foundation, Incorporated, USA
SOURCE: PCT Int. Appl., 115pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014159500	A1	20141002	WO 2014-US23934	20140312
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2912518	A1	20141002	CA 2014-2912518	20140312
AU 2014240467	A1	20151105	AU 2014-240467	20140312
EP 2968260	A1	20160120	EP 2014-775944	20140312
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 105377252	A	20160302	CN 2014-80028215	20140312
JP 2016514135	T	20160519	JP 2016-501388	20140312
US 20160038456	A1	20160211	US 2015-14775751	20150914
IN 2015DN09621	A	20160226	IN 2015-DN9621	20151014

PRIORITY APPLN. INFO.: US 2013-61784386 P 20130314
WO 2014-US23934 W 20140312
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The current invention is directed to a treatment of a proliferative disease comprising administering to a subject in need of such treatment, a composition comprising epigallocatechin-3-gallate (EGCG), curcumin, glucosinolates and, optionally Daikon radish sprout, alone or in combination with providing a ketogenic diet or a modified ketogenic diet to the subject. The invention also provides a composition comprising medium chain triglycerides, epigallocatechin-3-gallate, curcumin, compns. comprising glucosinolates and/or derivs. thereof, such as glucoraphanin and its breakdown product sulforaphane (SFN) (which are found at high levels in broccoli sprouts or sprouts of other cruciferous vegetables), and, optionally Daikon radish sprout.
IT 1140909-48-3, Cometriq
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cometriq; methods of treating proliferative diseases such as cancer using natural compds. and/or ketogenic diet)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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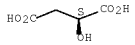
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

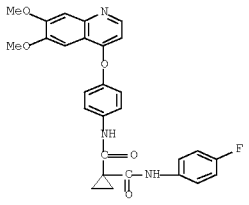


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 324 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1653556 CAPLUS Full-text
DOCUMENT NUMBER: 161:542164
TITLE: Articles and methods for preventing and treating dermatologic adverse events
INVENTOR(S): Lacouture, Mario E.; Abou-Alfa, Ghassan Khaled
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 22pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014160628	A2	20141002	WO 2014-US31545	20140324
WO 2014160628	A3	20141204		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2978412	A2	20160203	EP 2014-775469	20140324
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160101114	A1	20160414	US 2015-14888392	20151030

PRIORITY APPLN. INFO.: US 2013-61804907 P 20130325
WO 2014-US31545 W 20140324
AB The present invention provides articles and methods for preventing or treating dermatol. adverse events.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(articles and methods for preventing and treating dermatol. adverse events)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



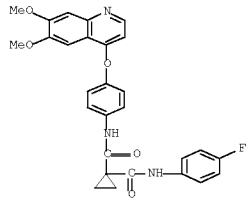
L4 ANSWER 325 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1651697 CAPLUS Full-text
DOCUMENT NUMBER: 161:710328
TITLE: Hepatocellular carcinoma: novel molecular targets in carcinogenesis for future therapies
AUTHOR(S): Bertino, Gaetano; Demma, Shirin; Ardiri, Annalisa; Proiti, Maria; Gruttadauria, Salvatore; Toro, Adriana; Malaguarnera, Giulia; Bertino, Nicoletta; Malaguarnera, Michele; Malaguarnera, Mariano; Di Carlo, Isidoro
CORPORATE SOURCE: Hepatology Unit, Department of Medical and Pediatric Sciences, University of Catania, Policlinic, Catania, 95123, Italy
SOURCE: BioMed Research International (2014) 203693/1-203693/15, 16 pp.
CODEN: BRIIDT; ISSN: 2314-6141
DIGITAL OBJECT ID: 10.1155/2014/203693
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background. Hepatocellular carcinoma is one of the most common and lethal malignant tumors worldwide. Over the past 15 years, the incidence of HCC has more than doubled. Due to late diagnosis and/or advanced underlying liver cirrhosis, only limited treatment options with marginal clin. benefit are available in up to 70% of patients. During the last decades, no effective conventional cytotoxic systemic therapy was available contributing to the dismal prognosis in patients with HCC. A better knowledge of mol. hepatocarcinogenesis provides today the opportunity for targeted therapy. Materials and Methods. A search of the literature was made using cancer literature, the PubMed, Scopus, and Web of Science (WOS) database for the following keywords: "hepatocellular carcinoma," "mol. hepatocarcinogenesis," "targeted therapy," and "immunotherapy." Discussion and Conclusion. Treatment decisions are complex and dependent upon tumor

staging, presence of portal hypertension, and the underlying degree of liver dysfunction. The knowledge of mol. hepatocarcinogenesis broadened the horizon for patients with advanced HCC. During the last years, several mol. targeted agents have been evaluated in clin. trials in advanced HCC. In the future, new therapeutic options will be represented by a blend of immunotherapy-like vaccines and T-cell modulators, supplemented by molecularly targeted inhibitors of tumor signaling pathways.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatocellular carcinoma as novel mol. targets in carcinogenesis for future therapies)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 326 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1600971 CAPLUS Full-text

DOCUMENT NUMBER: 161:533327

TITLE: c-met cancer biomarkers for patient prognosis and selection for the therapy with c-met antagonist, particularly anti-c-met antibody

INVENTOR(S): Yauch, Robert; Koeppen, Hartmut

PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG

SOURCE: PCT Int. Appl., 99pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014150819	A2	20140925	WO 2014-US24316	20140312
WO 2014150819	A3	20150108		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

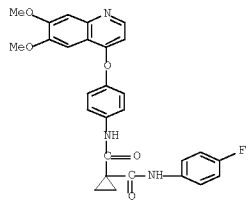
PRIORITY APPLN. INFO.: US 2013-61801276 P 20130315

AB The invention concerns c-met biomarkers for patient selection and prognosis in cancer, as well as methods of therapeutic treatment and diagnostic kits using anti-c-met antibodies.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-met antagonist; c-met cancer biomarkers for patient prognosis and selection for therapy with c-met antagonist, particularly anti-c-met antibody)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 327 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1599013 CAPLUS Full-text

DOCUMENT NUMBER: 161:533781

TITLE: Antibodies for treating angiogenesis-related disorders

INVENTOR(S): Gurewich, Victor

PATENT ASSIGNEE(S): FFE Therapeutics LLC, USA

SOURCE: PCT Int. Appl., 76pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014151917	A1	20140925	WO 2014-US26675	20140313

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2968550	A1	20160120	EP 2014-769535	20140313

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

US 20160024194	A1	20160128	US 2015-14775261	20150911

PRIORITY APPLN. INFO.: US 2013-61785345 P 20130314
WO 2014-US26675 W 20140313

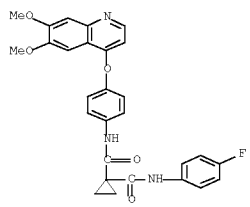
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The author discloses anti-angiogenic monoclonal antibodies and antigen-binding antibody fragments that selectively and specifically bind to an epitope in both fibronectin and either fibrinogen or fibrin fragment E. In one example, administration of the monoclonal antibodies is shown to inhibit tumor growth and vascularization in a colon adenocarcinoma xenograft model.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination therapy with cross-reactive monoclonal antibodies to fibronectin and fibrinogen)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 328 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1596401 CAPLUS Full-text

DOCUMENT NUMBER: 161:528901

TITLE: Stapling eIF4E-eIF4G interacting peptides and their therapeutic use in cancer treatment

INVENTOR(S): Brown, Christopher John; Lane, David Philip; Quah, Soo Tng; Lama, Dilraj; Verma, Chandra Shekhar

PATENT ASSIGNEE(S): Agency for Science, Technology and Research, Singapore

SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014149001	A1	20140925	WO 2014-SG94	20140228

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

SG 201400336	A1	20150828	SG 2014-336	20140115
CN 105263950	A	20160120	CN 2014-80029531	20140228
EP 2976354	A1	20160127	EP 2014-768664	20140228

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

US 20160046672	A1	20160218	US 2015-14778761	20150921

PRIORITY APPLN. INFO.: SG 2013-2065 A 20130321
SG 2014-336 A 20140115
WO 2014-SG94 W 20140228

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

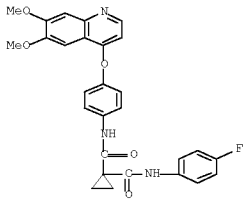
OTHER SOURCE(S): MARPAT 161:528901

AB The present invention relates to crosslinked peptides that are assocd. with human eIF4G and bind to eIF4E, uses thereof and pharmaceutical compns. comprising the peptides. Described below are crosslinked peptides related to a portion of human eIF4E. These crosslinked peptides contain at least two modified amino acids that together form an internal crosslink (also referred to as a staple) that can help to stabilize the alpha-helical secondary structure of a portion of eIF4G1 that is thought to be important for binding of eIF4E to eIF4G. Accordingly, a crosslinked peptide described herein can have improved biol. activity relative to a corresponding peptide that is not crosslinked. The crosslinked eIF4G1 peptides are thought to interfere with binding of eIF4G1 to eIF4G thereby inhibiting the increased

translation of mRNAs with highly structured 5'UTRs. The crosslinked eIF4G1 peptide described herein can be used therapeutically, e.g., to treat or prevent a variety of cancers in a subject.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stapling eIF4E-eIF4G interacting peptides and their therapeutic use in cancer treatment)

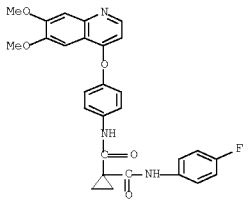
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

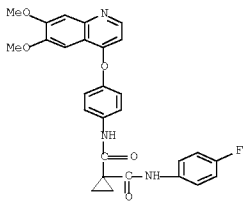
CRN 849217-68-1
CMF C28 H24 F N3 O5



increased risk of developing congestive heart failure in cancer patients. Clinicians should be aware of this risk and provide close monitoring in patients receiving these therapies.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(congestive heart failure risk in cancer patients treated with vascular endothelial growth factor tyrosine kinase inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 330 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1563739 CAPLUS Full-text
DOCUMENT NUMBER: 161:496846
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Gomis, Roger; Planet, Evarist; Pavlovic, Milica; Arnal, Anna; Tarragona, Maria
PATENT ASSIGNEE(S): Fundacio Privada Institut de Recerca Biomedica, Spain; Fundacio Privada Institucio Catalana de Recerca i Estudis Avancats
SOURCE: PCT Int. Appl., 97pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

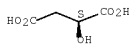
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014140933	A2	20140918	WO 2014-IB1253	20140314
WO 2014140933	A3	20141231		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE,

CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 329 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1594844 CAPLUS Full-text
DOCUMENT NUMBER: 162:544299
TITLE: Congestive heart failure risk in cancer patients treated with vascular endothelial growth factor tyrosine kinase inhibitors: a systematic review and meta-analysis of 36 clinical trials
AUTHOR(S): Qi, Wei-Xiang; Shen, Zan; Tang, Li-Na; Yao, Yang
CORPORATE SOURCE: Department of Oncology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE: British Journal of Clinical Pharmacology (2014), 78(4), 748-762
CODEN: BCPHBM; ISSN: 1365-2125
DIGITAL OBJECT ID: 10.1111/bcp.12387
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB Aims : Congestive heart failure (CHF) assocd. with vascular endothelial growth factor tyrosine-kinase inhibitors (VEGFR-TKIs) has emerged as a relevant problem in clin. and scientific communities. We performed an up-to-date, comprehensive meta-anal. to determine the overall incidence and risk of CHF in cancer patients receiving VEGFR-TKIs. Methods : The databases of PubMed, Web of Science and abstrs. presented at the American Society of Clin. Oncol. up to August 31 2013 were searched for relevant articles. Statistical analyses were conducted to calculate the summary incidence, odds ratio (OR) and 95% confidence intervals (CIs) by using either random effects or fixed effect models according to the heterogeneity of included studies. Results : A total of 10 553 patients from 36 clin. trials were included. The overall incidence of all grade and high grade CHF associated with VEGFR-TKIs was 3.2% (95% CI 1.8%, 5.8%) and 1.4% (95% CI 0.9%, 2.3%), resp. The use of VEGFR-TKIs significantly increased the risk of developing all grade (OR 2.37, 95% CI 1.76, 3.20, P < 0.001) and high grade (OR 3.51, 95% CI 1.74, 7.05, P < 0.001) CHF. In subgroup analyses, the risk of CHF did not significantly vary with tumor types (P = 0.071 for all grade; P = 0.72 for high grade) and VEGFR-TKIs (P = 0.55 for all grade; P = 0.99 for high grade). Meta-regression indicated that CHF might possibly occur early in the treatment of VEGFR-TKIs. No evidence of publication bias was observed Conclusion : The use of VEGFR-TKIs is associated with a significantly

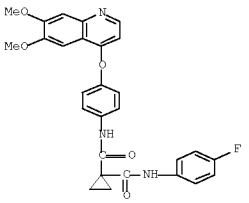
EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2906394	A1	20140918	CA 2014-2906394	20140314
AU 2014229505	A1	20150903	AU 2014-229505	20140314
KR 2015122731	A	20151102	KR 2015-7026432	20140314
EP 2971113	A2	20160120	EP 2014-747411	20140314
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 105324491	A	20160210	CN 2014-80015564	20140314
JP 2016516403	T	20160609	JP 2015-562411	20140314
MX 2015011362	A	20151216	MX 2015-11362	20150902
US 20160032400	A1	20160204	US 2015-14776412	20150914
PRIORITY APPLN. INFO.:			US 2013-61801718 P	20130315
			WO 2014-IB1253 W	20140314

AB The invention relates to a method for the prognosis of bone metastasis in cancer which comprises using a probe to determine if a gene of interest is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise using a probe to determine the expression level of a gene of interest, or the amplification or translocation of a gene of interest. The invention also relates to a method for predicting early bone metastasis in a subject suffering cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering cancer and for classifying a subject from cancer into a cohort.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for prognosis and treatment of cancer metastasis)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



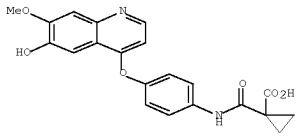
L4 ANSWER 331 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1554223 CAPLUS Full-text
DOCUMENT NUMBER: 161:496839
TITLE: Metabolites of n-[3-fluoro-4-({

6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-

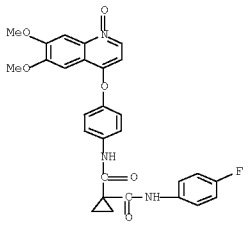
4-yl}oxy)phenyl]-n'-(4-fluorophenyl)cyclopropane-1,1-
dicarboxamide
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy,
Steven; Nguyen, Linh
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014145693	A1	20140918	WO 2014-US30498	20140317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

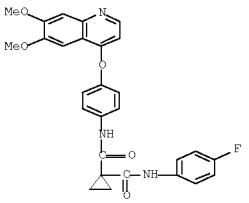
PRIORITY APPLN. INFO.: US 2013-61792562 P 20130315
OTHER SOURCE(S): CASREACT 161:496839; MARPAT 161:496839
GI



AB The invention relates to metabolites of foretinib as well as uses thereof.
IT 1621681-63-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metabolites of foretinib)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



IT 849217-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(metabolites of foretinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



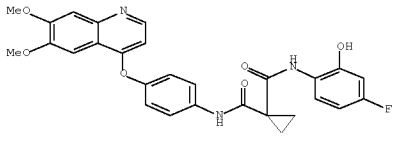
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 332 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1554191 CAPLUS Full-text
DOCUMENT NUMBER: 161:496838
TITLE: Metabolites of

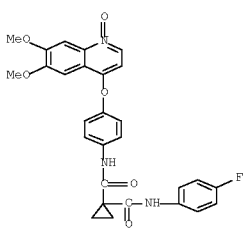
N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-
(4-fluorophenyl) cyclopropane-1,1-dicarboxamide
INVENTOR(S): Aftab, Dana T.; Naganathan, Sriram; Xu, Wei; Lacy,
Steven; Nguyen, Linh
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 65pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014145715	A1	20140918	WO 2014-US30524	20140317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2907334	A1	20140918	CA 2014-2907334	20140317
AU 2014232714	A1	20151008	AU 2014-232714	20140317
KR 2015130376	A	20151123	KR 2015-7027712	20140317
IL 241577	A	20151130	IL 2014-241577	20140317
CN 105121412	A	20151202	CN 2014-80021215	20140317
EP 2970126	A1	20160120	EP 2014-721149	20140317
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JP 2016516074	T	20160602	JP 2016-503412	20140317
MX 2015012490	A	20160524	MX 2015-12490	20150911
US 20160031818	A1	20160204	US 2015-14776337	20150914
IN 2015KN03380	A	20160318	IN 2015-KN3380	20151013

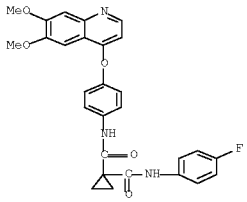
PRIORITY APPLN. INFO.: US 2013-61792413 P 20130315
WO 2014-US30524 W 20140317
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:496838; MARPAT 161:496838
GI



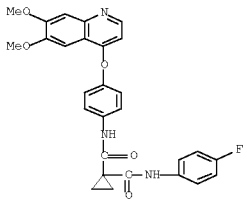
AB The invention relates to metabolites of cabozantinib as well as uses thereof.
IT 1621681-53-7P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metabolites of cabozantinib)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



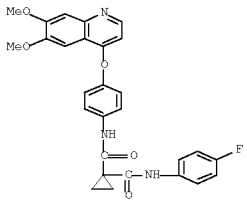
IT 1628542-34-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolites of cabozantinib)
RN 1628542-34-6 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-, monohydroxy deriv. (CA INDEX NAME)



IT 849217-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(metabolites of cabozantinib)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 334 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1476801 CAPLUS Full-text
DOCUMENT NUMBER: 161:446646
TITLE: Preparation of pyridine compounds as protein tyrosine kinase inhibitors for treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wang, Ruyong; Wang, Liang
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 118pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

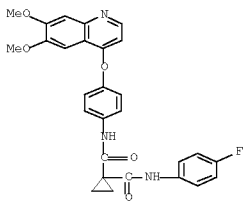
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 104016979	A	20140903	CN 2013-10597520	20131122
CN 104016979	B	20170503		
PRIORITY APPLN. INFO.:			CN 2012-10480698 A	20121123
			CN 2013-10116667 A	20130403
OTHER SOURCE(S):	MARPAT 161:446646			

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridinyl compds. of general formula I, pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. For I, each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; X is C6-C10 aryl or 5-10 membered heteroaryl that are optionally substituted; and Y is an (un)substituted bicyclic heterocyclyl. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 6-step reaction that culminated in coupling of intermediates III and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-ol. Example compds. of the invention were also tested in ALK and c-Met kinase inhibition assays. Pharmacokinetic profiles were also examined in rats, as was compound stability in human and rat liver microsomes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyridine compds. as protein tyrosine kinase inhibitors for treatment of proliferative diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 335 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1460877 CAPLUS Full-text
DOCUMENT NUMBER: 162:17927
TITLE: Comparison of the cancer gene targeting and biochemical selectivities of all targeted kinase inhibitors approved for clinical use
AUTHOR(S): Uitdehaag, Joost C. M.; de Roos, Jeroen A. D. M.; van Doornmalen, Antoon M.; Prinsen, Martine B. W.; de Man, Jos; Tanizawa, Yoshinori; Kawase, Yusuke; Yoshino, Kohichiro; Buijsman, Rogier C.; Zaman, Guido J. R.
CORPORATE SOURCE: Netherlands Translational Research Center B.V., Oss, Neth.
SOURCE: PLoS One (2014), 9(3), e92146/1-e92146/13, 13 pp.
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0092146
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 333 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1509904 CAPLUS Full-text
DOCUMENT NUMBER: 162:419468
TITLE: Antitumor Agent Cabozantinib Decreases RANKL Expression in Osteoblastic Cells and Inhibits Osteoclastogenesis and PTHrP-Stimulated Bone Resorption
AUTHOR(S): Stern, Paula H.; Alvares, Keith
CORPORATE SOURCE: Department of Pharmacology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
SOURCE: Journal of Cellular Biochemistry (2014), 115(11), 2033-2038
CODEN: JCEBD5; ISSN: 0730-2312
DIGITAL OBJECT ID: 10.1002/jcb.24879
PUBLISHER: Wiley-Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cabozantinib, an inhibitor of vascular endothelial growth factor and hepatocyte growth factor signaling, decreases bone lesions in patients with prostate cancer. To determine direct effects of cabozantinib on bone, resorption in neonatal mouse bone organ culture and on gene expression, proliferation, and phenotypic markers in osteoblast and osteoclast cell lines were examined Cabozantinib, 0.3 and 3 μM, prevented PTHrP-stimulated calcium release from neonatal mouse calvaria. Since the effect on resorption could reflect effects on osteoblasts to prevent osteoclast activation, or direct inhibition of osteoclasts, responses in osteoblastic and osteoclast precursor cell lines were examined Twenty-four-hour treatment of osteoblastic MC3T3-E1 cells with 3 μM cabozantinib decreased expression of receptor activator of NFkB ligand (RANKL) and alkaline phosphatase. Forty-eight-hour treatment of MC3T3-E1 cells with 3 μM cabozantinib inhibited cell proliferation and decreased MTT activity. Effects on alkaline phosphatase activity were biphasic, with small stimulatory effects at concns. below 3 μM. When RAW 264.7 osteoclast precursor cells differentiated with 20 ng/mL RANKL were co-treated for 24 h with 3 μM cabozantinib, expression of RANK, TRAP, cathepsin K, alpha v or beta 3 integrin, or NFATc1 were unaffected. Five-day treatment of RANKL-treated RAW 264.7 cells with 3 μM cabozantinib decreased TRAP and MTT activity. The results suggest that the osteoblast could be the initial target, with subsequent direct and indirect effects on osteoclastogenesis leading to decreased resorption. The multiple effects of cabozantinib on the cell microenvironment of bone are consistent with its effectiveness in reducing lesions from prostate cancer metastases. J. Cell. Biochem. 115: 2033-2038, 2014. © 2014 Wiley Periodicals, Inc.

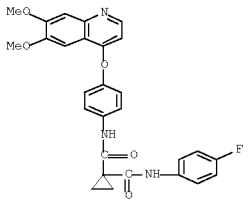
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agent cabozantinib decreases RANKL expression in osteoblastic cells and inhibits osteoclastogenesis and PTHrP-stimulated bone resorption)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

AB The anti-proliferative activities of all twenty-five targeted kinase inhibitor drugs that are in clin. use were measured in two large assay panels: (1) a panel of proliferation assays of forty-four human cancer cell lines from diverse tumor tissue origins; and (2) a panel of more than 300 kinase enzyme activity assays. This study provides a head-on comparison of all kinase inhibitor drugs in use, and for six of these drugs, the first kinome profiling data in the public domain. Correlation of drug activities with cancer gene mutations revealed novel drug sensitivity markers, suggesting that cancers dependent on mutant CTNNB1 will respond to trametinib and other MEK inhibitors, and cancers dependent on SMAD4 to small mol. EGFR inhibitor drugs. Comparison of cellular targeting efficacies reveals the most targeted inhibitors for EGFR-, ABL1- and BRAF(V600E)-driven cell growth, and demonstrates that the best targeted agents combine high biochem. potency with good selectivity. For ABL1 inhibitors, we computationally deduce optimized kinase profiles for use in a next generation of drugs. Our study shows the power of combining biochem. and cellular profiling data in the evaluation of kinase inhibitor drug action.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of cancer gene targeting and biochem. selectivities of all targeted kinase inhibitors approved for clin. use in human)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 336 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1425621 CAPLUS Full-text

DOCUMENT NUMBER: 161:400645

TITLE: Treatment of cancer using an oncolytic virus and a receptor tyrosine kinase inhibitor

INVENTOR(S): Conner, Joe

PATENT ASSIGNEE(S): Virttu Biologics Limited, UK

SOURCE: PCT Int. Appl., 310pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014128487	A1	20140828	WO 2014-GB50522	20140221
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
GB 2516521	A	20150128	GB 2014-3083	20140221
GB 2516521	B	20170111		
GB 2537053	A	20161005	GB 2016-7581	20140221
US 20150374767	A1	20151231	US 2015-14768549	20150818

PRIORITY APPLN. INFO.: GB 2013-3184 A 20130222
GB 2014-3083 A3 20140221
WO 2014-GB50522 W 20140221

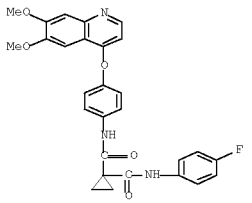
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A method of treating cancer is disclosed, the method comprising simultaneous or sequential administration of an oncolytic virus and a receptor tyrosine kinase (RTK) inhibitor.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of cancer using an oncolytic virus and a receptor tyrosine kinase inhibitor)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 337 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1416968 CAPLUS Full-text

DOCUMENT NUMBER: 162:442908

TITLE: High-Grade Undifferentiated Sarcomas of the Uterus: Diagnosis, Outcomes, and New Treatment Approaches

AUTHOR(S): Philip, Charles-Andre; Pautier, Patricia; Duffaud, Florence; Ray-Coquard, Isabelle

CORPORATE SOURCE: Department of Adult Medical Oncology, Centre Leon Berard, Lyon, 69008, Fr.

SOURCE: Current Oncology Reports (2014), 16(10), 1-8
CODEN: CORUAT; ISSN: 1534-6269

DIGITAL OBJECT ID: 10.1007/s11912-014-0405-1

PUBLISHER: Springer

DOCUMENT TYPE: Journal; General Review; (online computer file)

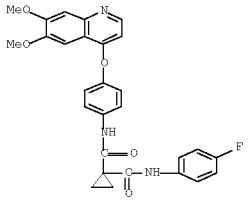
LANGUAGE: English

AB A review. High-grade undifferentiated sarcomas (HGUS) are rare malignancies accounting for 6 % of all uterine sarcomas and have a very poor outcome. Histol. classification of HGUS is currently debated as a subgroup with uniform nucleoli, and frequently YWHAE-FAM22 transcript has been described, constituting a potential target for new therapies. In localized HGUS, surgery involving total hysterectomy and bilateral oophorectomy is recommended. Adjuvant radiotherapy has recently been suggested in a retrospective study to decrease local recurrence and improve survival vs. observation in localized HGUS. In metastatic or recurrent disease, chemotherapy with doxorubicin with or without ifosfamide constitutes the standard of care. Gemcitabine plus docetaxel also seems to be an interesting alternative. Targeted therapies such as pazopanib are now available for soft tissue sarcomas and so could be proposed for uterine sarcoma patients after first- or second-line chemotherapy in the metastatic phase. Further investigations are needed to determine their indications and targets. A European Organization for Research and Treatment of Cancer (EORTC) randomized trial testing maintenance therapy with cabozantinib after first-line chemotherapy in HGUS is ongoing.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-Grade Undifferentiated Sarcomas of the Uterus: Diagnosis, Outcomes, and New Treatment Approaches)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 338 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:1390694 CAPLUS Full-text

DOCUMENT NUMBER: 161:375913

TITLE: Preparation of pyrazolopyridine compounds as protein kinase modulators useful for treatment of hyperproliferative disorders

INVENTOR(S): Xi, Ning

PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC

SOURCE: U.S. Pat. Appl. Publ., 41pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

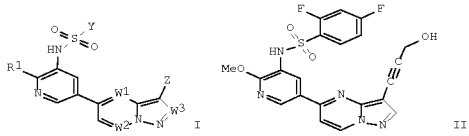
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140234254	A1	20140821	US 2014-14181670	20140215
US 9573953	B2	20170221		
CA 2898294	A1	20140828	CA 2014-2898294	20140215
WO 2014130375	A1	20140828	WO 2014-US16643	20140215
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2014219256	A1	20150730	AU 2014-219256	20140215
AU 2014219256	B2	20170216		
KR 2015118102	A	20151021	KR 2015-7019069	20140215

EP 2958564	A1	20151230	EP 2014-754663		20140215
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
JP 2016509056	T	20160324	JP 2015-558892		20140215
ZA 2015005085	A	20161221	ZA 2015-5085		20140215
MX 2015010700	A	20170123	MX 2015-10700		20150817
IN 2015CN05660	A	20160701	IN 2015-CN5660		20150916
PRIORITY APPLN. INFO.:			US 2013-61767721	P	20130221
			WO 2014-US16643	W	20140215

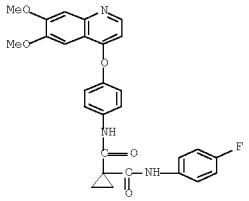
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:375913; MARPAT 161:375913
GI



AB The invention provides heteroarom. derivs. and pharmaceutically acceptable salts and formulations thereof useful in modulating the protein kinase activity, especially phosphatidylinositol 3-kinases (PI3K) and mammalian target of rapamycin (mTOR), and in modulating inter- and/or intra-cellular signaling activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Compds. of formula I [wherein W1, W2, and W3 are independently N or CRc; Z is D, CN, N3, etc.; Y is Cl-6 alkyl, C3-6 cycloalkyl, C3-C6 heterocyclyl, etc.; R1 is H, Cl, C3-6 cycloalkyl, etc.; each Rc is independently H, D, F, etc.] or stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, prodrugs, or pharmaceutically acceptable salts thereof are claimed and exemplified. Example compound II was prepared in seven steps (procedure given). Candidate compds. of I were assayed for their stability in liver microsomes, their oral and i.v. bioavailability, and inhibitory activity against PI3K and mTOR kinase (data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyrazolopyridine compds. as protein kinase modulators useful for treatment of hyperproliferative disorders)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 339 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER:	2014:1389525 CAPLUS Full-text
DOCUMENT NUMBER:	161:379820
TITLE:	Efflux inhibitor compositions containing effect transporter protein inhibitors
INVENTOR(S):	Bunt, Antonius Martinus Gustave; Tellingen, Olaf Van
PATENT ASSIGNEE(S):	Izumi Biosciences LLC, USA; The Netherlands Cancer Institute
SOURCE:	U.S. Pat. Appl. Publ., 33pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

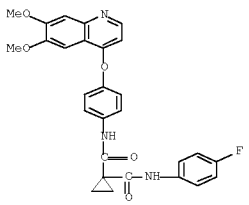
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140235631	A1	20140821	US 2013-13952476	20130726
PRIORITY APPLN. INFO.:			US 2013-61767689 P	20130221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to efflux inhibitor compns. and methods of using these agents for treating conditions where the activity of efflux transporter proteins (e.g., Breast Cancer Resistance Protein (BCRP) and P-Glycoprotein (P-GP)) inhibit effective delivery of a therapeutic agent to a target tissue (e.g., brain, spinal cord, nerves, cerebrospinal fluid, testis, eyeballs, retina, inner ear, placenta, mammary gland, liver, biliary tract, kidney, intestines, lung, adrenal cortex, endometrium, hematopoietic cells, and/or stem cells). E.g., elacridar nanoparticles were prepared

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kinase inhibitor; efflux inhibitor pharmaceuticals containing effect transporter protein inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 340 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER:	2014:1348855 CAPLUS Full-text
DOCUMENT NUMBER:	161:346659
TITLE:	Drug selection for non-small cell lung cancer therapy
INVENTOR(S):	Singh, Sharat; Kim, Phillip
PATENT ASSIGNEE(S):	Nestec S.A., Switz.
SOURCE:	PCT Int. Appl., 77pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014122582	A1	20140814	WO 2014-IB58790	20140204
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2954068	A1	20151216	EP 2014-706699	20140204
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20160032403	A1	20160204	US 2015-14812979	20150729
PRIORITY APPLN. INFO.:			US 2013-61761105 P	20130205
			WO 2014-IB58790 W	20140204

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

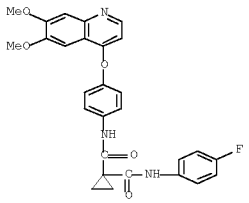
AB The invention provides methods for therapy selection for a patient with non-small cell lung cancer (NSCLC) based on detecting, quantifying, and comparing the activity of particular signal transduction pathways, and components thereof, which can be represented as the patient's analyte index (e.g., EGFR/cMET index) and can be used to determine whether the patient is likely to respond to a particular therapy such as EGFR inhibitor therapy alone, cMET inhibitor therapy alone, or a combination thereof. The EGFR inhibitor is selected from the group consisting of cetuximab, panitumumab, matuzumab, nimotuzumab, Erbl vaccine, erlotinib, gefitinib, CL-387785 and a combination thereof, wherein the c-MET inhibitor is selected from the group consisting of ARQ197, XL184, GSK1363089/XL880, MP470, MGCD265, SGX523, PF04217903, JNJ38877605, INCB28060, AMG-458, E7050, MK-2461, BMS-777607 and a combination thereof. The invention also provides methods for determining drug resistance in non-small cell lung cancer (NSCLC) patients receiving above mentioned therapy.

IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for non-small cell lung cancer therapy)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

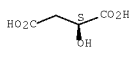
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 341 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1339983 CAPLUS Full-text
DOCUMENT NUMBER: 161:329247
TITLE: Improved treatment for adenoid cystic carcinoma comprising growth factor receptor kinase and MET kinase inhibitors
INVENTOR(S): Stenman, Goeran; Andersson, Mattias
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 116pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014123476	A1	20140814	WO 2014-SE50140	20140204

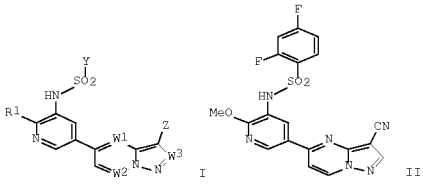
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2013-61849920 P 20130205

AB The present application relates to inhibitors of epidermal growth factor receptor (EGFR) kinase, MET kinase, insulin receptor (IR) kinase and insulin-like growth factor 1 (IGF1R) kinase for use in the treatment of neoplastic disease such as adenoid cystic carcinoma (ACC) and dermal cylindroma characterized by MYB activation. In an optional embodiment, the kinase inhibitor inhibits the MET kinase and the EGFR kinase and/or the IGF1R/IR kinase. In an optional embodiment, the kinase inhibitor is BMS-754807. In an optional embodiment, the IGF1R/IR kinase inhibitor is selected from a group consisting of linsitinib and BMS-754807. In an optional embodiment, the EGFR kinase inhibitor is selected from a group consisting of gefitinib, erlotinib, BMS-690514 and cetuximab. In an optional embodiment, the MET kinase inhibitor is selected from a group consisting of crizotinib, BMS-907351, BMS-777607 and BMS-754807.

IT 849217-68-1, BMS 907351
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BMS 907351; improved treatment for adenoid cystic carcinoma comprising growth factor receptor kinase and MET kinase inhibitors)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



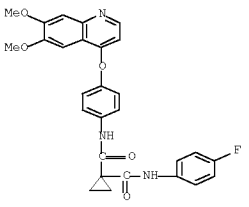
I

II

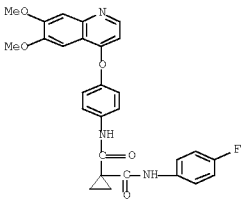
AB The present invention discloses aryl-heterocyclic compd. (with structure as shown in formula I), stereo isomers, geometrical isomers, tautomers, oxynitride, hydrates, solvates, metabolic products, pharmaceutically acceptable salts or prodrugs, pharmaceutical compns. containing thereof and application thereof in preparing agents for inhibiting or regulating the activity of protein kinases in biol. specimens. For example, compound II was prepared in a multi-step synthesis. The present invention also relates to pharmaceutical compns. containing the inventive compound, and application of the pharmaceutical compns. for treating mammal, particular human hyperproliferative disorders.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of aryl-heterocyclic compds. for treatment of hyperproliferative disorders)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 343 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1273412 CAPLUS Full-text
DOCUMENT NUMBER: 162:67014



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 342 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1274352 CAPLUS Full-text
DOCUMENT NUMBER: 161:361023
TITLE: Preparation of aryl-heterocyclic compounds for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 59pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CN 103965199	A	20140806	CN 2014-10041929		20140128
PRIORITY APPLN. INFO.:			CN 2013-10040391	A	20130202
			CN 2013-10117077	A	20130404

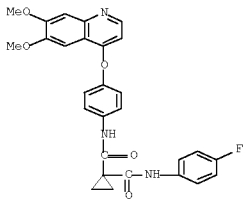
OTHER SOURCE(S): CASREACT 161:361023; MARPAT 161:361023
GI

TITLE: Development of cabozantinib for the treatment of prostate cancer
AUTHOR(S): Vaishampayan, Ulka N.
CORPORATE SOURCE: Department of Oncology, Wayne State University/Karmanos Cancer Institute, Detroit, MI, USA
SOURCE: Core Evidence (2014), 9, 61-67, 7 pp.
CODEN: CEOVAF; ISSN: 1555-1741
DIGITAL OBJECT ID: 10.2147/CE.S67095
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib (XL184) is a multitargeted receptor tyrosine kinase with predominantly MET and vascular endothelial growth factor inhibition properties. It is currently approved by the US Food and Drug Administration for the treatment of progressive metastatic medullary thyroid cancer. The agent has a convenient once-daily oral dosing schedule and has demonstrated encouraging activity in metastatic castrate-resistant prostate cancer (CRPC). A Phase I/II trial demonstrated responses in soft tissue, visceral disease, and bone metastases in CRPC. An objective response rate of 5%, a stable disease rate of 75%, and a median progression-free survival of 6 mo was observed As compared with the 140 mg daily dose used in thyroid cancer, a lower dose of 60 mg daily is currently being utilized in prostate cancer studies due to the fact that toxicity could be reduced without compromising efficacy. Randomized trials are ongoing in comparison with prednisone or with mitoxantrone and prednisone in pretreated metastatic CRPC. Cabozantinib has demonstrated a unique mechanism of action and preliminary efficacy in the crowded therapeutic field of prostate cancer. Since multiple therapies have recently demonstrated overall survival benefit in metastatic CRPC, cabozantinib will likely face some challenges in clin. application. At present, in this rapidly evolving field, it is unclear what proportion of patients with prostate cancer will be eligible to receive this therapy. The cost of cabozantinib is likely to be another deterrent, especially if it remains more expensive than other oral therapies, such as abiraterone and enzalutamide. Defining the role of MET overexpression and RET mutations as biomarkers in prostate cancer may help to guide patient selection, and enrich and enhance the future applications of this targeted novel agent.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of cabozantinib for treatment of prostate cancer in patients)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



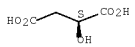
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 344 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1270460 CAPLUS Full-text
DOCUMENT NUMBER: 161:351479
TITLE: Degradation kinetics study of cabozantinib by a novel stability-indicating LC method and identification of its major degradation products by LC/TOF-MS and LC-MS/MS
AUTHOR(S): Wu, Chunyong; Xu, Xue; Feng, Chao; Shi, Yuanyuan; Liu, Wenyuan; Zhu, Xiaoyun; Zhang, Junying
CORPORATE SOURCE: Key Laboratory of Drug Quality Control and Pharmacovigilance, Ministry of Education, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2014), 98, 356-363
CODEN: JPBADA; ISSN: 0731-7085
DIGITAL OBJECT ID: 10.1016/j.jpba.2014.06.008
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The chem. stability of cabozantinib (CBZ) was investigated using a novel stability-indicating LC method. Forced degradation of CBZ was carried out under acidic, basic, thermal, oxidative and photolytic stress conditions. Hydrolysis and oxidation were the primary pathways for this compound and three major unknown degradation products were characterized by LC/TOF-MS and LC-MS/MS. The major oxidative degradation product was isolated by preparative LC and identified by UV, HRMS and NMR techniques to be N-{4-[(N-oxide-6,7-dimethoxyquinolin-4-yl)oxy]phenyl}-N'-(4-fluorophenyl)- cyclopropane-1,1-dicarboxamide. The developed method was validated as per ICH guidelines and then successfully applied to investigate the degradation kinetics of CBZ. Degradation of CBZ followed first-order kinetics under all exptl. conditions. A V-shaped pH-rate profile over the pH range 2-10 was observed with maximum stability at pH 6. The effect of temperature on the rate of CBZ degradation was characterized using the Arrhenius equation. The activation energy for hydrolysis was 57.31 kJ mol-1 in alkaline solution
IT 849217-68-1, Cabozantinib 1140909-48-3, Cabozantinib

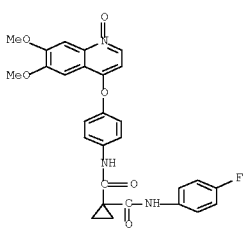
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

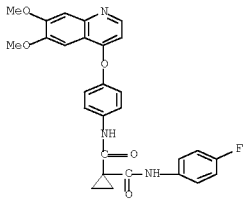


IT 1621681-63-7
RL: ANT (Analyte); FMU (Formation, unclassified); PRP (Properties); ANST (Analytical study); FORM (Formation, nonpreparative)
(degradation kinetics study of cabozantinib by novel stability-indicating LC method and identification of major degradation products by LC/TOF-MS and LC-MS/MS)
RN 1621681-63-7 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N-[4-[(6,7-dimethoxy-1-oxido-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

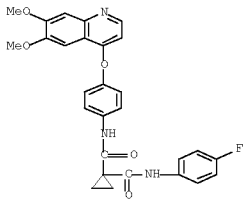
L4 ANSWER 345 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1237165 CAPLUS Full-text
DOCUMENT NUMBER: 162:55826
TITLE: Recent orphan drugs that are first-in-class
AUTHOR(S): Phillips, M. Ian; Lee, Jongserk R.
CORPORATE SOURCE: Keck Graduate Institute, Center for Rare Disease Therapies, 535 Watson Drive, Claremont, CA, 91711, USA
SOURCE: Expert Opinion on Orphan Drugs (2014), 2(8), 759-763
(S)-Malate
RL: AMX (Analytical matrix); PEP (Physical, engineering or chemical process); PRP (Properties); ANST (Analytical study); PROC (Process)
(degradation kinetics study of cabozantinib by novel stability-indicating LC method and identification of major degradation products by LC/TOF-MS and LC-MS/MS)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

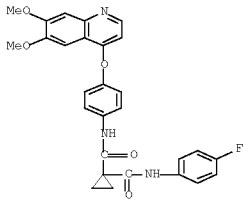
CRN 849217-68-1
CMF C28 H24 F N3 O5



CODEN: EOODAJ; ISSN: 2167-8707
DIGITAL OBJECT ID: 10.1517/21678707.2014.931806
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Although the pipeline for new drugs seemed to be drying up, the number of new 'first-in-class' drugs appeared to be increasing. First-in-class drugs are those which use a new and unique mechanism for treating a disease or medical condition. They are a subset of new mol. entities (NMEs). The FDA reports that in 2012, 39 NMEs were approved. Twenty of these NMEs (.apprx. 50%) were identified by the FDA as first-in-class drugs. Of the 39 NMEs, 13 were designated orphan drugs and 9 of those orphan drugs were first-in-class. In 2013, there were 27 NMEs of which 9 were first-in-class. In 2013, nos. of NMEs are lower than the 2011 or 2012 but are based on fewer applications than in those years. There were 33% of NMEs that were first-in-class and 33% of the NMEs were orphan drugs. The FDA data indicate that creative new products are being developed for rare diseases.
IT 1140909-48-3, Cometriq
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(movement toward first-in-class drugs, indicating more innovation in drug discovery and utilizing orphan drugs)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

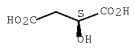
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



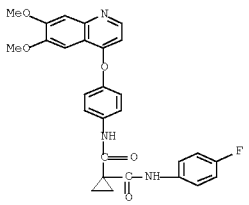
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 346 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1222486 CAPLUS Full-text
DOCUMENT NUMBER: 161:744871
TITLE: Cabozantinib-Induced Thyroid Dysfunction: A Review of Two Ongoing Trials for Metastatic Bladder Cancer and Sarcoma
AUTHOR(S): Yavuz, Sahzene; Apolo, Andrea B.; Kummar, Shivaani; del Rivero, Jaydira; Madan, Ravi A.; Shawker, Thomas; Reynolds, James; Celi, Francesco S.
CORPORATE SOURCE: National Institute of Diabetes and Digestive and Kidney Diseases, Diabetes, Endocrine, and Obesity Branch, National Institutes of Health, Bethesda, MD, USA
SOURCE: Thyroid (2014), 24(8), 1223-1231
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2013.0621
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Background: Thyroid dysfunction is a common adverse event associated with tyrosine kinase inhibitors (TKI), but its underlying pathophysiol. is unclear. Cabozantinib is a novel TKI currently Food and Drug Administration approved for advanced medullary thyroid cancer and tested in clin. trials on solid tumors including prostate, liver, bladder, breast, and ovarian cancer. Methods: We analyzed the thyroid function of patients enrolled in two phase 2 clin. trials using cabozantinib at the National Institutes of Health Clin. Center. Two cases of thyroiditis associated with cabozantinib therapy are presented in detail, and a systematic review of the literature on TKI-associated thyroid dysfunction is also discussed. Results: Between Sept. 2012 and Sept. 2013, 33 patients were treated with cabozantinib, and follow-up thyroid function tests were available for 31 (20 males, 11 females; age 59±1 years). Thyroid dysfunction was recorded in the majority of patients (93.1%), with a predominance of subclin. hypothyroidism. Two cases showed a biphasic pattern of thyroid dysfunction characterized by a transient thyrotoxicosis followed by hypothyroidism. Color Doppler demonstrated an increase in vascularization during the thyrotoxic phase, but no uptake was visualized on nuclear medicine imaging. A systematic review of the literature resulted in the identification of 40 original manuscripts, of which 13 were case series and 6 were case reports describing TKI-associated thyroid dysfunction. Conclusion: TKI therapy often results in clin. significant thyroid dysfunction. Cabozantinib treatment commonly results in thyroid dysfunction varying from subclin. hypothyroidism to symptomatic thyrotoxicosis. Early detection and characterization of cabozantinib-associated thyroid dysfunction and close follow-up are essential to provide adequate management of this common adverse event.

stabilization (i.e. a complete or partial response, or stable disease). The overall survival benefit with cabozantinib is as yet unclear, with no significant benefit observed in two interim analyses (one prespecified, and one unplanned and conducted at the request of the US FDA). The tolerability profile of oral cabozantinib is typical for a small mol. targeting the VEGFR and other tyrosine kinase-mediated pathways, with adverse events associated with the inhibition of the VEGF pathway (e.g. gastrointestinal perforation, hemorrhage, hypertension and venous thrombosis) reported in the phase III study. Treatment-emergent adverse events were generally managed with supportive therapy, dose redns. and/or dose interruptions. Although final overall survival data are awaited, current evidence suggests cabozantinib to be a valuable treatment option for adults with progressive, unresectable locally advanced or metastatic MTC.
IT 1140909-48-3, Cometriq
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cabozantinib in patients with medullary thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

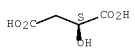
CRN 849217-68-1
CMF C28 H24 F N3 O5



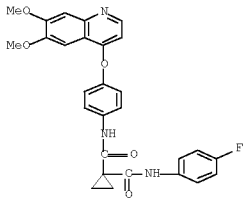
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(review of two ongoing trials for metastatic bladder cancer and sarcoma and cabozantinib-induced thyroid dysfunction)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 347 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1212244 CAPLUS Full-text
DOCUMENT NUMBER: 161:731791
TITLE: Cabozantinib: A Review of Its Use in Patients with Medullary Thyroid Cancer
AUTHOR(S): Hoy, Sheridan M.
CORPORATE SOURCE: Springer, Auckland, N. Z.
SOURCE: Drugs (2014), 74(12), 1435-1444
CODEN: DRUGAY; ISSN: 0012-6667
DIGITAL OBJECT ID: 10.1007/s40265-014-0265-x
PUBLISHER: Springer International Publishing AG
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (Cometriq) is an orally administered small mol. inhibitor of multiple tyrosine kinase receptors, including those involved in the pathogenesis of medullary thyroid cancer (MTC) [i.e. rearranged during transfection (RET), MET and vascular endothelial growth factor receptor (VEGFR)-2]. Cabozantinib is indicated for the treatment of adults with progressive, unresectable locally advanced (in the EU) or metastatic (in the EU and USA) MTC. Compared with placebo, cabozantinib significantly prolonged progression-free survival, reflecting a 72 % reduction in the risk of disease progression or death, in patients with unresectable, locally advanced or metastatic MTC participating in a multinational, phase III study. A significantly higher proportion of patients receiving cabozantinib than those receiving placebo achieved an objective response or disease

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 348 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1205266 CAPLUS Full-text
DOCUMENT NUMBER: 161:269288
TITLE: Hydrogen-bond surrogate peptides and peptidomimetics for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer
INVENTOR(S): Arora, Paramjit S.; Pan, Quintin; Mapp, Anna
PATENT ASSIGNEE(S): New York University, USA; The Ohio State University Research Foundation; University of Michigan
SOURCE: PCT Int. Appl., 98pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014113792	A1	20140724	WO 2014-US12331	20140121
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20140205681	A1	20140724	US 2014-14160018	20140121
US 20140220159	A1	20140807	US 2014-14160001	20140121
US 9605026	B2	20170328		
EP 2964245	A1	20160113	EP 2014-740418	20140121
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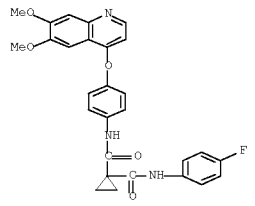
PRIORITY APPLN. INFO.: US 2013-61754574 P 20130119
US 2013-61874190 P 20130905
WO 2014-US12331 W 20140121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 161:269288
AB The present invention relates to peptidomimetics for reactivating p53. Methods of using the peptidomimetics are also disclosed. One aspect of the present invention relates to a peptidomimetic, where the peptidomimetic mimics a helix having the formula X1-X2-X2-X3-X2-X2-X1-X4, wherein each X1 is any neg. charged residue, each X2 is any hydrophobic residue, X3 is any pos.-charged residue, and X4 is any polar residue. Addnl., the peptidomimetic

may contain one or more bridges linking the side chains of its component amino acids. Another aspect of the present invention relates to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, the method comprising administering to the subject a peptidomimetic of the present invention under conditions effective to treat or prevent the disorder. Another aspect of the present invention relates to a method of inducing apoptosis and decreasing survival and/or proliferation of a cell, the method comprising contacting the cell with a peptidomimetic. In this study, the authors took a novel approach and functionally reactivated p53 in Human papillomaviruses (HPV)-pos. head and neck squamous cell carcinoma (HNSCC) by blocking the interaction between E6 and p300. Ectopic expression of the CH1 domain of p300 squelched E6 to disrupt E6-p300 association resulting in an increase in p53 acetylation, accumulation, and activity. CH1 domain inhibitors reactivated p53 and dramatically potentiated the efficacy of cisplatinum in HPV-pos. HNSCC. Taken together, the authors work revealed a novel druggable approach to reactivate p53 in HPV-pos. HNSCC that is expected to translate to other HPV-pos. carcinomas.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidomimetics for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer and combination with other agents)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

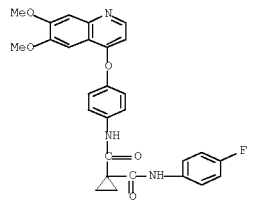
L4 ANSWER 349 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1202788 CAPLUS Full-text
DOCUMENT NUMBER: 161:269285
TITLE: Oligooxopiperazines for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer
INVENTOR(S): Arora, Paramjit S.; Pan, Quintin; Mapp, Anna
PATENT ASSIGNEE(S): New York University, USA; The Ohio State University

Taken together, the authors work revealed a novel druggable approach to reactivate p53 in HPV-pos. HNSCC that is expected to translate to other HPV-pos. carcinomas. HMD: helix αB of C-terminal transactivation domain, of HIF-1α, mimics.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligooxopiperazines for p53 reactivation by inhibiting interaction of E6 with CREB-binding protein and/or p300 to treat HPV-associated cancer and combination with other agents)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 350 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1160177 CAPLUS Full-text
DOCUMENT NUMBER: 161:239766
TITLE: Androgen receptor modulator for treatment of prostate cancer and other conditions
INVENTOR(S): Chen, Isan; Hager, Jeffrey H.; Maneval, Edna Chow; Herbert, Mark R.; Smith, Nicholas D.
PATENT ASSIGNEE(S): Aragon Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 46pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

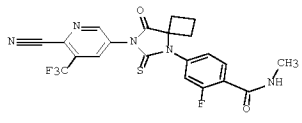
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140199236	A1	20140717	US 2014-14151106	20140109
US 9340524	B2	20160517		
CA 2898025	A1	20140724	CA 2014-2898025	20140109
WO 2014113260	A1	20140724	WO 2014-US10777	20140109
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2898329	A1	20140724	CA 2014-2898329	20140121
US 20140205655	A1	20140724	US 2014-14160037	20140121
AU 2014207311	A1	20150820	AU 2014-207311	20140121
EP 2945631	A2	20151125	EP 2014-741084	20140121
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 105246481	A	20160113	CN 2014-80010794	20140121
JP 2016510327	T	20160407	JP 2015-553892	20140121
IN 2015CN04978	A	20160701	IN 2015-CN4978	20150817

PRIORITY APPLN. INFO.: US 2013-61754575 P 20130119
WO 2014-US12337 W 20140121
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:269285; MARPAT 161:269285

AB The present invention relates to oligooxopiperazines for reactivating p53. Methods of using the oligooxopiperazines are also disclosed. A first aspect of the present invention relates to a method of treating or preventing in a subject a disorder mediated by interaction of E6 with CREB-binding protein and/or p300, the method comprising administering to the subject an oligooxopiperazine that substantially mimics helix αB of the C-terminal transactivation domain of Hypoxia-Inducible Factor Iα under conditions effective to treat or prevent the disorder. A second aspect of the present invention relates to a method of inducing apoptosis or decreasing survival and/or proliferation of a cell, the method comprising contacting the cell with an oligooxopiperazine. In this study, the authors took a novel approach and functionally reactivated p53 in Human papillomaviruses (HPV)-pos. head and neck squamous cell carcinoma (HNSCC) by blocking the interaction between E6 and p300. Ectopic expression of the CH1 domain of p300 squelched E6 to disrupt E6-p300 association resulting in an increase in p53 acetylation, accumulation, and activity. CH1 domain inhibitors reactivated p53 and dramatically potentiated the efficacy of cisplatinum in HPV-pos. HNSCC.

			MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW	
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AU 2014207839	A1	20150723	AU 2014-207839	20140109
IL 239741	A	20150831	IL 2014-239741	20140109
KR 2015105464	A	20150916	KR 2015-7021865	20140109
CN 105007920	A	20151028	CN 2014-80015802	20140109
EP 2945628	A1	20151125	EP 2014-701865	20140109
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JP 2016508991	T	20160324	JP 2015-552756	20140109
AR 94654	A1	20150819	AR 2014-100116	20140113
IN 2015DN05950	A	20160831	IN 2015-DN5950	20150707
CR 20150357	A	20150824	CR 2015-357	20150708
MX 2015009090	A	20151005	MX 2015-9090	20150714
US 20160220548	A1	20160804	US 2016-15094113	20160408

PRIORITY APPLN. INFO.: US 2013-61752842 P 20130115
US 2014-14151106 A1 20140109
WO 2014-US10777 W 20140109
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
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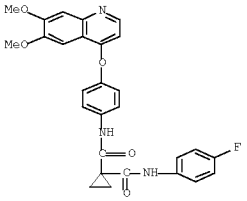
I

AB The invention discloses the androgen receptor modulator I for the treatment of prostate cancer in combination with other therapeutic options and for the treatment of diseases or conditions that are amenable to treatment with the androgen receptor modulator, as well as pharmaceutical compns. and medicaments that include I.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androgen receptor modulator for treatment of prostate cancer and other conditions)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L4 ANSWER 351 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1154296 CAPLUS Full-text
DOCUMENT NUMBER: 161:209516
TITLE: Predictive biomarker and method for combination therapy of EGFR and c-MET inhibitors in non-small cell lung cancer with wild type EGFR
INVENTOR(S): Lee, Mun Ja; Kim, Hyeon Jeong; Kang, Han Na
PATENT ASSIGNEE(S): JEUK Co., Ltd., S. Korea
SOURCE: Repub. Korea, 20pp.
CODEN: KRXXFC
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

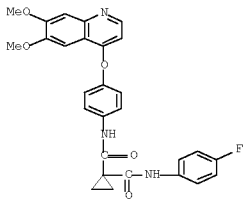
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 1418970	B1	20140711	KR 2013-29977	20130320

PRIORITY APPLN. INFO.: KR 2013-29977 20130320

AB The title method comprises the steps of: detg. the p53 genotypes of patients, separating out the patients having cooperation tumor effect probability of combination therapy according to EGFR and c-MET inhibitors. Therefore, the condition of p53 can be used as predicative factor for combination therapy of EGFR and c-MET inhibitors.

IT 849217-68-1, Cabozantinib, co-use with EGFR inhibitors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MET inhibitor; predictive biomarker and method for combination therapy of EGFR and c-MET inhibitors in non-small cell lung cancer with wild type EGFR)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 352 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1134083 CAPLUS Full-text
DOCUMENT NUMBER: 162:254986
TITLE: A Melanoma Cell State Distinction Influences Sensitivity to MAPK Pathway Inhibitors
AUTHOR(S): Konieczkowski, David J.; Johannessen, Cory M.; Abudayyeh, Omar; Kim, Jong Wook; Cooper, Zachary A.; Piris, Adriano; Frederick, Dennie T.; Barzily-Rokni, Michal; Straussman, Ravid; Haq, Rizwan; Fisher, David E.; Mesirov, Jill P.; Hahn, William C.; Flaherty, Keith T.; Wargo, Jennifer A.; Tamayo, Pablo; Garraway, Levi A.
CORPORATE SOURCE: Broad Institute of Harvard and MIT, Cambridge, MA, USA
SOURCE: Cancer Discovery (2014), 4(7), 816-827
CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID: 10.1158/2159-8290.CD-13-0424
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

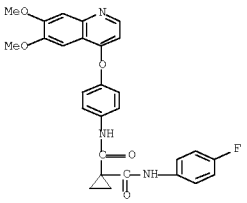
AB Most melanomas harbor oncogenic BRAFv600 mutations, which constitutively activate the MAPK pathway. Although MAPK pathway inhibitors show clin. benefit in BRAFV600-mutant melanoma, it remains incompletely understood why 10% to 20% of patients fail to respond. Here, we show that RAF inhibitor-sensitive and inhibitor-resistant BRAFv600-mutant melanomas display distinct transcriptional profiles. Whereas most drug-sensitive cell lines and patient biopsies showed high expression and activity of the melanocytic lineage transcription factor MITF, intrinsically resistant cell lines and biopsies displayed low MITF expression but higher levels of NF-κ signaling and the receptor tyrosine kinase AXL. In vitro, these MITF-low/NF-κβ-high melanomas were resistant to inhibition of RAF and MEK singly or in combination, and ERK. Moreover, in cell lines, NF- activation antagonized MITF expression and induced both resistance marker genes and drug resistance. Thus, distinct cell states characterized by MITF or NF-κβ activity may influence intrinsic resistance to MAPK pathway inhibitors in BRAFv600-mutant melanoma.

IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RAF inhibitor resistant human melanoma cells carrying mutant BRAF showed low MITF and high NFκB levels which influence intrinsic resistance to MAPK pathway inhibitors)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

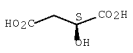
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



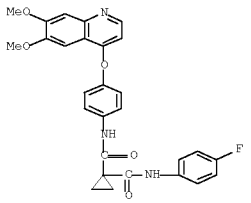
OS.CITING REF COUNT: 60 THERE ARE 60 CAPLUS RECORDS THAT CITE THIS RECORD (60 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 353 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1064742 CAPLUS Full-text
DOCUMENT NUMBER: 161:455975
TITLE: A targeted next-generation sequencing assay detects a high frequency of therapeutically targetable alterations in primary and metastatic breast cancers: implications for clinical practice
AUTHOR(S): Vasan, Neil; Yelensky, Roman; Wang, Kai; Moulder, Stacy; Dzimitrowicz, Hannah; Avritscher, Rony; Wang, Bauang; Wu, Yun; Cronin, Maureen T.; Palmer, Gary; Symmans, W. Fraser; Miller, Vincent A.; Stephens, Phiup; Pusztai, Lajos
CORPORATE SOURCE: Yale University School of Medicine, Connecticut, New Haven, USA
SOURCE: Oncologist (2014), 19(5), 453-458
CODEN: OCOLF6; ISSN: 1083-7159
DIGITAL OBJECT ID: 10.1634/theoncologist.2013-0377
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background. The aim of this study was to assess the frequency of potentially actionable genomic alterations in breast cancer that could be targeted with approved agents or investigational drugs in clin. trials using a next-generation sequencing-based genomic profiling assay performed in a Clin. Laboratory Improvement Amendments-certified and College of American Pathologists-accredited com. laboratory Methods. Fifty-one breast cancers were analyzed, including primary tumor biopsies of 33 stage I–II and 18 stage IV cancers (13 soft tissue, 3 liver, and 2 bone metastases). We assessed 3,230 exons in 182 cancer-related genes and 37 introns in 14 genes often rearranged in cancer for base substitutions, indels, copy number alterations, and gene fusions. The average median sequencing depth was 1,154×. Results. We observed 158 genomic alterations in 55 genes in 48 of 51 (94%) tumors (mean 3.1, range 0–9). The average number of potentially therapeutically relevant alterations was similar in primary (1.6, range 0–4) and in heavily pretreated metastatic cancers (2.0, range 0–4) (p = .24). The most common actionable alterations were in PIK3CA (n = 9, phosphatidylinositol 3-kinase [PI3K]/mammalian target of rapamycin [mTOR] inhibitors), NF1 (n = 7, PI3K/mTOR/mitogen-activated protein kinase inhibitors), v-akt murine thymoma viral oncogene homolog 1–3 (n = 7, PI3K/mTOR/AKT inhibitors), BRCA1/2 (n = 6, poly[ADP-ribose] polymerase inhibitors), and CCND1,2 and CCNE (n = 8)/cycline dependent kinase (CDK)6 (n = 1) (CDK4/6 inhibitors), KIT (n = 1, imatinib/sunitinib), ALK (n = 1, crizotinib), FGFR1,2 (n = 5, fibroblast growth factor receptor inhibitors), and EGFR (n = 2, epidermal growth factor receptor inhibitors). Our sequencing assay also correctly identified all six cases with HER2 (ERBB2) amplification by fluorescence in situ hybridization when tumor content was adequate. In addition, two known activating HER2 mutations were identified, both in unamplified cases. Conclusion. Overall, 84% of cancers harbored at least one genomic alteration linked to potential treatment options. Systematic evaluation of the predictive value of these genomic alterations is critically important for further progress in this field.

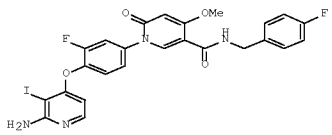
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeted next-generation sequencing assay detects a high frequency of therapeutically targetable alterations in primary and metastatic breast cancers and its implications for clin. practice)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



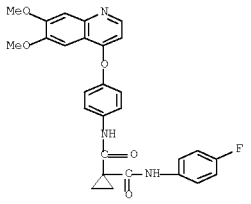
OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 354 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1049484 CAPLUS Full-text
DOCUMENT NUMBER: 161:246290
TITLE: Design, synthesis and evaluation of highly selective pyridone-based class II MET inhibitors
AUTHOR(S): She, Nengfang; Zhuo, Linsheng; Jiang, Wen; Zhu, Xiaolei; Wang, Jia; Ming, Zhihui; Zhao, Xinge; Cong, Xin; Huang, Wei
CORPORATE SOURCE: Key Laboratory of Pesticide and Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Wuhan, 430079, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2014), 24(15), 3351-3355
CODEN: BMCLE8; ISSN: 0960-894X
DIGITAL OBJECT ID: 10.1016/j.bmcl.2014.05.097
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 161:246290
GI



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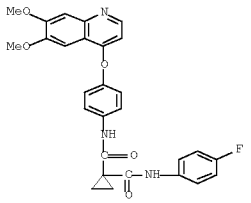
DIGITAL OBJECT ID: 10.1007/s12032-014-0049-x
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Since chemotherapy has been shown to be unsuccessful in case of advanced thyroid carcinomas, the research for new therapies is fundamental. Clin. trials of many tyrosine kinase inhibitors as well as anti-angiogenic inhibitors suggest that patients with thyroid cancer could have an advantage with new target therapy. Recently, Food and Drug Administration approved two targeted therapies, vandetanib and cabozantinib for the treatment of metastatic thyroid carcinomas with acceptable outcome. We summarized the results and the toxic effects associated with these treatments reported in clin. trials. Future trials should aim at combinations of targeted agents with or without other treatment modalities to obtain a more effective result in thyroid carcinoma treatment.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new era of treatment for advanced thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

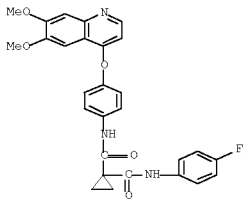
L4 ANSWER 356 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:969861 CAPLUS Full-text
DOCUMENT NUMBER: 161:455940
TITLE: Role of salvage targeted therapy in differentiated thyroid cancer patients who failed first-line sorafenib
AUTHOR(S): Dadu, Ramona; Devine, Catherine; Hernandez, Mike; Waguespack, Steven G.; Busaidy, Naifa L.; Hu, Mimi I.; Jimenez, Camilo; Habra, Mouhammad A.; Sellin, Rena V.; Ying, Anita K.; Cote, Gilbert J.; Sherman, Steven I.; Cabanillas, Maria E.
CORPORATE SOURCE: Departments of Endocrine Neoplasia and Hormonal Disorders, Baylor College of Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2014), 99(6), 2086-2094
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2013-3588
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Context: Sorafenib, a tyrosine kinase inhibitor, is a common first-line therapy for advanced differentiated thyroid cancer (DTC). However, responses are not durable and drug toxicity remains a problem. Objective: The objective of the study was to determine the efficacy of salvage therapy after first-line sorafenib failure. Design: This was a retrospective review at M. D. Anderson Cancer Center from Jan. 2005 to May 2013. Patients: The study included patients with metastatic DTC who received salvage therapy after their initial sorafenib failure (group 2). Patients who received first-line sorafenib only (group 1) were evaluated for comparison of overall survival (OS). Outcome Measures: Progression-free survival, best response, and median OS were measured. Results: Sixty-four patients with metastatic, radioactive iodine refractory DTC were included; 35 were in group 1 and 25 were in group 2, and the groups were well balanced. Median OS of all 64 patients receiving first line sorafenib was 37 mo; median OS was significantly longer with salvage therapy compared with sorafenib alone (58 vs 28 mo, P = .013). In group 2, 17 patients were evaluable for best response, although two patients had toxicity with sorafenib, which was discontinued before restaging. Best responses with first-line sorafenib were partial response in 2 of 15 (13%), stable disease in 10 of 15 (67%), and progressive disease in 3 of 15 (20%) patients. With salvage therapy, partial responses were seen in 7 of 17 (41%) and stable disease in 10 of 17 (59%) patients. Median progression-free survival was 7.4 mo with first-line sorafenib and 11.4 mo with salvage therapy. Salvage therapy included sunitinib (n = 4), pazopanib (n = 3), cabozantinib (n = 4), lenvatinib (n = 3), and vemurafenib (n = 3). Conclusions: Other targeted agents are effective salvage treatments after sorafenib failure, despite similar mechanisms of action, and should be offered to patients who are able to receive salvage therapy.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salvage targeted treatment with sunitinib, pazopanib, cabozantinib, lenvatinib and vemurafenib was effective in treatment of patient with metastatic differentiated thyroid cancer who failed first-line sorafenib therapy)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

AB The high incidence of MET oncogene activation in human malignancies has prompted researchers to develop MET inhibitors. As part of our efforts to developing effective and safe therapeutic agents against MET-dependent tumors, a pyridone-based class II MET inhibitor, namely, 1-(4-((2-amino-3-iodopyridin-4-yl)oxy)-3-fluorophenyl)-N-(4-fluorobenzyl)- 4-methoxy-6-oxo-1,6-dihydropyridine-3-carboxamide (3s, I), was identified. Knowledge of the binding mode of class II MET inhibitors led to the design of new inhibitors that utilize 2-pyridone to conformationally restrain key pharmacophoric groups within the mol. Integrated mol. docking and SAR studies resulted in the discovery of a novel class of pyridone MET inhibitors with high potency (IC50 of 0.005 μM) and efficient selectivity (>5000 fold) to VEGFR-2, c-Kit and RET kinases.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(docking and kinase selectivity study; design, synthesis and evaluation of highly selective pyridone-based class II MET inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 355 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:1006107 CAPLUS Full-text
DOCUMENT NUMBER: 161:238658
TITLE: Advanced thyroid cancers: new era of treatment
AUTHOR(S): Mohammed, Amrallah A.; El-Shentenawy, Ayman
CORPORATE SOURCE: Oncology Center, King Abdullah Medical City-Holy Capital, Makkah, 21995, Saudi Arabia
SOURCE: Medical Oncology (New York, NY, United States) (2014), 31(7), 1-8
CODEN: MONCEZ; ISSN: 1357-0560



OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 357 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:951549 CAPLUS Full-text
DOCUMENT NUMBER: 161:86164
TITLE: Preparation of pyridine compounds as protein tyrosine kinase inhibitors for treatment of proliferative diseases
INVENTOR(S): Xi, Ning; Wang, Ruyong; Wang, Liang
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 158pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

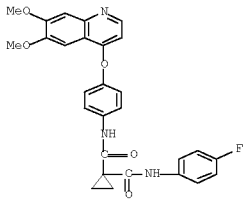
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014089324	A1	20140612	WO 2013-US73367	20131205

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61734903 P 20121207
US 2013-61880184 P 20130920
OTHER SOURCE(S): CASREACT 161:86164; MARPAT 161:86164
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides novel substituted pyridinyl compds. of general formula I, pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. For I, each of R1, R2, R3, R4, R5 and R6 is independently H, D or F; X is C6-C10 aryl or 5-10 membered heteroaryl that are optionally substituted; and Y is an (un)substituted bicyclic heterocyclyl. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Example compound II was prepared in a 6-step reaction that culminated in coupling of intermediates III and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-ol. Example compds. of the invention were tested in ALK and c-Met kinase inhibition assays. Pharmacokinetic profiles were also examined in rats, as was compound stability in human and rat liver microsomes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyridine compds. as protein tyrosine kinase inhibitors for treatment of proliferative diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

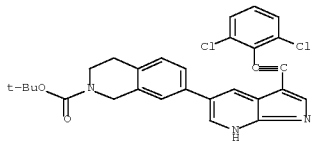
L4 ANSWER 358 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:951212 CAPLUS Full-text
DOCUMENT NUMBER: 161:94410

TITLE: Alkynyl compounds and methods of use
INVENTOR(S): Xi, Ning; Li, Xiaobo; Zhou, Shiqing
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 86pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014089280	A1	20140612	WO 2013-US73286	20131205

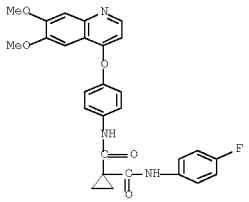
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7 RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61734897 P 20121207
OTHER SOURCE(S): CASREACT 161:94410; MARPAT 161:94410
GI



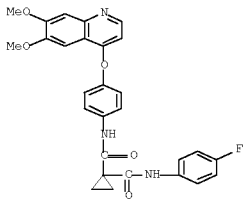
AB The present invention provides novel substituted alkynyl compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkynyl compds. and methods of use)
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 359 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:943695 CAPLUS Full-text
DOCUMENT NUMBER: 161:196584
TITLE: Adverse events of targeted therapies
AUTHOR(S): Klastersky, Jean A.
CORPORATE SOURCE: Institut Jules Bordet, Centre des Tumeurs de l'Universite Libre de Bruxelles, Brussels, Belg.
SOURCE: Current Opinion in Oncology (2014), 26(4), 395-402
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0000000000000096
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Purpose of review: There is currently an explosion in the no. of so-called targeted therapies. As new indications for these agents multiply, there is also an increase of new and less new side-effects. Recent findings: Given this rapidly evolving field, any literature on that topic is rapidly obsolete and needs re-evaluation. Summary: Targeted therapies are associated with a wide spectrum of adverse events, which cannot always be easily separated from the complications linked to cancer, its therapy, and comorbidities. A high awareness of these events might improve the patient's quality of life and contribute to the recognition of new syndromes.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adverse events of targeted therapies)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

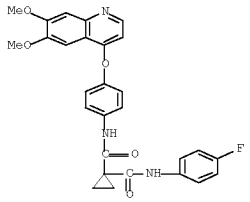


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 360 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:926742 CAPLUS Full-text
DOCUMENT NUMBER: 161:316322
TITLE: Cabozantinib Suppresses Tumor Growth and Metastasis in Hepatocellular Carcinoma by a Dual Blockade of VEGFR2 and MET
AUTHOR(S): Xiang, Qingfeng; Chen, Weiqiang; Ren, Meng; Wang, Jingnan; Zhang, Hongwu; Deng, David Y. B.; Zhang, Lei; Shang, Changzhen; Chen, Yajin
CORPORATE SOURCE: Departments of Hepatopancreatobiliary Surgery, Sun Yat-sen University, Guangzhou, Peop. Rep. China
SOURCE: Clinical Cancer Research (2014), 20(11), 2959-2970
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-2620
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB MET signaling was suggested a potential role in hepatocellular carcinoma (HCC) and associated with prometastasis during antiangiogenesis therapy. We investigated the potential association between MET expression and therapeutic response to sorafenib in patients with HCC. Antitumor effects of cabozantinib, a dual inhibitor of MET and VEGFR2, were examined in cultured HCC cells as well as in vivo models. Total MET and phosphorylated MET (p-MET) were measured in 29 resected HCC specimens, and correlated with response to sorafenib as postoperative adjuvant therapy. In the second set of expts. using cultured HCC cells, and mouse xenograft and metastatic models, effects of cabozantinib were examined High level of p-MET in resected HCC specimens was associated with resistance to adjuvant sorafenib therapy. In cultured HCC cells that expressed p-MET, cabozantinib inhibited the activity of MET and its downstream effectors, leading to G1-phase arrest. Cabozantinib inhibited tumor growth in p-MET-pos. and p-MET-neg. HCC by decreasing angiogenesis, inhibiting proliferation, and promoting apoptosis, but it exhibited more profound efficacy in p-MET-pos. HCC xenografts. Cabozantinib blocked the hepatocyte growth factor (HGF)-stimulated MET pathway and inhibited the migration and invasion of the HCC cells. Notably, cabozantinib reduced the number of metastatic lesions in the lung and liver in the exptl. metastatic mouse model. Patients with HCC with high level of p-MET are associated with resistance to adjuvant sorafenib treatment. The dual blockade of VEGFR2 and MET by cabozantinib has significant antitumor activities in HCC, and the activation of MET in HCC may be a promising efficacy-predicting biomarker. Clin Cancer Res; 20(11); 2959-70. ©2014 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib suppresses tumor growth and metastasis in hepatocellular carcinoma by dual blockade of VEGFR2 and MET)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

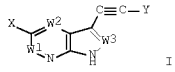


OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

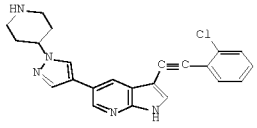
L4 ANSWER 361 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:923002 CAPLUS Full-text
DOCUMENT NUMBER: 161:99226
TITLE: Heterocyclic alkynyl compound, and its use and application as cell proliferation inhibitor and for regulating the activity of protein kinases
INVENTOR(S): Xi, Ning; Li, Xiaobo; Zhou, Shiqing
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China; Jiatuo Sciences Company
SOURCE: Faming Zhuanli Shenqing, 64pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103833753	A	20140604	CN 2013-10590780	20131121
CN 103833753	B	20170201		

PRIORITY APPLN. INFO.: CN 2012-10477798 A 20121122
CN 2013-10116694 A 20130403
OTHER SOURCE(S): MARPAT 161:99226
GI



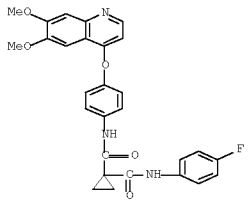
I



II

AB The present invention provides new substituted alkynyl compds. with the formula of I [W1-4 independently = N or CRc, wherein Rc = H, D, F, Cl, Br, etc.; X = Ph, pyridinyl, pyrrolyl, pyrazolyl, etc.; Y = (un)substituted aryl or heteroaryl], pharmaceutically acceptable salts thereof, pharmaceutical formulation thereof, and their use in regulating the activity of protein kinases and regulating the signal response in cells or between cells. Thus, e.g., II was prepared in a multi-step synthesis. Compds. of the invention were tested for their stability and Alk, c-Met kinase inhibitory activity, e.g., II showed IC50 value of 58 nM against Alkaline The present invention also relates to pharmaceutical compns. comprising a compound of the present invention, and using the pharmaceutical composition for treating a mammal, particularly to human hyperproliferative disorders.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; heterocyclic alkynyl compound, and its use and application as cell proliferation inhibitor and for regulating the activity of protein kinases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



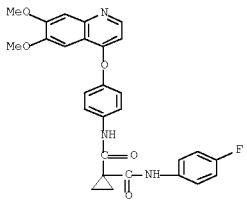
L4 ANSWER 362 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:913474 CAPLUS Full-text
DOCUMENT NUMBER: 161:46548
TITLE: Cabozantinib capsule composition and its production method
INVENTOR(S): Wang, Luanqiu; Wang, Xinyao
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103830203	A	20140604	CN 2014-10078549	20140305

PRIORITY APPLN. INFO.: CN 2014-10078549 20140305

AB The invention provides a cabozantinib capsule compn. and its prodn. method. The cabozantinib capsule composition is composed of cabozantinib 10-60wt%, carrier 15-70 wt%, organic solvent 10-30wt%, surfactant 0.5-3.0wt%, micronized silica gel 1.0-3.0wt% and starch 5.0-20wt%. The carrier comprises one or more of glycerol monostearate, polyethylene glycol 6000, cetyl alc. and octyl alc. The organic solvent comprises one or more of ethanol, methanol and acetone. The surfactant comprises one or more of sodium dodecyl sulfate, Tween 80 and lecithin. The production method includes adding carrier into organic solvent, heating to 60℃, adding cabozantinib and surfactant, vacuum drying at 40℃, comminution by gas stream to obtain powder with grain size of 1-8 μm, adding micronized silica gel and starch, mixing, and packaging in. The produced cabozantinib capsule preparation has good oral absorption, high dissoln. rate, high bioavailability, and can remarkably inhibit the growth of tumor volume The invention has simple preparation process, low cost, and applicability for com. process.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for producing cabozantinib capsule composition)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

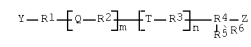


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

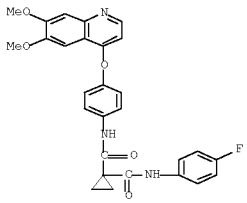
L4 ANSWER 363 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:873778 CAPLUS Full-text
DOCUMENT NUMBER: 161:77594
TITLE: Hydrophilic linkers and their uses for conjugation of drugs to cell binding molecules
INVENTOR(S): Zhao, R. Yongxin
PATENT ASSIGNEE(S): Hangzhou Dac Biotech Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 102pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014080251	A1	20140530	WO 2012-IB56700	20121124
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2891280	A1	20140530	CA 2012-2891280	20121124
AU 2012395148	A1	20150521	AU 2012-395148	20121124
AU 2012395148	B2	20161027		
EP 2922818	A1	20150930	EP 2012-888899	20121124
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2016501859	T	20160121	JP 2015-543532	20121124
CN 105849086	A	20160810	CN 2012-80076481	20121124
US 20150250896	A1	20150910	US 2015-14432073	20150327

PRIORITY APPLN. INFO.: WO 2012-IB56700 W 20121124
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 161:77594; MARPAT 161:77594
GI

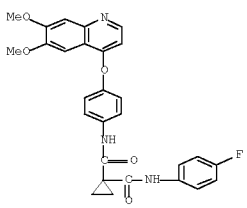


AB Prepn. of cell binding agent-drug conjugates comprising hydrophilic linker of formula (I), wherein:Y represents a functional group that enables reaction with a cell-binding agent; Q and T are either -P(=O)(OM)-, or -S(O)-;m and n are integer from 0 to 5, but not 0 at the same time; In addition, when m = 1, n = 0, Q is not -P(=O)(OM)-; or when n = 1, m = 0, T is not -P(=O)(OM)-;Z represents a functional group that enables linkage of a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ether, ester, carbamate, carbonate, amine (secondary, tertiary, or quartary), imine, cycloheteroalkyane, heteroarom., alkoxime or amide bond; R1, R2, R3, R4, R5 and R6, are the same or different and are H, linear alkyl having from 1-6 carbon atoms, branched or cyclic alkyl having from 3 to 6 carbon atoms, linear, branched or cyclic alkenyl or alkynyl, or 1-6 carbon atoms of esters, ether, amide, or polyethyleneoxy unit of formula (OCH2CH2)p, wherein p is an integer from 0 to about 1000, or combination thereof and methods of using such linkers and conjugates in pharmaceutical dosage forms for combination therapy of cancer, autoimmune and infectious diseases are provided.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(hydrophilic linkers and their uses in preparation of cell binding agent-drug conjugates useful in combination therapy of cancer, autoimmune and infectious diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 364 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:814874 CAPLUS Full-text
DOCUMENT NUMBER: 161:466864
TITLE: Aerodigestive Fistula Formation as a Rare Side Effect of Antiangiogenic Tyrosine Kinase Inhibitor Therapy for Thyroid Cancer
AUTHOR(S): Blevins, Dean P.; Dadu, Ramona; Hu, Mimi; Baik, Christina; Balachandran, Diwakar; Ross, William; Gunn, Brandon; Cabanillas, Maria E.
CORPORATE SOURCE: Department of Internal Medicine, University of Texas Health Science Center at Houston, Houston, TX, USA
SOURCE: Thyroid (2014), 24(5), 918-922
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2012.0598
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: In the past decade, targeted therapy with antiangiogenic drugs has become standard of care for most types of metastatic, progressive thyroid cancer. While these drugs were thought initially to be less toxic than traditional chemotherapy, they can have rare but serious and fatal toxicities. Once such toxicity that has been reported in other tumor types is upper airway fistula formation, which can be life-threatening. Summary: Here, we describe three patients treated with antiangiogenic tyrosine kinase inhibitors at two academic institutions who developed aerodigestive fistula. All three patients had risk factors for fistula formation, which included external beam radiation and/or large tumor with invasion of the tracheal wall. Conclusions: Fistula formation is a known but rare side effect of antiangiogenic tyrosine kinase inhibitors. Knowledge of the risk factors that may predispose thyroid cancer patients to this serious adverse event is vital prior to prescribing antiangiogenics. Particular caution should be observed when using these drugs in patients undergoing radiation therapy or surgery, or in patients whose tumor is invading vital structures of the neck, as they may be at higher risk of developing this rare complication. In these patients, antiangiogenic tyrosine kinase inhibitors should be used cautiously, patients should be aware of the risk, and physicians should monitor patients for symptoms of fistula.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aerodigestive fistula formation as a rare side effect of antiangiogenic tyrosine kinase inhibitor therapy for thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 365 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:794981 CAPLUS Full-text
DOCUMENT NUMBER: 160:740120
TITLE: Preparation of heteroaromatic compounds as protein kinase modulators for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 57pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

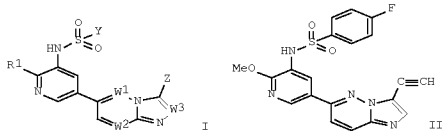
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140134133	A1	20140515	US 2013-14076256	20131110
CA 2889346	A1	20140522	CA 2013-2889346	20131110
WO 2014078211	A1	20140522	WO 2013-US69366	20131110
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR,				

IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

AU 2013345107	A1	20150430	AU 2013-345107		20131110
AU 2013345107	B2	20160225			
CN 104755085	A	20150701	CN 2013-80054625		20131110
KR 2015083833	A	20150720	KR 2015-7008264		20131110
EP 2919784	A1	20150923	EP 2013-855522		20131110
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
JP 2015536994	T	20151224	JP 2015-541973		20131110
ZA 2015002575	A	20161130	ZA 2015-2575		20131110
IN 2015CN03339	A	20160701	IN 2015-CN3339		20150609
PRIORITY APPLN. INFO.:			US 2012-61726139	P	20121114
			WO 2013-US69366	W	20131110

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:740120; MARPAT 160:740120
GI

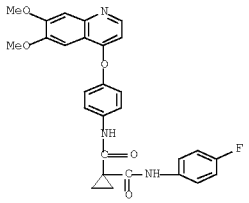


I II

AB The invention provides heteroarom. derivs. and pharmaceutically acceptable salts and formulations thereof useful in modulating the protein kinase activity, especially phosphatidylinositol 3-kinases (PI3K) and mTOR kinase, and in modulating inter- and/or intra-cellular signaling activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Compds. of formula I [wherein W1, W2, and W3 are independently N or CRc; Z is D CN, N3, etc.; Y is C1-C6 alkyl, C3-C6 cycloalkyl, C3-C6 heterocyclyl, etc.; R1 is H, Cl, C3-C6 cycloalkyl, etc.; each Rc is independently H, D, F, etc.] or stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, prodrugs, or pharmaceutically acceptable salts thereof are claimed and exemplified. For example, II was prepared in five steps (procedure given). Candidate compds. of I were assayed for their stability in liver microsomes, their oral and i.v. bioavailability, and inhibitory activity against PI3K and mTOR kinase (data given).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of heteroarom. compds. as protein kinase modulators for treatment of hyperproliferative disorders)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 366 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:718961 CAPLUS Full-text
DOCUMENT NUMBER: 160:630742
TITLE: Replication-competent retroviral vectors for gene therapy using mini-promoters
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Lin, Amy H.; Logg, Christopher R.; Kasahara, Noriyuki
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: PCT Int. Appl., 89pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014066700	A1	20140501	WO 2013-US66709	20131024

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2909324	A1	20150826	EP 2013-849839		20131024
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME					
CN 104884627	A	20150902	CN 2013-80067486		20131024
JP 2015533510	T	20151126	JP 2015-539817		20131024
US 20150273029	A1	20151001	US 2015-14438564		20150424
PRIORITY APPLN. INFO.:			US 2012-61718610	P	20121025
			WO 2013-US66709	W	20131024

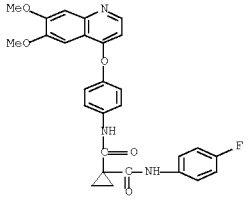
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Compact replicating retroviral vectors using a minimal promoter to express a therapeutic gene with a size of 0.9-1.9 kb are described. An internal ribosome entry sequence may be used for polycistronic expression cassettes. The vectors do not use the prior art SCP1, Ad, or CMV core promoters. Development and optimization of vectors is described.

IT 1140909-48-3, XL-184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in cancer therapy with retroviral gene therapy vectors; retroviral vectors for gene therapy using mini-promoters)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

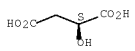
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

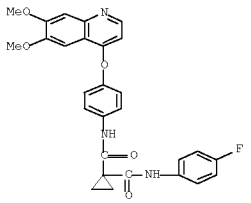
L4 ANSWER 367 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:711027 CAPLUS full-text
DOCUMENT NUMBER: 160:643049
TITLE: Cabozantinib dispersible tablet and preparation method thereof
INVENTOR(S): Peng, Zongyu; Li, Ran; Zheng, Feibo
PATENT ASSIGNEE(S): Qingdao Cancer Hospital, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 11pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103751140	A	20140430	CN 2014-10017920	20140115
PRIORITY APPLN. INFO.:			CN 2014-10017920	20140115

AB The invention discloses Cabozantinib dispersible tablet and prepn. method and application thereof. The inventive Cabozantinib dispersible tablet consists of the following component according to weight percentage: Cabozantinib 10-60%, filler 10-40%, disintegrant 10-50%, acidulant 10-50%, binder 0.1-10%, and lubricant and glidant 0.1-20%. Compared with the common tablet, the inventive dispersible tablet contains no surfactant, its solubility, dispersivity, and disintegrability are good, and it can be completely disintegrated within 1 min. The prepared Cabozantinib dispersible tablet has high dissoln. rate, high bioavailability, rapid distribution in vivo, stable quality, and good taste. The preparation method is simple, and suitable for industrial production

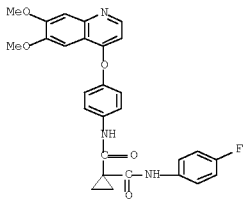
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib dispersible tablet)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

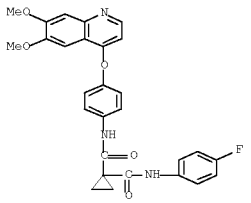


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 368 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:679549 CAPLUS Full-text
DOCUMENT NUMBER: 161:30896
TITLE: Cabozantinib: a new molecular targeted antitumor drug
AUTHOR(S): Zhang, Xiu-ying; Liu, Yao; Bai, Qiu-jiang; Wang, Nan
CORPORATE SOURCE: Department of Pharmacy, Kailuan General Hospital, Tangshan, Hebei Province, 063000, Peop. Rep. China
SOURCE: Yiyao Daobao (2013), 32(11), 1468-1470
CODEN: YDIAAL; ISSN: 1004-0781
DIGITAL OBJECT ID: 10.3870/yydb.2013.11.021
PUBLISHER: Yiyao Daobao Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. Cabozantinib, a new mol. targeted antitumor drug, was introduced with several subsections as follow: action mechanisms, pharmacokinetics, adverse reactions, drug interactions, clin. trials, and conclusions.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib: a new mol. targeted antitumor drug)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 369 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:653844 CAPLUS Full-text
DOCUMENT NUMBER: 161:257408
TITLE: Preclinical Evaluation of Imaging Biomarkers for Prostate Cancer Bone Metastasis and Response to Cabozantinib
AUTHOR(S): Graham, Timothy J.; Box, Gary; Tunariu, Nina; Crespo, Mateus; Spinks, Terry J.; Miranda, Susana; Attard, Gerhardt; de Bono, Johann; Eccles, Suzanne A.; Davies, Faith E.; Robinson, Simon P.
CORPORATE SOURCE: Division of Radiotherapy and Imaging, Institute of Cancer Research and Royal Marsden NHS Trust, Surrey, SM2 5NG, UK
SOURCE: Journal of the National Cancer Institute (2014), 106(4), ???
CODEN: JNCIEQ; ISSN: 0027-8874
DIGITAL OBJECT ID: 10.1093/jnci/dju033
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background Prostate cancer is incurable once it has metastasized to the bone. Appropriate preclin. models are lacking. The therapeutic efficacy of the multikinase inhibitor cabozantinib was assessed in an orthotopic xenograft model of castration-resistant prostate cancer (CRPC) bone metastasis using noninvasive, multimodality functional imaging. Methods NOD/SCID mice were injected intratibially with luciferase-expressing ERG (v-ets avian erythroblastosis virus E26 oncogene homolog) rearranged VCaP human prostate carcinoma cells. The response of VCaP xenografts (n = 7 per group) to cabozantinib was investigated using bioluminescence imaging and anatomical and diffusion weighted magnetic resonance imaging. This enabled quantitation of tumor volume and apparent diffusion coefficient (ADC). Bone uptake of technetium-methylene diphosphonate (99mTc-MDP) was assessed by single-photon emission computed tomog. Ex vivo micro computed tomog. was used to quantify bone volume and correlated with appropriate histopathol. Statistical significance was determined using the two-sided Mann-Whitney test or Wilcoxon signed rank test. Results VCaP xenografts were predominantly osteosclerotic with some osteolytic activity. Fluorescent in situ hybridization anal. confirmed retention of ERG oncogene rearrangements. Cabozantinib induced a statistically significant 52% reduction in tumor luminance (P = .02) and stasis in tumor volume after 15 days of treatment. Tumor ADC statistically significantly increased with cabozantinib and was associated with extensive necrosis (after 10 days, mean tumor ADC ± SD = 556±43×10-6 mm2/s vs pretreatment ADC = 485±43×10-6 mm2/s; P = .02). Tumor-associated uptake of 99mTc-MDP was statistically significantly reduced after 3 days of treatment (P = .02), sustained over 15 days treatment, and associated with a statistically significant (P = .048) reduction in bone growth on the tibial cortex, yet a highly statistically significant (P = .001) increase in trabecular bone volume Conclusions The intratibial VCaP model faithfully emulates clin. disease. Cabozantinib exerts potent effects on both tumor and tumor-induced bone matrix remodeling, and quantitation of ADC provides a clin. translatable imaging biomarker for early, sensitive assessment of treatment response in CRPC bone metastasis.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(noninvasive, multimodality functional imaging was effective in imaging biomarkers in response to cabozantinib in xenografted mouse model of human bone metastatic castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 370 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:628215 CAPLUS Full-text
DOCUMENT NUMBER: 160:542029
TITLE: Method for the diagnosis, prognosis and treatment of prostate cancer metastasis
INVENTOR(S): Gomis, Roger; Jean-Mairet, Joel
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 140pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

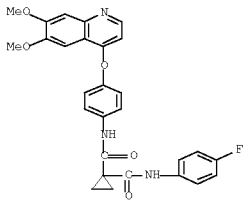
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014057357	A2	20140417	WO 2013-IB2866	20131009
WO 2014057357	A3	20140530		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM			
CA 2888122	A1	20140417	CA 2013-2888122	20131009
US 20140105918	A1	20140417	US 2013-14050262	20131009
AU 2013328385	A1	20150507	AU 2013-328385	20131009
EP 2906718	A2	20150819	EP 2013-821939	20131009
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2015105297	A	20150916	KR 2015-7012297	20131009
CN 104995313	A	20151021	CN 2013-80060218	20131009
JP 2016500517	T	20160114	JP 2015-536237	20131009
JP 6074049	B2	20170201		
MX 2015004610	A	20151022	MX 2015-4610	20150410
US 20150362495	A1	20151217	US 2015-14435128	20150410
JP 2016105731	A	20160616	JP 2016-48499	20160311
US 20170121777	A1	20170504	US 2016-15183419	20160615
AU 2016213773	A1	20160901	AU 2016-213773	20160810

PRIORITY APPLN. INFO.:	US 2012-61713318	P	20121012
	AU 2013-328385	A3	20131009
	JP 2015-536237	A3	20131009
	WO 2013-IB2866	W	20131009
	US 2015-14435128	A2	20150410

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention relates to a method for the diagnosis or the prognosis of metastasis in prostate cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for the diagnosis or the prognosis of metastasis in prostate cancer, as well as to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which, comprise determining the c-MAF expression level. Finally, the invention relates to the use of a c-MAF inhibitor as therapeutic target for treating the prostate cancer.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-MAF gene for diagnosis, prognosis and treatment of prostate cancer metastasis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-

quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 371 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:581585 CAPLUS Full-text
DOCUMENT NUMBER: 160:555604
TITLE: Phage display derived peptides highly specific against Mdm2/Mdm4 and methods for treating cancer
INVENTOR(S): Joseph, Thomas Leonard; Verma, Chandra Shekhar; Lane, David Phillip; Brown, Christopher John
PATENT ASSIGNEE(S): Agency for Science, Technology and Research, Singapore
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014055039	A1	20140410	WO 2013-SG428	20131001
WO 2014055039	A9	20141106		

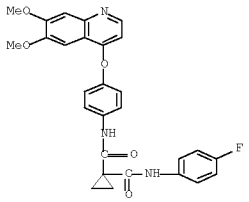
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2904000	A1	20150812	EP 2013-844064	20131001

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

US 20150246946	A1	20150903	US 2015-14432729	20150331
PRIORITY APPLN. INFO.:			SG 2012-7302	A 20121001
			WO 2013-SG428	W 20131001

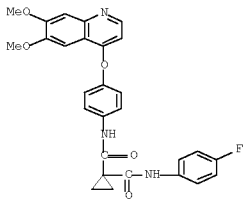
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 160:555604
AB By using a phage display derived peptide as an initial template, compds. have been developed that are highly specific against Mdm2/Mdm4. These compds. exhibit greater potency in p53 activation and protein-protein interaction assays than a compound derived from the p53 wild-type sequence. Unlike nutlin, a small mol. inhibitor of Mdm2/Mdm4, the phage derived compds. can arrest cells resistant to p53 induced apoptosis over a wide concentration range without cellular toxicity, suggesting they are highly suitable for cyclo-therapy. In one embodiment, there is disclosed the peptide comprising or consisting o f the amino acid sequence of SEQ ID NO 1 (TSFXaaiEYWXaa3LLXaai), wherein Xaa3 can be N or A and wherein in case Xaa3 is N, Xaai is not A and/or Xaa2 is not S. In one embodiment, Xaa3 can be any type of amino acid other than A and wherein in case Xaa3 is N, Xaaj is not A and/or Xaa2 is not S. Those peptides have been shown to inhibit the p53:Mdm2 interactions with a nanomolar affinity.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL184; phage display derived peptides highly specific against Mdm2/Mdm4 and methods for treating cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 372 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:565947 CAPLUS Full-text
DOCUMENT NUMBER: 161:208503
TITLE: First-, second-, third-line therapy for mRCC: benchmarks for trial design from the IMDC

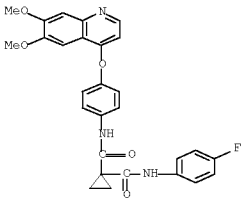
AUTHOR(S): Ko, J. J.; Choueiri, T. K.; Rini, B. I.; Lee, J.-L.; Kroeger, N.; Srinivas, S.; Harshman, L. C.; Knox, J. J.; Bjarnason, G. A.; MacKenzie, M. J.; Wood, L.; Vaishampayan, U. N.; Agarwal, N.; Pal, S. K.; Tan, M.-H.; Rha, S. Y.; Yuasa, T.; Donskov, F.; Bamias, A.; Heng, D. Y. C.
CORPORATE SOURCE: Tom Baker Cancer Center, University of Calgary, Calgary, AB, Can.
SOURCE: British Journal of Cancer (2014), 110(8), 1917-1922
CODEN: BJCAAI; ISSN: 0007-0920
DIGITAL OBJECT ID: 10.1038/bjc.2014.25
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Limited data exist on outcomes for metastatic renal cell carcinoma (mRCC) patients treated with multiple lines of therapy. Benchmarks for survival are required for patient counselling and clin. trial design. Methods: Outcomes of mRCC patients from the International mRCC Database Consortium database treated with 1, 2, or 3+ lines of targeted therapy (TT) were compared by proportional hazards regression. Overall survival (OS) and progression-free survival (PFS) were calculated using different population inclusion criteria. Results: In total, 2705 patients were treated with TT of which 57% received only first-line TT, 27% received two lines of TT, and 16% received 3+ lines of TT. Overall survival of patients who received 1, 2, or 3+ lines of TT were 14.9, 21.0, and 39.2 mo, resp., from first-line TT (P<0.0001). On multivariable anal., 2 lines and 3+ lines of therapy were each associated with better OS (HR=0.738 and 0.626, P<0.0001). Survival outcomes for the subgroups were as follows: for all patients, OS 20.9 mo and PFS 7.2 mo; for those similar to eligible patients in the first-line ADAPT trial, OS 14.7 mo and PFS 5.6 mo; for those similar to patients in first-line TIVO-1 trial, OS 24.8 mo and PFS 8.2 mo; for those similar to patients in second-line INTORSECT trial, OS 13.0 mo and PFS 3.9 mo; and for those similar to patients in the third-line GOLD trial, OS 18.0 mo and PFS 4.4 mo. Conclusions: Patients who are able to receive more lines of TT live longer. Survival benchmarks provide context and perspective when interpreting and designing clin. trials.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(first-, second-, third-line therapy for metastatic renal cell carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 373 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:542996 CAPLUS Full-text
DOCUMENT NUMBER: 161:267984
TITLE: Bone-targeted therapies in metastatic castration-resistant prostate cancer: evolving paradigms
AUTHOR(S): El-Amm, Joelle; Freeman, Ashley; Patel, Nihar; Aragon-Ching, Jeanny B.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Medicine, George Washington University Medical Center, Washington, DC, 20037, USA
SOURCE: Prostate Cancer (2013) 210686/1-210686/11, 11 pp.
CODEN: PCRACU; ISSN: 2090-312X
DIGITAL OBJECT ID: 10.1155/2013/210686
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Majority of patients with metastatic castrate resistant prostate cancer (mCRPC) develop bone metastases which results in significant morbidity and mortality as a result of skeletal-related events (SREs). Several bone-targeted agents are either in clin. use or in development for prevention of SREs. Bisphosphonates were the first class of drugs investigated for prevention of SREs and zoledronic acid is the only bisphosphonate that is FDA-approved for this indication. Another bone-targeted agent is denosumab which is a fully humanized monoclonal antibody that binds to the RANK-L thereby inhibiting RANK-L mediated bone resorption.While several radiopharmaceuticals were a approved for pain palliation in mCRPC including strontium and samarium, alpharadin is the first radiopharmaceutical to show significant overall survival benefit. Contemporary therapeutic options including enzalutamide and abiraterone have effects on pain palliation and SREs as well. Other novel bone-targeted agents are currently in development, including the receptor tyrosine kinase inhibitors cabozantinib and dasatinib. Emerging therapeutics in mCRPC has resulted in great strides in preventing one of the most significant sources of complications of bone metastases.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evolving paradigms of bone-targeted therapies in metastatic castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

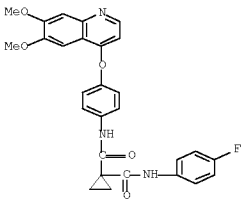


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 374 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:479457 CAPLUS Full-text
DOCUMENT NUMBER: 160:515456
TITLE: Synthesis method of antitumor therapeutic drug of cabozantinib
INVENTOR(S): Cai, Jianping; Chen, Zengfei; Zhang, Lifeng; Fang, Ying
PATENT ASSIGNEE(S): Suzhou Moer Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 9pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103664778	A	20140326	CN 2013-10631287	20131127
CN 103664778	B	20170405		
PRIORITY APPLN. INFO.:			CN 2013-10631287	20131127
OTHER SOURCE(S):	CASREACT 160:515456; MARPAT 160:515456			

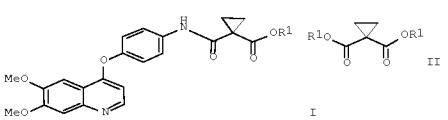
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L4 ANSWER 375 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:478399 CAPLUS Full-text
DOCUMENT NUMBER: 160:501685
TITLE: Process for the preparation of cabozantinib and its intermediate
INVENTOR(S): Shi, Xiangfei; Zhao, Rui; Meng, Qingyi; Zhang, Xiquan
PATENT ASSIGNEE(S): Chia Tai Tianqing Pharmaceutical Group Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 18pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

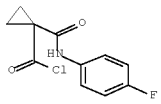
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103664776	A	20140326	CN 2012-10374723	20120926
CN 103664776	B	20160504		
PRIORITY APPLN. INFO.:			CN 2012-10374723	20120926
OTHER SOURCE(S):	MARPAT 160:501685			

GI



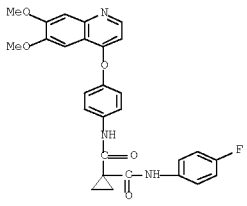
I II

AB The invention relates to process for the prepn. of cabozantinib and its intermediate of formula I from 1,1-cyclopropane dicarboxylic acid diester of formula II [R1 = C1-10 alkyl]. For example, cabozantinib was prepared by hydrolysis of compound II [R1 = Et] to afford



AB The invention discloses a synthesis method of antitumor therapeutic drug of cabozantinib., comprising: using 4-(6, 7- dimethoxy quinoline -4- oxy)-phenylamine to react with 1-((4- fluorophenyl) carbamoyl) cyclopropyl acyl halide, an acid-binding agent in organic solvent at -5~20 ℃ for 0.5~2h to obtain cabozantinib; the inventive method uses cheap raw materials, has mild conditions, simple and convenient operation, stable process, good repeatability, high molar yield, low cost, so invention is an applicable method for com. production of cabozantinib. Cabozantinib was prepared via chlorination of 6,7-dimethoxyquinolin-4-ol; the resulting 4-chloro-6,7-dimethoxyquinoline underwent condensation with 4-aminophenol or 4-nitrophenol to give the corresponding ethers, which underwent redn and/or acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropylcarbonyl halides to give cabozantinib. The said 1-[(4-fluorophenyl)carbamoyl]cyclopropylcarbonyl halides were prepared via condensation of 1,1-cyclopropanedicarboxylic acid with p-fluoroaniline followed by halogenation. The inventive method uses cheap raw materials, has mild conditions, simple and convenient operation, stable process, good repeatability, high molar yield, low cost, so invention is an applicable method for com. production of cabozantinib.
IT 849217-68-1P, Cabozantinib
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor drug cabozantinib starting from (dimethoxy)quinolinol and cyclopropanedicarboxylic acid by using etherification and amidation as the key steps)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

1-(ethoxycarbonyl)cyclopropanecarboxylic acid, which underwent amidation reaction with 4-aminophenol followed by arylation with 4-chloro-6,7-dimethoxyquinoline to afford compound I [R1 = Et], which underwent hydrolysis followed by amidation with 4-fluoroaniline to afford cabozantinib.
IT 849217-68-1P, Cabozantinib
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of cabozantinib and its intermediate)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 376 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:448281 CAPLUS full-text
DOCUMENT NUMBER: 160:480988
TITLE: Inhibition of viral infection-triggered asthma with c-kit inhibitor
INVENTOR(S): Umetsu, Dale T.; Chang, Ya-Jen; De Kruyff, Rosemarie Helena; Baumgarth, Nicole
PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA
SOURCE: PCT Int. Appl., 128pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014043442	A1	20140320	WO 2013-US59609	20130913
WO 2014043442	A9	20160623		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,

VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2895170 A1 20150722 EP 2013-836850 20130913
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

US 20150297593 A1 20151022 US 2015-14428272 20150313
PRIORITY APPLN. INFO.: US 2012-61701296 P 20120914
WO 2013-US59609 W 20130913

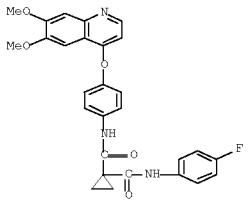
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods, compns., and kits featuring a c-Kit kinase inhibitor for use in preventing or treating virus-induced respiratory pathol.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-kit inhibitors for treatment of viral infection-triggered asthma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 377 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:443739 CAPLUS Full-text

DOCUMENT NUMBER: 160:485576

TITLE: Combination therapy for prevention or treatment of c-met or angiogenesis factor induced diseases

INVENTOR(S): Jeong, Yun Ju; Kim, Kyung Ah; Song, Yun Jeong; Lee, Ji Min; Lee, Hyo Seon; Choi, Jae Hyun; Lee, Saet Byoul

PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea

SOURCE: Eur. Pat. Appl., 168pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

EP 2708556 A1 20140319 EP 2013-184072 20130912
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

KR 2014035266 A 20140321 KR 2013-108913 20130911

US 20140086926 A1 20140327 US 2013-14025403 20130912

PRIORITY APPLN. INFO.: KR 2012-101177 A 20120912
KR 2013-108913 A 20130911

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The authors disclose combination therapy for prevention or treatment of c-Met-induced or angiogenesis factor-induced diseases. The therapy comprises the co-administration of an angiogenesis inhibitor and an anti-c-Met antibody. In one example, the metastatic potential (migration) of HUVEC cells is shown to be inhibited by the combined effects of an anti-c-Met antibody and an anti-VEGF antibody.

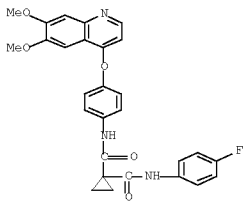
IT 1140909-48-3, XL 184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination therapy with anti-MET receptor antibodies)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

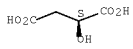
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5



Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 378 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:431636 CAPLUS Full-text

DOCUMENT NUMBER: 163:325757

TITLE: Effects of Cabozantinib on Pain and Narcotic Use in Patients with Castration-resistant Prostate Cancer: Results from a Phase 2 Nonrandomized Expansion Cohort

AUTHOR(S): Basch, Ethan; Autio, Karen A.; Smith, Matthew R.; Bennett, Antonia V.; Weitzman, Aaron L.; Scheffold, Christian; Sweeney, Christopher; Rathkopf, Dana E.; Smith, David C.; George, Daniel J.; Higano, Celestia S.; Harzstark, Andrea L.; Sartor, A. Oliver; Gordon, Michael S.; Vogelzang, Nicholas J.; de Bono, Johann S.; Haas, Naomi B.; Corn, Paul G.; Schimmoller, Frauke; Scher, Howard I.

CORPORATE SOURCE: Cancer Outcomes Research Program, Lineberger Cancer Center, University of North Carolina, Chapel Hill, NC, USA

SOURCE: European Urology (2015), 67(2), 310-318
CODEN: EUURAV; ISSN: 0302-2838

DIGITAL OBJECT ID: 10.1016/j.eururo.2014.02.013

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; (online computer file)

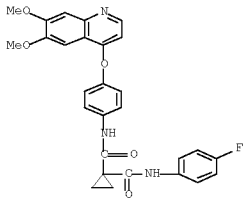
LANGUAGE: English

AB Pain neg. affects quality of life for cancer patients. Preliminary data in metastatic castration-resistant prostate cancer (mCRPC) suggested a benefit of the oral tyrosine kinase inhibitor cabozantinib to pain palliation. Prospective evaluation of cabozantinib's benefits on pain and narcotic use in mCRPC.This was a nonrandomized expansion (NRE) cohort (n = 144) of a phase 2 randomized discontinuation trial in docetaxel-refractory mCRPC patients. Pain and interference of symptoms with sleep and general activity were electronically self-reported daily for 7-d intervals at baseline and regularly scheduled throughout the study. Mean per-patient scores were calculated for each interval. Narcotic use was recorded daily during the same intervals.Open-label cabozantinib (100 mg or 40 mg). The following stringent response definition was used: clin. meaningful pain reduction (≥30% improvement in mean scores from baseline) confirmed at a later interval without concomitant increases in narcotics. Only patients with moderate or severe baseline pain were analyzed.Sixty-five patients with moderate or severe baseline pain were evaluable. Of these, 27 (42%) experienced pain palliation according to the stringent response definition. Thirty-seven patients (57%) had clin. meaningful pain relief at two consecutive intervals, reported ≥6 wk apart in the majority. Forty-four patients (68%) had palliation at one or more intervals; 36 (55%) decreased narcotics use during one or more intervals. Clin. meaningful pain reduction was associated with significant ($p \leq 0.001$) improvements in sleep quality and general activity. A limitation of this study was its open-label design. Cabozantinib demonstrated clin. meaningful pain palliation, reduced or eliminated patients' narcotic use, and improved patient functioning, thus meriting prospective validation in phase 3 studies.We evaluated the potential of cabozantinib to improve symptoms in patients with metastatic prostate cancer that no longer responds to standard therapies. We saw a promising reduction in pain and reduced need for narcotic painkillers. Larger, well-controlled trials are necessary to confirm these findings.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase 2 nonrandomized expansion cohort study on effects of cabozantinib on pain and narcotic use in patients with castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 379 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:410366 CAPLUS Full-text

DOCUMENT NUMBER: 160:451706

TITLE: Inhibitors of Met, VEGFR and Ret for use in the treatment of lung adenocarcinoma

INVENTOR(S): Aftab, Dana T.

PATENT ASSIGNEE(S): Exelixis, Inc., USA

SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2014039971 A1 20140313 WO 2013-US58768 20130909
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

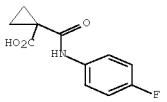
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20140121239	A1	20140501	US 2013-14021614	20130909
CN 104703600	A	20150610	CN 2013-80052164	20130909
EP 2892532	A1	20150715	EP 2013-765886	20130909
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015530389	T	20151015	JP 2015-531283	20130909
US 20150238477	A1	20150827	US 2015-14426580	20150306

PRIORITY APPLN. INFO.: US 2012-61698143 P 20120907
WO 2013-US58768 W 20130909

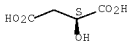
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:451706; MARPAT 160:451706
GI



AB This invention is directed to the treatment of cancer in a patient, particularly a patient with lung adenocarcinoma, and more particularly a patient with KIF5B-RET fusion-pos. non-small cell lung cancer, with an inhibitor of MET, VEGF, and RET.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

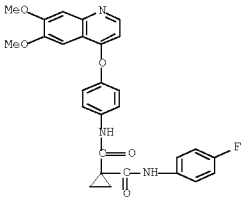
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

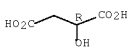
CRN 849217-68-1
CMF C28 H24 F N3 O5



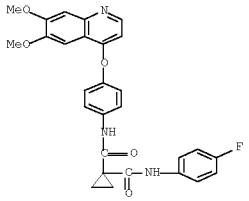
CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



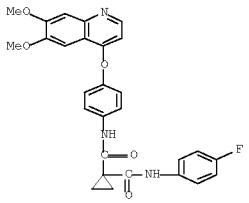
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD



IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors of Met, VEGFR and Ret for use in treatment of lung adenocarcinoma)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

(3 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 380 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:327215 CAPLUS Full-text
DOCUMENT NUMBER: 160:370140
TITLE: Preparation of substituted azaindole prodrugs, salts, pharmaceutical compositions thereof and methods of use in treating cancer and other proliferative disorders
INVENTOR(S): Xi, Ning; Wang, Tingjin; Tang, Yin; Sun, Mingming; Wang, Qian
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 53pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20140056849	A1	20140227	US 2013-13975371	20130826
US 9399639	B2	20160726		
CA 2882157	A1	20140306	CA 2013-2882157	20130826
WO 2014035846	A2	20140306	WO 2013-US56548	20130826
WO 2014035846	A3	20150625		

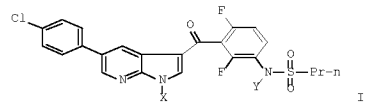
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

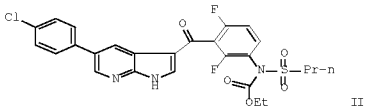
AU 2013309143	A1	20150212	AU 2013-309143	20130826
AU 2013309143	B2	20170309		
EP 2888260	A2	20150701	EP 2013-832403	20130826

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

PRIORITY APPLN. INFO.: US 2012-61693335 P 20120827
WO 2013-US56548 W 20130826
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:370140; MARPAT 160:370140
GI



I



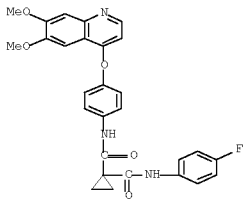
II

AB The present invention provides substituted azaindole prodrugs of vemurafenib, methods of making said prodrugs, pharmaceutical compns. of said prodrugs and methods of using said prodrugs and pharmaceutical compns. thereof to treat or prevent diseases or disorders such as cancer. The prodrugs have general formula I, wherein each of X and Y is independently H, -C(:O)R3, -C(:O)OR4, -C(R1R2)OC(:O)R3, -C(R1R2)OC(:O)OR4 or -C(R1R2)OP(:O)(OR4)(OR4a), with the proviso that when Y is H, X is not -C(:O)CH3 or H; each R1 and R2 is independently H, D, C1-6alkyl, etc.; each R3 is independently H, D, C1-10alkyl, etc.; and each R4 and R4a is independently H, C1-10alkyl, C3-8cycloalkyl, etc. Example compound II was prepared by reacting vemurafenib with Et chloroformate. Various prodrugs of the invention were studied for their stability in liver microsomes, their oral and i.v. bioavailability, and their antitumor properties.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted azaindole prodrugs., salts, pharmaceutical compns. thereof and methods of use in treating cancer and other proliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 381 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:211024 CAPLUS Full-text

DOCUMENT NUMBER: 161:316285

TITLE: Cabozantinib Inhibits Prostate Cancer Growth and Prevents Tumor-Induced Bone Lesions

AUTHOR(S): Dai, Jinlu; Zhang, Honglai; Karatsinides, Andreas; Keller, Jill M.; Kozloff, Kenneth M.; Aftab, Dana T.; Schimmoller, Frauke; Keller, Evan T.

CORPORATE SOURCE: Departments of Urology and Orthopaedic Surgery, University of Michigan, Ann Arbor, MI, USA

SOURCE: Clinical Cancer Research (2014), 20(3), 617-630
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-0839

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

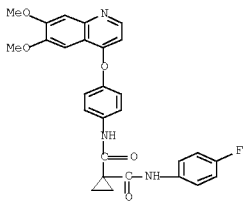
LANGUAGE: English

AB Purpose: Cabozantinib, an orally available multityrosine kinase inhibitor with activity against mesenchymal epithelial transition factor (MET) and VEGF receptor 2 (VEGFR2), induces resolution of bone scan lesions in men with castration-resistant prostate cancer bone metastases. The purpose of this study was to determine whether cabozantinib elicited a direct antitumor effect, an indirect effect through modulating bone, or both. Exptl. Design: Using human prostate cancer xenograft studies in mice, we determined the impact of cabozantinib on tumor growth in soft tissue and bone. In vitro studies with cabozantinib were performed using (i) prostate cancer cell lines to evaluate its impact on cell growth, invasive ability, and MET and (ii) osteoblast cell lines to evaluate its impact on viability and differentiation and VEGFR2. Results: Cabozantinib inhibited progression of multiple prostate cancer cell lines (Ace-1, C4-2B, and LuCaP 35) in bone metastatic and soft tissue murine models of prostate cancer, except for PC-3 prostate cancer cells in which it inhibited only s.c. growth. Cabozantinib directly inhibited prostate cancer cell viability and induced apoptosis in vitro and in vivo and inhibited cell invasion in vitro. Cabozantinib had a dose-dependent biphasic effect on osteoblast activity and inhibitory effect on osteoclast production in vitro that was reflected in vivo. It blocked MET and VEGFR2 phosphorylation in prostate cancer cells and osteoblast-like cells, resp. Conclusion: These data indicate that cabozantinib has direct antitumor activity, and that its ability to modulate osteoblast activity may contribute to its antitumor efficacy. Clin Cancer Res; 20(3); 617-30. ©2013 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib inhibits prostate cancer growth and prevents tumor-induced bone lesions)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 382 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:211001 CAPLUS Full-text

DOCUMENT NUMBER: 161:316087

TITLE: Cabozantinib and Prostate Cancer: Inhibiting Seed and Disrupting Soil?

AUTHOR(S): Lee, Richard J.; Smith, Matthew R.

CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA

SOURCE: Clinical Cancer Research (2014), 20(3), 525-527
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-2636

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal; General Review

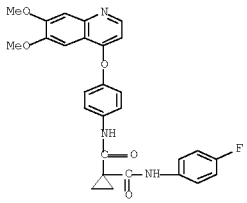
LANGUAGE: English

AB A review. Treatment with cabozantinib, an inhibitor of MET and VEGFR2 signaling, has demonstrated clin. benefit in early trials in men with metastatic prostate cancer. Preclin. evidence suggests that cabozantinib can kill cancer cell seeds while disrupting angiogenesis and stromal cells in the metastatic soil.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cabozantinib in treatment of prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 383 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:175942 CAPLUS Full-text

DOCUMENT NUMBER: 160:310859

TITLE: Preparation of substituted pyrazolone compounds as protein tyrosine kinase modulators useful in treatment of proliferative diseases

INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming

PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.

SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

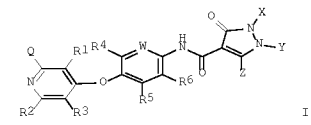
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022117	A1	20140206	WO 2013-US51175	20130719

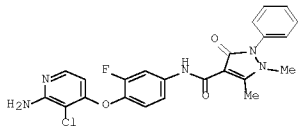
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW,

SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
US 20150050239 A1 20150219 US 2013-13945925 20130719
US 8969388 B2 20150303
EP 2879676 A1 20150610 EP 2013-825325 20130719
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
JP 2015523390 T 20150813 JP 2015-524334 20130719
PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
WO 2013-US51175 W 20130719
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:310859; MARPAT 160:310859
GI



I



II

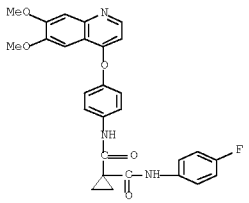
AB The invention provides substituted pyrazolone compds.of formula I, stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, and pharmaceutical preparation for regulating the activity of protein kinases and adjusting the signal response in the cell or between cells. The invention also relates to pharmaceutical compns. comprising the compds. and a method for treating hyperproliferative disorder of mammal, particularly human using the compns. Compds. of formula I [wherein Q is H, NH2 and derivative, OH and derivs., -NHCOR, etc.; W is (un)substituted CH or N; X, Y, and Z are independently H, D, C1-6 alkyl, C3-8 cycloalkyl-C1-4 alkylene, etc.; R1-R6 are independently H, D, F, Cl, Br, CN, etc.; R is H, C1-6 alkyl, C3-8 cycloalkyl-C1-4 alkylene, C3-7 heterocycloalkyl, etc.] and their stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, are claimed and exemplified. For example, II was prepared in a multistep process (procedure given). I were evaluated for stability in liver microsomes and pharmacokinetic properties in mice, rats, dogs, and monkeys (data given). Binding of I to receptor tyrosine kinases was determined using KINOMEscan where II exhibited binding constant (Kd) values of 23 nM for KDR tyrosine kinase and 4.4 nM for c-Met tyrosine kinase.

IT 849217-68-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolone compds. useful as protein tyrosine kinase modulators for treatment of proliferative disorders)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



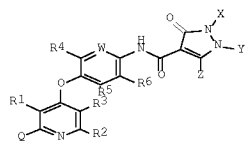
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 384 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:175941 CAPLUS Full-text
DOCUMENT NUMBER: 160:310858
TITLE: Preparation of substituted pyrazolone compounds as protein tyrosine kinase modulators for treatment of proliferative disease
INVENTOR(S): Xi, Ning; Wu, Yanjun; Liao, Min; Feng, Yanming
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.
SOURCE: PCT Int. Appl., 110pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

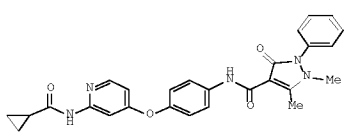
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WO 2014022116	A2	20140206	WO 2013-US51174	20130719
WO 2014022116	A3	20150716		

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MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM
CA 2876246 A1 20140206 CA 2013-2876246 20130719
AU 2013296897 A1 20141218 AU 2013-296897 20130719
AU 2013296897 B2 20150917
US 20150050239 A1 20150219 US 2013-13945925 20130719
US 8969388 B2 20150303
EP 2879677 A2 20150610 EP 2013-826459 20130719
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME
JP 2015530975 T 20151029 JP 2015-524333 20130719
MX 2015001424 A 20160309 MX 2015-1424 20150128
IN 2015CN01040 A 20160701 IN 2015-CN1040 20150223
PRIORITY APPLN. INFO.: US 2012-61676944 P 20120728
US 2012-61679416 P 20120803
WO 2013-US51174 W 20130719
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 160:310858; MARPAT 160:310858
GI



I

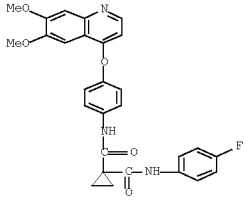


II

AB The invention provides substituted pyrazolone compds.of formula I, stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, and pharmaceutical preparation for regulating the activity of protein kinases and adjusting the signal response in the cell or between cells. The invention also relates to pharmaceutical compns. comprising the compds. and a method for treating hyperproliferative disorder of mammal, particularly human using the compns. Compds. of formula I [wherein Q is D, NH2 and derivs., -NHCOR, etc.; W is (un)substituted CH or N; each X, Y, and Z is independently H, D, C1-6 alkyl, C3-8 cycloalkyl, etc.; each R1-R6 is independently H, D, F, Cl, Br, CN, etc.; R is D, C3-8 cycloalkyl, -C1-4 alkylene -C6-10 aryl, etc.] and their stereoisomers, geometric isomers, tautomers, oxynitrides, hydrates, solvates, metabolites, pharmaceutically acceptable salts or prodrugs thereof, are claimed and exemplified. For example, II was prepared in a multistep process (procedure given). Candidate compds. of I were evaluated for stability in liver microsomes and pharmacokinetic properties in mice, rats, dogs, and monkeys (data given). Binding of I to receptor tyrosine kinases was determined using KINOMEscan where II exhibited binding constant (Kd) values of 2.9 nM for KDR tyrosine kinase and 0.21 nM for c-Met tyrosine kinase.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolone compds. useful as protein tyrosine kinase modulators for treatment of proliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



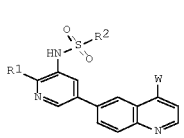
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

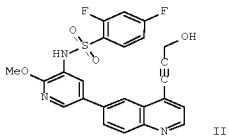
L4 ANSWER 385 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:173876 CAPLUS full-text
DOCUMENT NUMBER: 160:294980
TITLE: Preparation of N-[3-(quinolin-6-yl)pyridin-5-yl] benzenesulfonamides as PI3 kinase modulators
INVENTOR(S): Xi, Ning; Li, Zhuo; Wang, Tingjin; Wu, Zuping; Wen, Qiuling
PATENT ASSIGNEE(S): Calitor Sciences, LLC, USA; Sunshine Lake Pharma Co., Ltd.

SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014022128	A1	20140206	WO 2013-US51405	20130719
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2012-61676966 P 20120729
OTHER SOURCE(S): CASREACT 160:294980; MARPAT 160:294980
GI

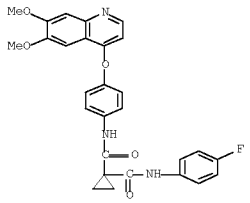

I


II

AB This invention relates to the field of lipid kinases and modulators thereof. In particular, the invention relates to compds. I [W = D, CN, N3, (un)substituted C5-12 spirobicyclyl or C≡CX; X = H, D, alkyl, cycloalkyl, etc.; R1 = H, D, Cl, alkyl, etc.; R2 = alkyl, cycloalkyl, aryl, etc.] as modulators of phosphatidylinositol 3-kinases (PI3 kinases or PBKs) signaling pathways, and methods of their use. Twenty-nine compds. I were prepared and disclosed. E.g., a multi-step synthesis of II, starting from 5-bromo-2-chloro-3-nitropyridine, was described. Exemplified compds. I exhibited potent activities in the PI3Kα(h) and mTOR(h) assays (data given for representative compds. I). The invention also provides pharmaceutically acceptable compns. comprising compds. I and methods of using the compns. in modulating of PI3K signaling pathways and their related disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-[3-(quinolin-6-yl)pyridin-5-yl] benzenesulfonamides as PI3 kinase modulators)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L4 ANSWER 386 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:151402 CAPLUS Full-text
DOCUMENT NUMBER: 160:242457
TITLE: In-frame fusion of genes CEP55 and RET associated with diffuse-type gastric cancer and their use in drug discovery and cancer therapy
INVENTOR(S): Shibata, Tatsuhiro; Hosoda, Fumie
PATENT ASSIGNEE(S): National Cancer Center, Japan
SOURCE: PCT Int. Appl., 53pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014017491	A1	20140130	WO 2013-JP69929	20130723
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CN 104619841	A	20150513	CN 2013-80039589	20130723
EP 2878672	A1	20150603	EP 2013-822713	20130723
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
US 20150177246	A1	20150625	US 2015-14417052	20150123

PRIORITY APPLN. INFO.: JP 2012-165694 A 20120726
WO 2013-JP69929 W 20130723
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

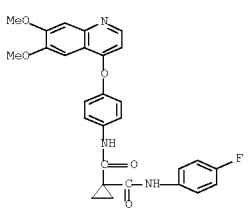
AB Through transcriptome an in-frame fusion of 2 genes (CEP55 and RET) of human chromosome 10 was found in patients with diffuse-type gastric cancer. The fused genes can be used for evaluation of the effectiveness of an antitumor agent such as RET tyrosine kinase inhibitors. Antibody to CEP55 or RET protein is also claimed.

IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RET tyrosine kinase inhibitors; in-frame fusion of genes CEP55 and RET associated with diffuse-type gastric cancer and their use in drug discovery and cancer therapy)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

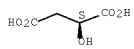
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5



Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 387 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2014:146206 CAPLUS Full-text
DOCUMENT NUMBER: 160:225648
TITLE: Efflux inhibitor compositions and methods of treatment using the same
INVENTOR(S): Bunt, Antonius Martinus Gustave; Van Tellingen, Olaf
PATENT ASSIGNEE(S): Neth.
SOURCE: PCT Int. Appl., 74pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2014018932	A2	20140130	WO 2013-US52402	20130726
WO 2014018932	A3	20140320		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2880236	A1	20140130	CA 2013-2880236	20130726
AU 2013295549	A1	20150319	AU 2013-295549	20130726
EP 2877159	A2	20150603	EP 2013-745549	20130726
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104736144	A	20150624	CN 2013-80050643	20130726
JP 2015523400	T	20150813	JP 2015-524485	20130726
MX 2015001194	A	20151123	MX 2015-1194	20150126
IN 2015MN00408	A	20150904	IN 2015-MN408	20150225

PRIORITY APPLN. INFO.: US 2012-61676689 P 20120727
WO 2013-US52402 W 20130726

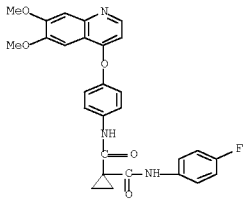
AB The present invention relates to efflux inhibitor compns. and methods of using these agents for treating conditions where the activity of efflux transporter proteins (e.g., Breast Cancer Resistance Protein (BCRP) and P-Glycoprotein (P-GP)) inhibit effective delivery of a therapeutic agent to a target tissue (e.g., brain, spinal cord, nerves, cerebrospinal fluid,

testis, eyeballs, retina, inner ear, placenta, mammary gland, liver, biliary tract, kidney, intestines, lung, adrenal cortex, endometrium, hematopoietic cells, and/or stem cells).

IT 849217-68-1, Cabozantinib
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efflux inhibitor compns. and methods of treatment using same)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 388 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:127915 CAPLUS Full-text

DOCUMENT NUMBER: 160:362955

TITLE: Novel tyrosine kinase inhibitors for renal cell carcinoma

AUTHOR(S): Dorff, Tanya B.; Pal, Sumanta K.; Quinn, David I.

CORPORATE SOURCE: Department of Medicine, USC Norris Comprehensive Cancer Center, USC Keck School of Medicine, Los Angeles, CA, 90033, USA

SOURCE: Expert Review of Clinical Pharmacology (2014), 7(1), 67-73
CODEN: ERCPAG; ISSN: 1751-2433

DIGITAL OBJECT ID: 10.1586/17512433.2014.862496

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal; General Review; (online computer file)

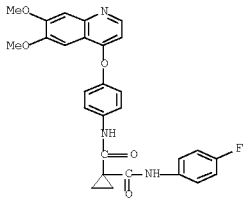
LANGUAGE: English

AB A review. Although targeted therapy against VEGF and mTOR have revolutionized the treatment of advanced renal cell carcinoma (RCC), addnl. agents are required due to toxicity and resistance to currently available drugs. Some next-generation tyrosine kinase inhibitors have focused on VEGF, narrowing the spectrum of receptors which are inhibited and enhancing binding affinity. However, targeting novel receptors with tyrosine kinase inhibition of addnl. receptor targets has also emerged as an important future therapeutic strategy for RCC, both clear cell and variant histol. New pathways being targeted include FGF, angiopoietin and MET. In this review, we highlight five novel tyrosine kinase inhibitors in development for RCC: tivozanib; dovitinib; regorafenib; cabozantinib; and tivantinib.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel tyrosine kinase inhibitors for renal cell carcinoma)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 389 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2014:93138 CAPLUS Full-text

DOCUMENT NUMBER: 160:289739

TITLE: c-MET kinase inhibitors: a patent review (2011 - 2013)

AUTHOR(S): Zhu, Kongkai; Kong, Xiangqian; Zhao, Dan; Liang, Zhongjie; Luo, Cheng

CORPORATE SOURCE: Center for Systems Biology, Soochow University, Jiangsu, 215006, Peop. Rep. China

SOURCE: Expert Opinion on Therapeutic Patents (2014), 24(2), 217-230
CODEN: EOTPEG; ISSN: 1354-3776

DIGITAL OBJECT ID: 10.1517/13543776.2014.864279

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal; General Review; (online computer file)

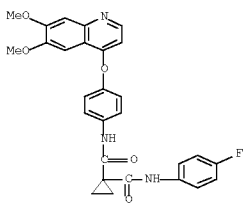
LANGUAGE: English

AB A review. Introduction: The receptor tyrosine kinase c-MET displays aberrant activation in the malignant phenotype of various tumors, and thus, has drawn considerable attention as drug target for cancer therapy. Many c-MET inhibitors are now under clin. investment, and one of them - Cabozantinib - has been approved by US FDA in 2012 for the treatment of medullary thyroid cancer, which further proved the feasibility of c-MET inhibition method in cancer therapy. Areas covered: This article briefly outlines the role of c-MET in oncogenesis and provides a broad overview of the assays used to characterize new inhibitors. Then, a series of representative small-mol. inhibitors of c-MET, especially from the published patent literature from 2011 to 2013, are recorded. Herein, the challenges in the kinase inhibitor design, such as the inhibitor selectivity and resistance mutations, are also discussed. Expert opinion: Up to now, at least 17 inhibitors of c-MET are under clin. evaluation, and several agents exhibit encouraging results. Thus, inhibiting c-MET signaling has major therapeutic value in cancer therapy. Focus on the selectivity of both types of inhibitors, with potent selectivity or multi-targets, have demonstrated antitumor efficacy. The network pharmacol. and clin. trials integrated would provide powerful tools to further evaluate the superiority of both inhibitors in continued efficacy and toxicity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(application of c-MET kinase inhibitors for the treatment of medullary thyroid cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 390 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:2007812 CAPLUS Full-text

DOCUMENT NUMBER: 160:380536

TITLE: Newly approved antitumor drugs by FDA in 2012

AUTHOR(S): Yang, Minglun

CORPORATE SOURCE: Department of Pharmacy, Linqu County People's Hospital, Linqu, Shandong Province, 262600, Peop. Rep. China

SOURCE: Yaoxue Fuwu Yu Yanjiu (2013), 13(4), 304-306
CODEN: YFYYAH; ISSN: 1671-2838

DIGITAL OBJECT ID: 10.5428/pcar20130420

PUBLISHER: Yaoxue Fuwu Yu Yanjiu Zazhishe

DOCUMENT TYPE: Journal; General Review

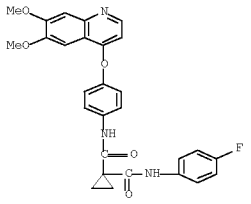
LANGUAGE: Chinese

AB A review. Newly approved antitumor drugs by FDA in 2012 were introduced.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(newly approved antitumor drugs by FDA in 2012)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 391 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:2006727 CAPLUS Full-text

DOCUMENT NUMBER: 160:380516

TITLE: Pharmacological and clinical studies of cabozantinib

AUTHOR(S): Zheng, Xi-yuan; Jiang, Han-jie; Pu, Xiao-ping

CORPORATE SOURCE: Department of Molecular and Cellular Pharmacology, School of Pharmaceutical Sciences, Peking University, Beijing, 100191, Peop. Rep. China

SOURCE: Zhongguo Xinyao Zazhi (2013), 22(17), 1990-1993
CODEN: ZXZHA6; ISSN: 1003-3734

PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi

DOCUMENT TYPE: Journal; General Review

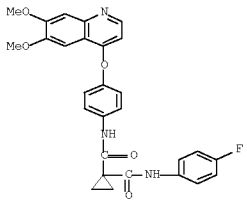
LANGUAGE: Chinese

AB A review. Cabozantinib, a new drug for medullary thyroid cancer treatment, is a potent inhibitor of MET, RET, and vascular endothelial factor receptor 2 (VEGFR2) as well as other tyrosine kinases that have been implicated in tumor development and progression. The mechanism, pharmacokinetics, drug interaction, clin. evaluation, and safety of cabozantinib were reviewed.

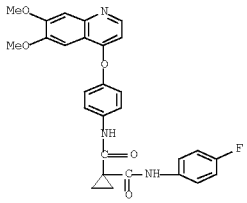
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. and clin. studies of cabozantinib)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

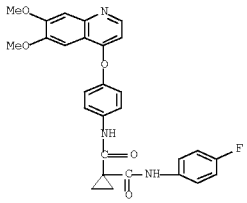


L4 ANSWER 392 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1965166 CAPLUS Full-text
DOCUMENT NUMBER: 160:155703
TITLE: Metastatic castration-resistant prostate cancer reveals intrapatient similarity and interpatient heterogeneity of therapeutic kinase targets
AUTHOR(S): Drake, Justin M.; Graham, Nicholas A.; Lee, John K.; Stoyanova, Tanya; Faltermeier, Claire M.; Sud, Sudha; Titz, Bjorn; Huang, Jiaoti; Pienta, Kenneth J.; Graeber, Thomas G.; Witte, Owen N.
CORPORATE SOURCE: Department of Microbiology, Immunology, and Molecular Genetics, David Geffen School of Medicine, University of California, Los Angeles, CA, 90095, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2013), 110(49), E4762-E4769,SE4762/1-SE4762/23
CODEN: PNASA6; ISSN: 0027-8424
DIGITAL OBJECT ID: 10.1073/pnas.1319948110
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In prostate cancer, multiple metastases from the same patient share similar copy number, mutational status, erythroblast transformation specific (ETS) rearrangements, and methylation patterns supporting their clonal origins. Whether actionable targets such as tyrosine kinases are also similarly expressed and activated in anatomically distinct metastatic lesions of the same patient is not known. We evaluated active kinases using phosphotyrosine peptide enrichment and quant. mass spectrometry to identify druggable targets in metastatic castration-resistant prostate cancer obtained at rapid autopsy. We identified distinct phosphopeptide patterns in metastatic tissues compared with treatment-naive primary prostate tissue and prostate cancer cell line-derived xenografts. Evaluation of metastatic castration-resistant prostate cancer samples for tyrosine phosphorylation and upstream kinase targets revealed SRC, epidermal growth factor receptor (EGFR), rearranged during transfection (RET), anaplastic lymphoma kinase (ALK), and MAPK1/3 and other activities while exhibiting intrapatient similarity and interpatient heterogeneity. Phosphoproteomic analyses and identification of kinase activation states in metastatic castration-resistant prostate cancer patients have allowed for the prioritization of kinases for further clin. evaluation.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphokinase profiling for drug targets of metastatic castration-resistant prostate cancer reveals intrapatient similarity and interpatient heterogeneity)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

L4 ANSWER 393 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1898455 CAPLUS Full-text
DOCUMENT NUMBER: 160:555100
TITLE: In Vitro and In Vivo Activity of Cabozantinib (XL184), an Inhibitor of RET, MET, and VEGFR2, in a Model of Medullary Thyroid Cancer
AUTHOR(S): Bentzien, Frauke; Zuzow, Marcus; Heald, Nathan; Gibson, Anna; Shi, Yongchang; Goon, Leanne; Yu, Peiwen; Engst, Stefan; Zhang, Wentao; Huang, Donghui; Zhao, Lora; Vysotskaia, Valentina; Chu, Felix; Bautista, Rajana; Cancilla, Belinda; Lamb, Peter; Joly, Alison H.; Yakes, F. Michael
CORPORATE SOURCE: ., Exelixis, Inc., South San Francisco, CA, USA
SOURCE: Thyroid (2013), 23(12), 1569-1577
CODEN: THYRER; ISSN: 1050-7256
DIGITAL OBJECT ID: 10.1089/thy.2013.0137
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: A limited no. of approved therapeutic options are available to metastatic medullary thyroid cancer (MTC) patients, and the response to conventional chemotherapy and/or radiotherapy strategies is inadequate. Sporadic and inherited mutations in the tyrosine kinase RET result in oncogenic activation that is associated with the pathogenesis of MTC. Cabozantinib is a potent inhibitor of MET, RET, and vascular endothelial factor receptor 2 (VEGFR2), as well as other tyrosine kinases that have been implicated in tumor development and progression. The object of this study was to determine the in vitro biochem. and cellular inhibitory profile of cabozantinib against RET, and in vivo antitumor efficacy using a xenograft model of MTC.Methods: Cabozantinib was evaluated in biochem. and cell-based assays that determined the potency of the compound against wild type and activating mutant forms of RET. Addnl., the pharmacodynamic modulation of RET and MET and in vivo antitumor activity of cabozantinib was examined in a MTC tumor model following subchronic oral administration.Results: In biochem. assays, cabozantinib inhibited multiple forms of oncogenic RET kinase activity, including M918T and Y791F mutants. Addnl., it inhibited proliferation of TT tumor cells that harbor a C634W activating mutation of RET that is most often associated with MEN2A and familial MTC. In these same cells grown as xenograft tumors in nude mice, oral administration of cabozantinib resulted in dose-dependent tumor growth inhibition that correlated with a reduction in circulating plasma calcitonin levels. Moreover, immunohistochem. analyses of tumors revealed that cabozantinib reduced levels of phosphorylated MET and RET, and decreased tumor cellularity, proliferation, and vascularization.Conclusions: Cabozantinib is a potent inhibitor of RET and prevalent mutationally activated forms of RET known to be associated with MTC, and effectively inhibits the growth of a MTC tumor cell model in vitro and in vivo.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of in vitro and in vivo antitumor efficacy of cabozantinib in preclin. model of medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



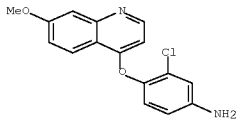
OS.CITING REF COUNT: 27 THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (27 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 394 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1873443 CAPLUS Full-text
DOCUMENT NUMBER: 160:50465
TITLE: Substituted quinoline compounds and use as Antitumor agents
INVENTOR(S): Xi, Ning; Wang, Tingjin; Zeng, Shan; Sun, Mingming; Wang, Kunrui
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 80pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013180949	A1	20131205	WO 2013-US41036	20130515

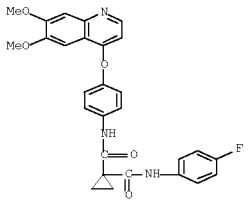
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61652210 P 20120527
OTHER SOURCE(S): CASREACT 160:50465; MARPAT 160:50465
GI



AB The present invention provides novel substituted quinoline compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted quinoline compds. and methods of use)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

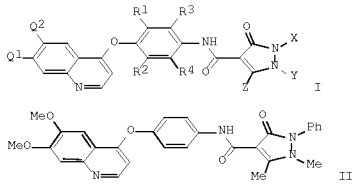


OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

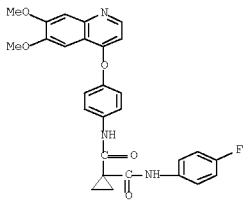
L4 ANSWER 395 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1866363 CAPLUS Full-text
DOCUMENT NUMBER: 160:33885
TITLE: Substituted quinoline compound useful in treatment of hyperproliferative diseases and its preparation
INVENTOR(S): Xi, Ning; Wang, Tingjin; Zeng, Shan; Sun, Mingming; Wang, Kunrui
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 57pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103420986	A	20131204	CN 2013-10179608	20130515
PRIORITY APPLN. INFO.:			CN 2012-10154478 A	20120518
			CN 2013-10118880 A	20130403

OTHER SOURCE(S): CASREACT 160:33885; MARPAT 160:33885
GI

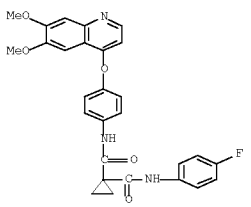


AB The invention relates to substituted quinoline compds. of formula I as protein kinase regulator useful in treatment of proliferative diseases and their preparation Compound I, wherein R1, R2, R3, and R4 are independently H, D, F, Cl, or Br; Q1 and Q2 are independently H, D, C1-6 alkyl, etc.; X and Z are independently H, D, C1-6 alkyl, etc.; Y is H, D, C2-6 alkynyl, etc.; their stereoisomers, N-oxides, solvates, pharmaceutically acceptable salts, are claimed. Compound II was prepared by multi-step procedure (procedure given). The present invention also relates to the pharmaceutical compns. containing the inventive compds., and method of application of the pharmaceutical composition for treatment of a mammal, especially hyperproliferative disease.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted quinoline compound useful in treatment of hyperproliferative diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 396 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:1864045 CAPLUS Full-text
DOCUMENT NUMBER: 161:30833
TITLE: An update on clinical trials of targeted therapies in thyroid cancer
AUTHOR(S): Haraldsdottir, Sigurdis; Shah, Manisha H.
CORPORATE SOURCE: The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA
SOURCE: Current Opinion in Oncology (2014), 26(1), 36-44
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0000000000000029
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Purpose of review: Several new targeted therapies with multikinase inhibitors targeting vascular endothelial growth factor (VEGF), rearranged during transfection and v-raf murine sarcoma viral oncogene homolog B1 pathways have been tested in clin. trials for radioiodine-refractory differentiated thyroid cancer (DTC) and medullary thyroid cancer (MTC) in the past 10 years. Recent findings: Results of the first phase III trial of VEGF-targeted therapy (sorafenib) in DTC were presented in June 2013, and two phase III trials with VEGF and rearranged during transfection-targeted therapies (vandetanib and cabozantinib) in MTC have led to approval by US Food and Drug Administration in the past 2 years. Whereas such therapies increase median progression-free survival compared to placebo, there is no therapy proven to improve overall survival yet. Significant potential adverse event risks associated with such therapies need to be recognized. Dissemination of knowledge about targeted therapies is critical for various medical specialists as patient care for thyroid cancers is best delivered in a multidisciplinary setting. Summary: Successful development of targeted systemic therapies in DTC and MTC in the past 5 years is incredibly exciting in the field and patients with advanced DTC/MTC now have new standard-of-care therapy options.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(update on clin. trials of targeted therapies in thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



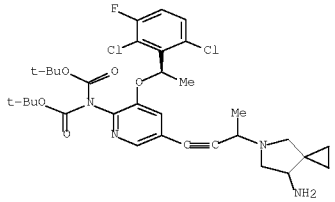
OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 397 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1837363 CAPLUS Full-text
DOCUMENT NUMBER: 160:28188
TITLE: Substituted alkynyl pyridine compounds and methods of use
INVENTOR(S): Xi, Ning; Yin, Lihua; Li, Xiaobo; Yu, Na; Wu, Yanjun
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013177092	A1	20131128	WO 2013-US41918	20130521

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61650513 P 20120523
OTHER SOURCE(S): CASREACT 160:28188; MARPAT 160:28188
GI

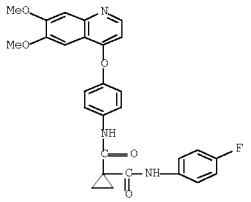


AB The present invention provides novel substituted alkynyl pyridine compds., pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted alkynyl pyridine compds. and methods of use)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 398 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:1836624 CAPLUS Full-text

DOCUMENT NUMBER: 160:28252

TITLE: Compounds and methods of use thereof for treating neurodegenerative disorders

INVENTOR(S): Zack, Donald J.; Welsbie, Derek Stuart; Yang, Zhiyong

PATENT ASSIGNEE(S): The Johns Hopkins University, USA

SOURCE: PCT Int. Appl., 106pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

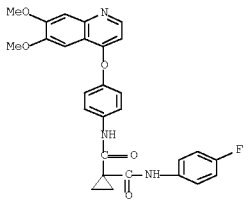
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013177367	A2	20131128	WO 2013-US42367	20130523

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY,



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 399 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:1823382 CAPLUS Full-text

DOCUMENT NUMBER: 161:178446

TITLE: Ocular adverse events of molecularly targeted agents approved in solid tumours: A systematic review

AUTHOR(S): Huillard, Olivier; Bakalian, Silvin; Levy, Christine; Desjardins, Laurence; Lumbroso-Le Rouic, Livia; Pop, Simona; Sablin, Marie-Paule; Le Tourneau, Christophe

CORPORATE SOURCE: Department of Medical Oncology, Clinical Trial Unit, Institut Curie, Paris, Fr.

SOURCE: European Journal of Cancer (2014), 50(3), 638-648
CODEN: EJCAEL; ISSN: 0959-8049

DIGITAL OBJECT ID: 10.1016/j.ejca.2013.10.016

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB When using molecularly targeted agents (MTAs), oncologists and patients face new and sometimes unexpected toxicities. Though ocular adverse events (OAEs) are not uncommon with chemotherapy, they are rarely severe or dose limiting. Ocular toxicity profile may differ with MTAs, indeed severe and dose limiting toxicities have been described with targeted therapies currently under investigation. Our study aimed to review OAEs experienced with MTAs approved in solid tumors. This review revealed that many OAEs, frequent and potentially severe, exist and concern most MTAs. The suggestion is prompt referral of patients with severe pain and/or visual impairment to the ophthalmologist since these symptoms can be associated with potentially severe OAE and need ophthalmic assessment. Oncologists must be aware of such events and their potential severity for better treatment and better diagnosis in daily practice as well as in clin. trials.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ocular adverse events of molecularly targeted agents approved in solid tumors)

RN 849217-68-1 CAPLUS

MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

EP 2852388	A2	20150401	EP 2013-793466	20130523

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

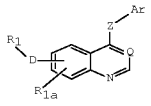
US 20150164906	A1	20150618	US 2014-14403523	20141124
US 9539259	B2	20170110		

PRIORITY APPLN. INFO.:

US 2012-61650613	P	20120523
US 2012-61680931	P	20120808
WO 2013-US42367	W	20130523

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

GI



I

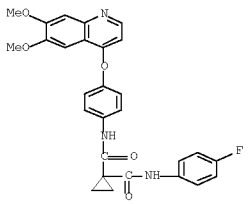
AB In some embodiments, the presently disclosed subject matter provides a method for treating or preventing a neurodegenerative disease, disorder, or condition in a subject in need thereof, the method comprising administering to the subject a 15 therapeutically effective amount of a compound of Formula I (wherein D is selected from the group consisting of O, S(O)0-2, and NR1b; R1a is selected from the group consisting of H, substituted or unsubstituted alkyl, halogen, OR1b, NO2, NR1bR1c; wherein: R1b and R1c are each independently selected from the group consisting of H or substituted or unsubstituted alkyl, aryl, etc.; R1 is H, substituted alkyl, aryl, etc.; Q is CR2a or N wherein R2a is H, alkyl or cyano; Z is O, NR1b and S(O)0-2; and Ar is substituted aryl or substituted heteroaryl), or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, thereby treating or preventing the neurodegenerative disease, disorder, or condition.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. and methods of use thereof for treating neurodegenerative disorders in relation to use of other agents and diagnosis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 400 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:1802363 CAPLUS Full-text

DOCUMENT NUMBER: 160:509021

TITLE: Multivoxel 1H MR spectroscopy is superior to contrast-enhanced MRI for response assessment after anti-angiogenic treatment of orthotopic human glioma xenografts and provides handles for metabolic targeting

AUTHOR(S): Hamans, Bob; Navis, Anna Catharina; Wright, Alan; Wesseling, Pieter; Heerschap, Arend; Leenders, William

CORPORATE SOURCE: Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.

SOURCE: Neuro-Oncology (Cary, NC, United States) (2013), 15(12), 1615-1624
CODEN: NEURJR; ISSN: 1522-8517

DIGITAL OBJECT ID: 10.1093/neuonc/not129

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; (online computer file)

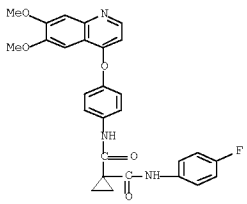
LANGUAGE: English

AB Background Anti-angiogenic treatment of glioblastoma characteristically results in therapy resistance and tumor progression via diffuse infiltration. Monitoring tumor progression in these patients is thwarted because therapy results in tumor invisibility in contrast-enhanced (CE) MRI. To address this problem, we examined whether tumor progression could be monitored by metabolic mapping using 1H MR spectroscopic imaging (MRSI). Methods We treated groups of BALB/c nu/nu mice carrying different orthotopic diffuse-infiltrative glioblastoma xenografts with bevacizumab (anti-vascular endothelial growth factor [VEGF] antibody, n = 13), cabozantinib (combined VEGF receptor 2/c-Met tyrosine kinase inhibitor, n = 11), or placebo (n = 15) and compared CE-MRI with MRS-derived metabolic maps before, during, and after treatment. Metabolic maps and CE-MRIs were

subsequently correlated to histol. and immunohistochem. Results In vivo imaging of choline/n-acetyl aspartate ratios via multivoxel MRS is better able to evaluate response to therapy than CE-MRI. Lactate imaging revealed that diffuse infiltrative areas in glioblastoma xenografts did not present with excessive glycolysis. In contrast, glycolysis was observed in hypoxic areas in angiogenesis-dependent compact regions of glioma only, especially after anti-angiogenic treatment. Conclusion Our data present MRSI as a powerful and feasible approach that is superior to CE-MRI and may provide handles for optimizing treatment of glioma. Furthermore, we show that glycolysis is more prominent in hypoxic areas than in areas of diffuse infiltrative growth. The Warburg hypothesis of persisting glycolysis in tumors under normoxic conditions may thus not be valid for diffuse glioma.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolic mapping via multivoxel magnetic resonance spectroscopy imaging than contrast-enhanced MRI showed better tumor progression after antiangiogenic Avastin and Exelixis treatment in mouse xenografted with human glioma cell)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



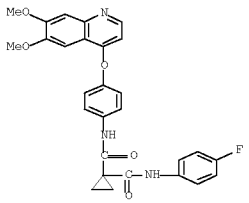
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 401 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1792084 CAPLUS Full-text
DOCUMENT NUMBER: 159:737215
TITLE: Cabozantinib in progressive medullary thyroid cancer
AUTHOR(S): Elisei, Rossella; Schlumberger, Martin J.; Mueller, Stefan P.; Schoffski, Patrick; Brose, Marcia S.; Shah, Manisha H.; Licitra, Lisa; Jarzab, Barbara; Medvedev, Viktor; Kreissl, Michael C.; Niederle, Bruno; Cohen, Ezra E. W.; Wirth, Lori J.; Ali, Haythem; Hessel, Colin; Yaron, Yifah; Ball, Douglas; Nelkin, Barry; Sherman, Steven I.
CORPORATE SOURCE: University of Pisa, Pisa, Italy
SOURCE: Journal of Clinical Oncology (2013), 31(29), 3639-3646
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.48.4659
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: Cabozantinib, a tyrosine kinase inhibitor (TKI) of hepatocyte growth factor receptor (MET), vascular endothelial growth factor receptor 2, and rearranged during transfection (RET), demonstrated clin. activity in patients with medullary thyroid cancer (MTC) in phase I. Patients and Methods: We conducted a double-blind, phase III trial comparing cabozantinib with placebo in 330 patients with documented radiog. progression of metastatic MTC. Patients were randomly assigned (2:1) to cabozantinib (140 mg per day) or placebo. The primary end point was progression-free survival (PFS). Addnl. outcome measures included tumor response rate, overall survival, and safety. Results: The estimated median PFS was 11.2 mo for cabozantinib vs. 4.0 mo for placebo (hazard ratio, 0.28; 95% CI, 0.19 to 0.40; P < .001). Prolonged PFS with cabozantinib was observed across all subgroups including by age, prior TKI treatment, and RET mutation status (hereditary or sporadic). Response rate was 28% for cabozantinib and 0% for placebo; responses were seen regardless of RET mutation status. Kaplan-Meier ests. of patients alive and progression-free at 1 yr are 47.3% for cabozantinib and 7.2% for placebo. Common cabozantinib-associated adverse events included diarrhea, palmar-plantar erythrodysesthesia, decreased weight and appetite, nausea, and fatigue and resulted in dose redns. in 79% and holds in 65% of patients. Adverse events led to treatment discontinuation in 16% of cabozantinib-treated patients and in 8% of placebo-treated patients. Conclusion: Cabozantinib (140 mg per day) achieved a statistically significant improvement of PFS in patients with progressive metastatic MTC and represents an important new treatment option for patients with this rare disease. This dose of cabozantinib was associated with significant but manageable toxicity.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in progressive medullary thyroid cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 145 THERE ARE 145 CAPLUS RECORDS THAT CITE THIS RECORD (147 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 402 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1772555 CAPLUS Full-text
DOCUMENT NUMBER: 159:738209
TITLE: Methods for determining nucleotide sequence
INVENTOR(S): Iafrate, Anthony John; Le, Long Phi; Zheng, Zongli
PATENT ASSIGNEE(S): The General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013169339	A1	20131114	WO 2013-US30201	20130311
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2873176	A1	20131114	CA 2013-2873176	20130311
US 20130303461	A1	20131114	US 2013-13793564	20130311
US 9487828	B2	20161108		
EP 2847353	A1	20150318	EP 2013-787745	20130311
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CN 104603287	A	20150506	CN 2013-80037100	20130311
JP 2015517307	T	20150622	JP 2015-511444	20130311
PRIORITY APPLN. INFO.:			US 2012-61645364 P	20120510
			US 2012-61679302 P	20120803
			WO 2013-US30201 W	20130311

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

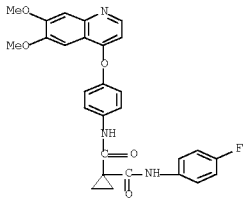
AB The technol. described herein is directed to methods of detg. oligonucleotide sequences, e.g. by enriching target sequences prior to sequencing the sequences. The invention provides the sequences of the DNA primers used for sequencing anal. The target sequence may be genomic DNA, RNA or cDNA with or without gene rearrangement.

IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for determining nucleotide sequence)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

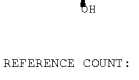
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



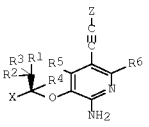
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

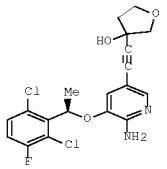
L4 ANSWER 403 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1771791 CAPLUS Full-text
DOCUMENT NUMBER: 159:742705
TITLE: Substituted alkynyl pyridine compounds as protein kinase regulator useful in treatment various diseases and their preparation
INVENTOR(S): Xi, Ning; Yin, Lihua; Li, Xiaobo; Yu, Na; Wu, Yanjun
PATENT ASSIGNEE(S): HEC Pharm Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing, 65pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103387535	A	20131113	CN 2013-10173770	20130510
CN 103387535	B	20160601		

PRIORITY APPLN. INFO.: CN 2012-10141993 A 20120510
CN 2013-10116652 A 20130403
OTHER SOURCE(S): CASREACT 159:742705; MARPAT 159:742705
GI

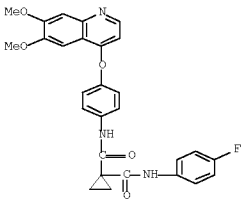

I


II

AB The invention relates to substituted alkynyl pyridine compds. of formula I as protein kinase regulator useful in treatment of various diseases and their preparation Compds. I, wherein R1, R2, R3, R4, R5 and R6 are independently H, D or F; X is C6-10 aryl or heteroaryl containing 5-10 atoms; Z is C1-6 alkyl, C3-6 cycloalkyl, C3-6 heterocyclic radical, etc.; their stereoisomers, solvates, N-oxidants, pharmaceutically acceptable salts, are claimed. Compound II was prepared by multi-step procedure (procedure given). The invention compds. were evaluated for their ALK(h) kinase activity. From assay, it was determined that II exhibited the IC50 value of 52 nM against ALK(h).

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted alkynyl pyridine compds. as protein kinase regulator useful in treatment of various diseases)

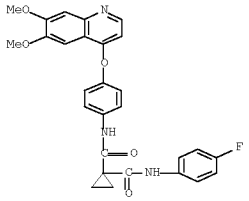
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 405 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1734775 CAPLUS Full-text
DOCUMENT NUMBER: 159:691817
TITLE: A dual MET-VEGF modulator for treating osteolytic bone metastases
INVENTOR(S): Aftab, Dana T.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013166296	A1	20131107	WO 2013-US39284	20130502
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2844254	A1	20150311	EP 2013-722238	20130502
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2015515988	T	20150604	JP 2015-510456	20130502
US 20150133494	A1	20150514	US 2014-14398188	20141031



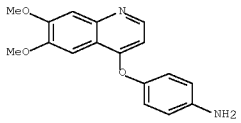
L4 ANSWER 404 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1746648 CAPLUS Full-text
DOCUMENT NUMBER: 160:200751
TITLE: Cabozantinib: a novel agent with a dual mechanism of action for castration-resistant prostate carcinoma
AUTHOR(S): Pinto, Alvaro
CORPORATE SOURCE: Medical Oncology Department, University Hospital La Paz-IdiPAZ, Madrid, Spain
SOURCE: Cancer Chemotherapy and Pharmacology (2014), 73(2), 219-222
CODEN: CCPHDZ; ISSN: 0344-5704
DIGITAL OBJECT ID: 10.1007/s00280-013-2343-2
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. The landscape of castration-resistant prostate carcinoma has changed completely in the last few years, with the approval of four new agents with proven benefit in overall survival. Abiraterone, cabazitaxel, enzalutamide and radium-223 dichloride have been added to the armamentarium of available agents for the treatment of these patients. We still lack information about which agent works best in an individual patient and how to optimally use them in a sequential strategy. Cabozantinib, a targeted agent against MET and vascular endothelial growth factor receptor-2, has shown promising results and could become the first targeted therapy to be approved for castration-resistant prostate carcinoma. This paper reviews the clin. development of cabozantinib in prostate cancer and future research possibilities for this drug.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib, a novel agent with a dual mechanism of action for castration-resistant prostate carcinoma)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

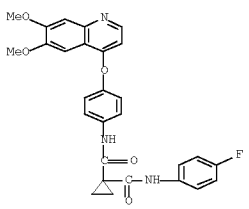
PRIORITY APPLN. INFO.: US 2012-61641837 P 20120502
WO 2013-US39284 W 20130502
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 159:691817; MARPAT 159:691817
GI



AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and osteolytic bone metastases, with a dual inhibitor of MET and VEGF.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



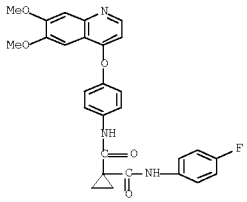
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with

N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

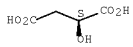
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CM 2

CRN 97-67-6
CMF C4 H6 O5

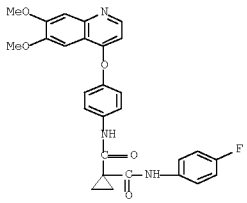
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual MET-VEGF modulator for treating osteolytic bone metastases)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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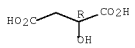
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CMF C28 H24 F N3 O5



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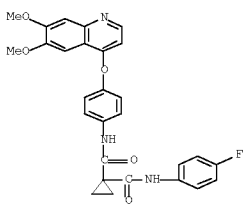
CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 406 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1717033 CAPLUS Full-text
DOCUMENT NUMBER: 160:363229
TITLE: Cabozantinib inhibits growth of androgen-sensitive and castration-resistant prostate cancer and affects bone remodeling
AUTHOR(S): Nguyen, Holly M.; Ruppender, Nazanin; Zhang, Xiaotun; Brown, Lisha G.; Gross, Ted S.; Morrissey, Colm; Gulati, Roman; Vessella, Robert L.; Schimmoller, Frauke; Aftab, Dana T.; Corey, Eva
CORPORATE SOURCE: Department of Urology, University of Washington, Seattle, WA, USA
SOURCE: PLoS One (2013), 8(10), e78881
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0078881
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Cabozantinib is an inhibitor of multiple receptor tyrosine kinases, including MET and VEGFR2. In a phase II clin. trial in advanced prostate cancer (PCa), cabozantinib treatment improved bone scans in 68% of evaluable patients. Our studies aimed to determine the expression of cabozantinib targets during PCa progression and to evaluate its efficacy in hormone-sensitive and castration-resistant PCa in preclin. models while delineating its effects on tumor and bone. Using immunohistochem. and tissue microarrays containing normal prostate, primary PCa, and soft tissue and bone metastases, our data show that levels of MET, P-MET, and VEGFR2 are increasing during PCa progression. Our data also show that the expression of cabozantinib targets are particularly pronounced in bone metastases. To evaluate cabozantinib efficacy on PCa growth in the bone environment and in soft tissues we used androgen-sensitive LuCaP 23.1 and castration-resistant C4-2B PCa tumors. In vivo, cabozantinib inhibited the growth of PCa in bone as well as growth of s.c. tumors. Furthermore, cabozantinib treatment attenuated the bone response to the tumor and resulted in increased normal bone volume In summary, the expression pattern of cabozantinib targets in primary and castration-resistant metastatic PCa, and its efficacy in two different models of PCa suggest that this agent has a strong potential for the effective treatment of PCa at different stages of the disease.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET, VEGFR2, RET expressions were found higher while cabozantinib by inhibiting these targets, it safely, effectively inhibited tumor growth, improved bone remodeling in human androgen-sensitive, metastatic CRPC tumor xenografted mouse)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

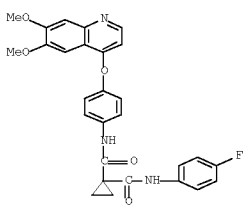


OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 407 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1698309 CAPLUS Full-text
DOCUMENT NUMBER: 159:662217
TITLE: Detection of RET fusions in cancer
INVENTOR(S): Doebele, Robert; Garcia, Marileila Varella; Le, Anh T.; Xu, Liangguo
PATENT ASSIGNEE(S): University of Colorado, USA
SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013163428	A1	20131031	WO 2013-US38215	20130425
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2012-61638452 P 20120425
AB Disclosed are methods and assay systems for the identification of chromosomal rearrangements involving the RET kinase gene in cellular samples. Further described are methods for identifying cancer patients who are predicted to respond, or not respond to the therapeutic administration of a chemotherapeutic regimen including one or more kinase inhibitor(s), to treat cancer in the patient.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detection of RET fusions in cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



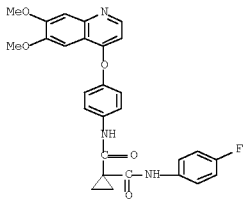
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 408 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1679191 CAPLUS Full-text
DOCUMENT NUMBER: 160:82446
TITLE: Commentary on "Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial." Smith DC, Smith MR, Sweeney C, Elfiky AA, Logothetis C, Corn PG, Vogelzang NJ, Small EJ, Harzstark AL, Gordon MS, Vaishampayan UN, Haas NB, Spira AI, Lara PN Jr, Lin CC, Srinivas S, Sella A, SchoffskiSchoeffski P, Scheffold C, Weitzman AL, Hussain M, University of Michigan, Ann Arbor, MI
AUTHOR(S): Trump, Donald L.
CORPORATE SOURCE: Neth.
SOURCE: Urologic Oncology: Seminars and Original Investigations (2013), 31(8), 1848
CODEN: UOSOAA; ISSN: 1078-1439
DIGITAL OBJECT ID: 10.1016/j.urolonc.2013.07.012
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Cabozantinib (XL184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. Patients received 100 mg of cabozantinib daily. Those with stable disease per RECIST at 12 wk were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 wk and progression-free survival (PFS) after random assignment. One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 wk was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 wk (95% CI, 10.7 to 62.4 wk) with cabozantinib and 5.9 wk (95% CI, 5.4 to 6.6 wk) with placebo (hazard ratio, 0.12; P<.001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by≥50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot syndrome (8%). Cabozantinib has clin. activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and redns. in bone turnover markers, pain, and narcotic use.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in patients with advanced prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

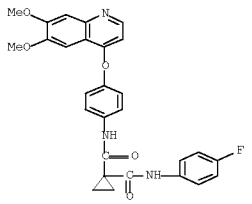
L4 ANSWER 409 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1655693 CAPLUS Full-text
DOCUMENT NUMBER: 159:632725
TITLE: Menainv and cancer invasion and metastasis diagnosis and antitumor screening
INVENTOR(S): Gertler, Frank B.; Hughes-Alford, Shannon K.; Lauffenburger, Douglas A.; Neil, Jason; White, Forest; Condeelis, John S.; Oudin, Madeleine J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA; Albert Einstein College of Medicine of Yeshiva University
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013158485	A1	20131024	WO 2013-US36336	20130412
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
US 20150044234	A1	20150212	US 2014-14390113	20141002
PRIORITY APPLN. INFO.:			US 2012-61625985 P	20120418
			US 2013-61778767 P	20130313
			WO 2013-US36336 W	20130412

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods and compns. are provided for diagnosing or inhibiting invasion or metastasis of a cancer in a subject based on MenaINV. A method is provided of identifying an agent as an inhibitor of sarcoma or carcinoma cell invasion or as an inhibitor of metastasis of a carcinoma or sarcoma, comprising contacting a preparation comprising a growth factor receptor and a protein tyrosine phosphatase 1b (PTP1b) in the presence of an amount of MenaINV and an amount of Mena and quantifying the association of the growth factor receptor and PTP1b in the presence of the agent and in the absence of the agent. An agent that increases the association of growth factor receptor and PTP1b in the presence of the agent as compared to in the absence of the agent is identified as an inhibitor of sarcoma or carcinoma cell invasion or of metastasis, and an agent that does not increase, or decreases, the association of growth factor receptor and PTP1b in the presence of the agent as compared to in the absence of the agent is not identified as an inhibitor of sarcoma or carcinoma cell invasion or metastasis. A further method is provided of identifying an agent as an inhibitor of sarcoma or carcinoma cell invasion or of metastasis of a carcinoma or sarcoma, the method comprising contacting a preparation comprising an amount of MenaINV, an amount of Mena, and a protein, wherein the protein is phosphorylated, with the agent and PTP1b and quantifying phosphorylation of the protein at the site or sites. A decrease in phosphorylation in (a) the presence of the agent and PTP1b as compared to (b) in the absence of the agent and presence of PTP1b identifies the agent as an inhibitor of sarcoma or carcinoma cell invasion or metastasis, and wherein an increase in, or no change in, phosphorylation in (i) the presence of the agent and PTP1b as compared to (ii) in the absence of the agent and presence of PTP1b does not identify the agent as an inhibitor of sarcoma or carcinoma cell invasion or metastasis.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Menainv and cancer invasion and metastasis diagnosis and antitumor screening)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 410 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1629334 CAPLUS Full-text
DOCUMENT NUMBER: 159:602931
TITLE: Method for the prognosis and treatment of cancer metastasis
INVENTOR(S): Arnal, Anna; Tarragona, Maria; Pavlovic, Milica; Planet, Evarist; Gomis, Roger
PATENT ASSIGNEE(S): Inbiomotion S.L., Spain
SOURCE: PCT Int. Appl., 150pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013153458	A2	20131017	WO 2013-IB1204	20130315
WO 2013153458	A3	20140227		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
EP 2650682	A1	20131016	EP 2012-382139	20120409
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CA 2891609	A1	20131017	CA 2013-2891609	20130315
AU 2013246618	A1	20141106	AU 2013-246618	20130315
KR 2015014919	A	20150209	KR 2014-7031148	20130315
EP 2836837	A2	20150218	EP 2013-731875	20130315
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104797935	A	20150722	CN 2013-80027292	20130315
JP 2015520606	T	20150723	JP 2015-505034	20130315
US 20150293100	A1	20151015	US 2014-14391085	20141007
US 20160139126	A9	20160519		
MX 2014012233	A	20150617	MX 2014-12233	20141009
PRIORITY APPLN. INFO.:			EP 2012-382139 A	20120409
			US 2012-61621949 P	20120409
			US 2012-61724807 P	20121109
			US 2012-61732175 P	20121130
			WO 2013-IB1204 W	20130315

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

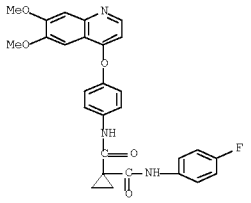
AB The present invention relates to a method for the prognosis of bone metastasis in triple neg. (including basal-like) breast cancer or, alternatively, ER+

breast cancer (including luminal A and β) which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level, amplification or translocation. The invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of triple neg. (including basal-like) breast cancer metastasis or, alternatively, ER+ breast cancer (including luminal A and B) metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for the prognosis and treatment of cancer metastasis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 411 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:1622779 CAPLUS Full-text

DOCUMENT NUMBER: 160:260019

TITLE: Novel Modeling of Cancer Cell Signaling Pathways Enables Systematic Drug Repositioning for Distinct Breast Cancer Metastases

AUTHOR(S): Zhao, Hong; Jin, Guangxu; Cui, Kemi; Ren, Ding; Liu, Timothy; Chen, Peikai; Wong, Solomon; Li, Fuhai; Fan, Yubo; Rodriguez, Angel; Chang, Jenny; Wong, Stephen T. C.

CORPORATE SOURCE: Department of Systems Medicine and Bioengineering; NCI Center for Modeling Cancer Development, The Methodist Hospital Research Institute, Weill Cornell Medical College; Methodist Cancer Center, The Methodist Hospital, Dan L. Duncan Cancer Center, Baylor College of Medicine, Houston, TX, USA

SOURCE: Cancer Research (2013), 73(20), 6149-6163
CODEN: CNREA8; ISSN: 0008-5472

DIGITAL OBJECT ID: 10.1158/0008-5472.CAN-12-4617

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

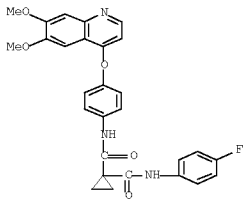
LANGUAGE: English

AB A new type of signaling network element, called cancer signaling bridges (CSB), has been shown to have the potential for systematic and fast-tracked drug repositioning. On the basis of CSBs, we developed a computational model to derive specific downstream signaling pathways that reveal previously unknown target-disease connections and new mechanisms for specific cancer subtypes. The model enables us to reposition drugs based on available patient gene expression data. We applied this model to repurpose known or shelved drugs for brain, lung, and bone metastases of breast cancer with the hypothesis that cancer subtypes have their own specific signaling mechanisms. To test the hypothesis, we addressed specific CSBs for each metastasis that satisfy (i) CSB proteins are activated by the maximal number of enriched signaling pathways specific to a given metastasis, and (ii) CSB proteins are involved in the most differential expressed coding genes specific to each breast cancer metastasis. The identified signaling networks for the three types of breast cancer metastases contain 31, 15, and 18 proteins and are used to reposition 15, 9, and 2 drug candidates for the brain, lung, and bone metastases. We conducted both in vitro and in vivo preclin. expts. as well as anal. on patient tumor specimens to evaluate the targets and repositioned drugs. Of special note, we found that the Food and Drug Administration-approved drugs, sunitinib and dasatinib, prohibit brain metastases derived from breast cancer, addressing one particularly challenging aspect of this disease.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel developed cancer signaling bridges-based computational model enabled systematic drug repositioning for brain, lung and bone metastasis in human breast cancer cell and in xenografted mouse model)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 412 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:1619978 CAPLUS Full-text

DOCUMENT NUMBER: 159:634400

TITLE: Method for the prognosis and treatment of cancer metastasis

INVENTOR(S): Gomis Cabre, Roger; Planet, Evarist; Pavlovic, M. Milica

PATENT ASSIGNEE(S): Fundacio Privada Institut de Recerca Biomedica, Spain; Fundacio Privada Institucio Catalana de Recerca i Estudis Avancats

SOURCE: Eur. Pat. Appl., 51pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2650682	A1	20131016	EP 2012-382139	20120409
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CA 2891609	A1	20131017	CA 2013-2891609	20130315
WO 2013153458	A2	20131017	WO 2013-IB1204	20130315
WO 2013153458	A3	20140227		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
AU 2013246618	A1	20141106	AU 2013-246618	20130315
KR 2015014919	A	20150209	KR 2014-7031148	20130315
EP 2836837	A2	20150218	EP 2013-731875	20130315
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 104797935	A	20150722	CN 2013-80027292	20130315
JP 2015520606	T	20150723	JP 2015-505034	20130315
US 20150293100	A1	20151015	US 2014-14391085	20141007
US 20160139126	A9	20160519		
MX 2014012233	A	20150617	MX 2014-12233	20141009

PRIORITY APPLN. INFO.: EP 2012-382139 A 20120409
US 2012-61621949 P 20120409
US 2012-61724807 P 20121109
US 2012-61732175 P 20121130
WO 2013-IB1204 W 20130315

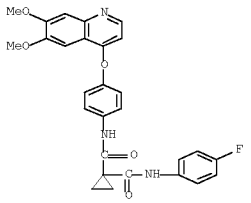
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to a method for the prognosis of bone metastasis in triple neg. (including basal-like) breast cancer which comprises determining if the c-MAF gene is amplified in a primary tumor sample. Likewise, the invention also relates to a method for determining the tendency to develop bone metastasis with respect to metastasis in other organs, which comprise determining the c-MAF gene expression level. The invention also relates to a method for predicting early bone metastasis in a subject suffering breast cancer. The invention also relates to a c-MAF inhibitor as therapeutic agent for use in the treatment of triple neg. (including basal-like) breast cancer metastasis. The invention relates to kits for predicting bone metastasis and predicting the clin. outcome of a subject suffering from bone metastasis. Finally, the invention relates to a method for typing of a subject suffering breast cancer and for classifying a subject from breast cancer into a cohort.

IT 849217-68-1, CAbozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for the prognosis and treatment of cancer metastasis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 413 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:1549396 CAPLUS Full-text

DOCUMENT NUMBER: 159:577130

TITLE: Preparation of spirobicyclyl substituted pyrazolyl pyridinamine compounds as tyrosine kinase inhibitors for treating hyperproliferative disorders

INVENTOR(S): Xi, Ning; Li, Minxiong; Zhou, Xuan; Wu, Yanjun

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 90pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013148537	A1	20131003	WO 2013-US33633	20130325

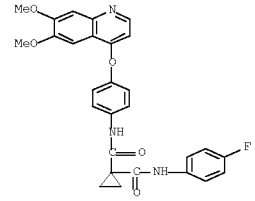
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61617626 P 20120329
OTHER SOURCE(S): CASREACT 159:577130; MARPAT 159:577130
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

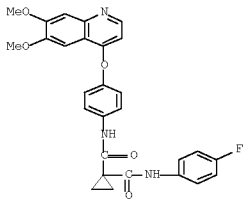
AB The present invention provides spirobicyclic compds. of general formula I (wherein R1-R6 are independently H, D, or F; each X and Y is independently (un)substituted C6-10aryl or (un)substituted 5-10 membered heteroaryl; Z is (un)substituted C5-12spirobicyclyl or (un)substituted -(C1-4alkylene)-(C5-12spirobicyclyl)-, with provisos), pharmaceutical acceptable salts and formulations thereof useful in modulating protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. The invention also provides pharmaceutically acceptable compns. comprising such compds. and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans. Synthetic procedures for preparing I are exemplified. For example, II was prepared in a 12-step synthesis that culminated in reaction of intermediates III and IV. II inhibited ALK kinase and c-Met kinase with IC50 values of 15 and 9 nM, resp.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of spirobicyclyl substituted pyrazolyl pyridinamine compds. as tyrosine kinase inhibitors for treating hyperproliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 415 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 414 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1459937 CAPLUS Full-text
DOCUMENT NUMBER: 159:472093
TITLE: Preparation of substituted pyrazolylpyridinamine compounds as protein tyrosine kinase modulators for treatment of hyperproliferative disorders
INVENTOR(S): Xi, Ning; Wang, Tingjin; Yi, Lei
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 141pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013138210	A1	20130919	WO 2013-US30096	20130311

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2012-61610473 P 20120314
US 2012-61617626 P 20120329
OTHER SOURCE(S): CASREACT 159:472093; MARPAT 159:472093
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides substituted pyrazolylpyridinamine compds. of formula I as protein tyrosine kinase modulators capable of regulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion for use in the treatment of hyperproliferative disorders. Compds. of formula I [wherein each R1, R2, R3, R4, R5, and R6 are independently H, D, or F; Z is substituted C3-7 heterocyclyl, substituted (C1-4 alkylene)-(C3-7 heterocyclyl), (un)substituted C5-12 fused bicyclyl, etc.;] stereoisomers, geometric isomers, tautomers, N-oxides, solvates, metabolites, or pharmaceutically acceptable salts or prodrugs thereof are claimed and prepared For example, II was prepared by the reaction of 4-iodo-1-(4-((tetrahydro-2H-pyran-2-yl)oxy)tetrahydrofuran-3-yl)-1H-pyrazole with III followed by removal of the tetrahydro-2H-pyran and deprotection of the amine group to afford II in 80% yield. Pharmacodynamic and pharmacokinetic assays were performed on II. II inhibited ALK kinase and c-Met kinase with IC50 of 5 nM and 4 nM resp., demonstrated 82% inhibition of glioblastoma tumor growth when dosed orally at 60 mg/kg to mice, and exhibited a half-life of 35.37 min in human microsomes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of substituted pyrazolylpyridinamine compds. as protein tyrosine kinase modulators for treatment of hyperproliferative disorders)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

ACCESSION NUMBER: 2013:1270627 CAPLUS Full-text
DOCUMENT NUMBER: 159:384885
TITLE: Epithelial membrane protein 2 (EMP2) regulates angiogenesis in cancer cells through induction of VEGF
INVENTOR(S): Wadehra, Madhuri; Braun, Jonathan; Gordon, Lynn K.
PATENT ASSIGNEE(S): University of California, USA; United States Dept. of Veterans Affairs
SOURCE: PCT Int. Appl., 84pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013119693	A1	20130815	WO 2013-US24968	20130206

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2863986	A1	20130815	CA 2013-2863986	20130206
AU 2013203424	A1	20130822	AU 2013-203424	20130206
EP 2812354	A1	20141217	EP 2013-747090	20130206

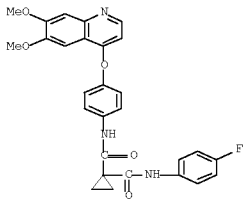
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2015508066	T	20150316	JP 2014-555854	20130206
US 20150079089	A1	20150319	US 2014-14376724	20140805
AU 2016204335	A1	20160721	AU 2016-204335	20160624

PRIORITY APPLN. INFO.: US 2012-61595617 P 20120206
AU 2013-203424 A3 20130206
WO 2013-US24968 W 20130206
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

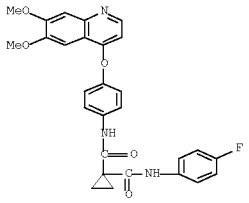
AB The authors disclose the targeting of epithelial membrane protein 2 (EMP2) for the treatment and prevention of endometrial cancer. In one example, EMP2 expression directly correlated with VEGF protein levels as well as with secreted protein expression by endometrial adenocarcinoma cells. Ribozyme-mediated reduction of EMP2 resulted in undetectable levels of VEGF.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with anti-EMP2 antibodies for treatment of uterine cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 416 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1255893 CAPLUS Full-text
DOCUMENT NUMBER: 159:660795
TITLE: Ponatinib is a potent inhibitor of wild-type and drug-resistant gatekeeper mutant RET kinase
AUTHOR(S): Mologni, Luca; Redaelli, Sara; Morandi, Andrea; Plaza-Menacho, Ivan; Gambacorti-Passerini, Carlo
CORPORATE SOURCE: Dept. of Health Sciences, University of Milano-Bicoccavia Cadore, Monza, 20900, Italy
SOURCE: Molecular and Cellular Endocrinology (2013), 377(1-2), 1-6
CODEN: MCEND6; ISSN: 0303-7207
DIGITAL OBJECT ID: 10.1016/j.mce.2013.06.025
PUBLISHER: Elsevier Ireland Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB RET kinase is aberrantly activated in thyroid cancers and in rare cases of lung and colon cancer, and has been validated as a mol. target in these tumors. Vandetanib was recently approved for the treatment of medullary thyroid cancer. However, vandetanib is ineffective in vitro against RET mutants carrying bulky aminoacids at position 804, the gatekeeper residue, similarly to drug-resistant BCR-ABL mutants in chronic myeloid leukemia. Ponatinib is a multi-target kinase inhibitor that was recently approved for treatment-refractory Philadelphia-pos. leukemia. We show here potent inhibition of oncogenic RET by ponatinib, including the drug-insensitive V804M/L mutants. Ponatinib inhibited the growth of RET+ and BCR-ABL+ cells with similar potency, while not affecting RET-neg. cells. Both in biochem. and in cellular assays ponatinib compared favorably with known RET inhibitors, such as vandetanib, cabozantinib, sorafenib, sunitinib and motesanib, used as reference compds. We suggest that ponatinib should be considered for the treatment of RET+ tumors, in particular those expressing vandetanib-resistant V804M/L mutations.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 418 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1227139 CAPLUS Full-text
DOCUMENT NUMBER: 159:329544
TITLE: Methods for predicting tumor response to targeted therapies with signal transduction pathway inhibitors using biomarkers
INVENTOR(S): Cohen, Jonathan M.; Derrien-Colemyn, Alexandrine Josephe; Gillespie, John Williams; Park, Soon Sik
PATENT ASSIGNEE(S): 20/20 Gene Systems, Inc., USA
SOURCE: PCT Int. Appl., 146pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013116735	A1	20130808	WO 2013-US24456	20130201

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

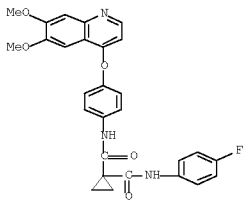
US 20140378500	A1	20141225	US 2014-14375827	20140731

PRIORITY APPLN. INFO.:

US 2012-61593688	P	20120201
US 2012-61654400	P	20120601
US 2012-61660305	P	20120615
US 2012-61660692	P	20120616
US 2012-61665943	P	20120629
US 2012-61699760	P	20120911
US 2012-61699874	P	20120912
WO 2013-US24456	W	20130201

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A method for identifying cancer patients that are likely to be responders or non-responders to a signal transduction pathway inhibitor is described. The present invention is directed to methods and tests that help predict the likelihood that a tumor will respond to a targeted therapy so that those cancer patients most likely to benefit can receive that drug in a timely manner and those patients unlikely to benefit from a particular drug can instead be prescribed alternative therapies. The test comprises a panel of two or more biomarkers that are part of a signal transduction pathway. The biomarkers included in the panel, in combination, express differently in tumors that respond the drug from those that do not respond. The drugs to which these tests predict response may be designed or determined to target the signal transduction pathway of which the biomarker panel is associated Examples of such drugs are those that target angiogenesis pathways like VEGF or cellular growth pathways like mTOR. Alternatively, the drugs might target something other than the pathway with which the biomarkers are associated but activation of that pathway might otherwise limit or defeat the effectiveness of that drug. Examples of such drugs are those that block cellular receptors but for which activation of downstream signaling pathways nevertheless maintains cellular growth.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for predicting tumor response to targeted therapies with signal transduction pathway inhibitors using biomarkers)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

(multi-target tyrosine kinase inhibitor ponatinib exposure inhibited both wild-type and drug-resistant gatekeeper mutant RET kinase activity and inhibited growth of RET+ and BCR-ABL+ human cancer but not RET-cancer or normal cell)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



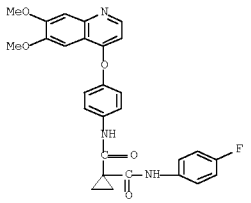
OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 417 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1254595 CAPLUS Full-text
DOCUMENT NUMBER: 159:353569
TITLE: Combination therapy comprising selective VEGFR-2 inhibitors and MEK inhibitors
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 106pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2626066	A1	20130814	EP 2012-154880	20120210

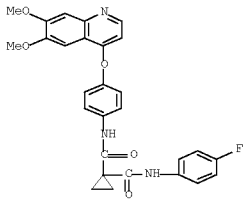
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

PRIORITY APPLN. INFO.: EP 2012-154880 20120210
AB The present invention relates to a combination therapy comprising selective inhibitors of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase and inhibitors of MAP kinase kinase (MEK). Accordingly, a pharmaceutical composition is provided that comprises a selective inhibitor of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase or a pharmaceutically acceptable salt, solvate and/or hydrate thereof, and an inhibitor or a pharmaceutically acceptable salt, solvate and/or hydrate thereof, for use in medicine, especially in the treatment of cancer, like lung cancer, such as non-small cell lung cancer, lung adenocarcinoma or small cell lung cancer. Also a method for identifying patients that are particularly susceptible to such a combination therapy is subject of the present invention. The method comprises the evaluation of the expression level of VEGFR-2 and/or VEGF. An increase in said expression level indicates susceptibility to the combination therapy.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy comprising selective VEGFR-2 inhibitors and MEK inhibitors)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



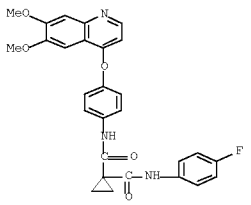
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 419 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1191423 CAPLUS Full-text
DOCUMENT NUMBER: 159:508181
TITLE: Cabozantinib (XL184) for the treatment of locally advanced or metastatic progressive medullary thyroid cancer
AUTHOR(S): Viola, David; Cappagli, Virginia; Elisei, Rossella
CORPORATE SOURCE: Endocrinology Unit, Department of Clinical & Experimental Medicine, WHO Collaborating Center for the Study & Treatment of Thyroid Diseases & other Endocrine & Metabolic Disorders, University of Pisa, Via Paradisa 2, Pisa, 56124, Italy
SOURCE: Future Oncology (2013), 9(8), 1083-1092
CODEN: FOUNBN; ISSN: 1479-6694
DIGITAL OBJECT ID: 10.2217/fon.13.128
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib (XL184) is an oral multiple receptor tyrosine kinase inhibitor manufactured by Exelixis Inc., CA, USA. It mainly inhibits three tyrosine kinase receptors: MET, VEGFR2 and RET. In both preclin. and clin. studies it has been shown to inhibit tumor angiogenesis, invasiveness and metastases. The most frequent side effects are fatigue, diarrhea, decreased appetite, nausea, weight loss and palmar-plantar erythrodysesthesia. A Phase III clin. trial (EXAM study) of XL184 vs. placebo in advanced and progressive medullary thyroid cancer showed a 28 vs. 0% overall response rate and a progression-free survival of 11.2 vs. 4.0 mo (hazard ratio: 0.28; 95% CI: 0.19-0.40; $p < 0.0001$) in patients treated with cabozantinib and placebo, resp. The drug has been approved by the US FDA for the treatment of advanced/progressive metastatic medullary thyroid cancer in the USA. The EMA is now evaluating its approval in Europe.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for treatment of locally advanced or metastatic progressive medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



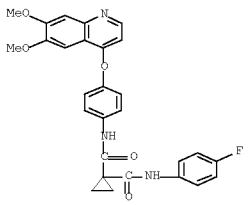
OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 420 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:1087476 CAPLUS Full-text
DOCUMENT NUMBER: 159:649618
TITLE: The novel c-Met inhibitor cabozantinib overcomes gemcitabine resistance and stem cell signaling in pancreatic cancer
AUTHOR(S): Hage, C.; Rausch, V.; Giese, N.; Giese, T.; Schoensiegel, F.; Labsch, S.; Nwaeburu, C.; Mattern, J.; Gladkich, J.; Herr, I.
CORPORATE SOURCE: Department of Experimental Medicine, Molecular OncoSurgery Group, University of Heidelberg and German Cancer Research Center, Heidelberg, Germany
SOURCE: Cell Death & Disease (2013), 4(May), e627
CODEN: CDDEA4; ISSN: 2041-4889
DIGITAL OBJECT ID: 10.1038/cddis.2013.158
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Pancreatic ductal adenocarcinoma (PDA) is one of the most lethal malignancies. Cancer stem cells (CSCs), which are not targeted by current therapies, may be the reason for pronounced therapy resistance. A new treatment option in phase II trials is cabozantinib that inhibits the pancreatic CSC surface marker and tyrosine kinase receptor c-Met. The purpose of this study was to evaluate the effect of cabozantinib to stem-like features and therapy resistance. Established PDA cell lines, a gemcitabine-resistant subclone, non-malignant pancreatic ductal cells and primary spheroidal cultures from patient tumors were analyzed by MTT-assay, flow cytometry, colony and spheroid formation assays, western blotting, qRT-PCR, antibody protein array, immunohistochem. and morphol. features. Cabozantinib inhibited viability and spheroid formation and induced apoptosis in malignant cells with minor effects in non-malignant cells. After long-term cabozantinib treatment, PDA cells had altered anti- and pro-apoptotic signaling, but still responded to cabozantinib, as apoptosis only slightly decreased and viability only slightly increased suggesting a low resistance-inducing potential of cabozantinib. In parallel, c-Met expression and the pluripotency transcription factor SOX2 were downregulated, which might counteract development of full therapy resistance in long-term treated subclones. In single-treatment studies, cabozantinib increased efficacy of gemcitabine. Most importantly, cabozantinib strongly induced apoptosis and reduced viability in PDA cell lines, which are completely resistant toward gemcitabine. In primary, CSC-enriched spheroidal cultures cabozantinib downregulated CSC markers SOX2, c-Met and CD133 and induced apoptosis. These findings suggest that the clin. use of cabozantinib may be more effective than current chemotherapeutics.
IT 849217-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel c-mesenchymal-epithelial transition factor inhibitor cabozantinib overcomes gemcitabine resistance and stem cell signaling in pancreatic cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 28 THERE ARE 28 CAPLUS RECORDS THAT CITE THIS RECORD (28 CITINGS)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 421 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:948019 CAPLUS Full-text
DOCUMENT NUMBER: 159:312293
TITLE: Drug monographs: cabozantanib and omacetaxine
AUTHOR(S): Solimando, Dominic A., Jr.; Ho, Kristin V.; Waddell, J. Aubrey
CORPORATE SOURCE: Walter Reed National Military Medical Center, Bethesda, MD, USA
SOURCE: Hospital Pharmacy (2013), 48(5), 373-377
CODEN: HOPHAZ; ISSN: 0018-5787
DIGITAL OBJECT ID: 10.1310/hpj4805-373
PUBLISHER: Thomas Land Publishers, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The complexity of cancer chemotherapy requires pharmacists be familiar with the complicated regimens and highly toxic agents used. This column reviews various issues related to preparation, dispensing, and administration of antineoplastic therapy, and the agents, both com. available and investigational, used to treat malignant diseases. Questions or suggestions for topics should be addressed to Dominic A. Solimando, Jr, President, Oncol. Pharmacy Services, Inc, 4201 Wilson Blvd #110-545, Arlington, VA 22203, e-mail: OncRxSvc@aol.com; or J. Aubrey Waddell, Professor, University of Tennessee College of Pharmacy; Oncol. Pharmacist, Pharmacy Department, Blount Memorial Hospital, 907 E. Lamar Alexander Parkway, Maryville, TN 37804, e-mail: waddfour@charter.net.
IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug monographs of cabozantinib and omacetaxine)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 422 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:909480 CAPLUS Full-text
DOCUMENT NUMBER: 159:736844
TITLE: Prostate cancer progression after androgen deprivation therapy: mechanisms of castrate resistance and novel therapeutic approaches
AUTHOR(S): Karantanos, T.; Corn, P. G.; Thompson, T. C.
CORPORATE SOURCE: Department of Genitourinary Medical Oncology-Research, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Oncogene (2013), 32(49), 5501-5511

CODEN: ONCNES; ISSN: 0950-9232
DIGITAL OBJECT ID: 10.1038/onc.2013.206
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

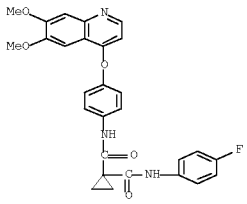
AB A review. Prostate cancer is the second-leading cause of cancer-related mortality in men in Western societies. Androgen receptor (AR) signaling is a critical survival pathway for prostate cancer cells, and androgen-deprivation therapy (ADT) remains the principal treatment for patients with locally advanced and metastatic disease. Although a majority of patients initially respond to ADT, most will eventually develop castrate resistance, defined as disease progression despite serum testosterone levels of <20 ng/dL. The recent discovery that AR signaling persists during systemic castration via intratumoral production of androgens led to the development of novel anti-androgen therapies including abiraterone acetate and enzalutamide. Although these agents effectively palliate symptoms and prolong life, metastatic castration-resistant prostate cancer remains incurable. An increased understanding of the mechanisms that underlie the pathogenesis of castrate resistance is therefore needed to develop novel therapeutic approaches for this disease. The aim of this review is to summarize the current literature on the biol. and treatment of castrate-resistant prostate cancer.

IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cabozatinib; prostate cancer progression after androgen deprivation therapy in relation to mechanisms of castrate resistance and novel therapeutic approaches)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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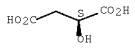
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CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



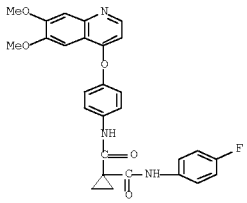
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REFERENCE COUNT: 158 THERE ARE 158 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 423 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:907853 CAPLUS Full-text
DOCUMENT NUMBER: 160:94029
TITLE: Response to Cabozantinib in Patients with RET Fusion-Positive Lung Adenocarcinomas
AUTHOR(S): Drilon, Alexander; Wang, Lu; Hasanovic, Adnan; Suehara, Yoshiyuki; Lipson, Doron; Stephens, Phil; Ross, Jeffrey; Miller, Vincent; Ginsberg, Michelle; Zakowski, Maureen F.; Kris, Mark G.; Ladanyi, Marc; Rizvi, Naiyer
CORPORATE SOURCE: Department of Medicine Thoracic Oncology Service, Lenox Hill Hospital, New York, NY, USA
SOURCE: Cancer Discovery (2013), 3(6), 630-635
CODEN: CDAIB2; ISSN: 2159-8274
DIGITAL OBJECT ID: 10.1158/2159-8290.CD-13-0035
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The discovery of RET fusions in lung cancers has uncovered a new therapeutic target for patients whose tumors harbor these changes. In an unselected population of non-small cell lung carcinomas (NSCLCs), RET fusions are present in 1%to2% of cases. This incidence increases substantially, however, in never-smokers with lung adenocarcinomas that lack other known driver oncogenes. Although preclin. data provide exptl. support for the use of RET inhibitors in the treatment of RET fusion-pos. tumors, clin. data on response are lacking. We report preliminary data for the first three patients treated with the RET inhibitor cabozantinib on a prospective phase II trial for patients with RET fusion-pos. NSCLCs (NCT01639508). Confirmed partial responses were observed in 2 patients, including one harboring a novel TRIM33-RET fusion. A third patient with a KIF5B-RET fusion has had prolonged stable disease approaching 8 mo (31 wk). All three patients remain progression-free on treatment.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response to cabozantinib in patients with RET fusion-pos. lung adenocarcinomas)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



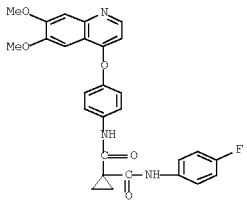
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REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 424 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:884114 CAPLUS Full-text
DOCUMENT NUMBER: 161:430953
TITLE: Tumour angiogenesis: an elusive target in castration-resistant prostate cancer
AUTHOR(S): Galsky, Matthew D.; Oh, William K.
CORPORATE SOURCE: The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA
SOURCE: Lancet Oncology (2013), 14(8), 681-682
CODEN: LOANBN; ISSN: 1470-2045
DIGITAL OBJECT ID: 10.1016/S1470-2045(13)70239-0
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

AB In this article, tumor angiogenesis an attractive target in castration-resistant prostate cancer is studied. Indeed, impressive single-agent activity has been reported with cabozantinib, a small mol. inhibitor of the tyrosine kinases MET and VEGFR2. The author reports on randomly allocated 1050 patients with castration-resistant prostate cancer to treatment with docetaxel plus prednisone with or without bevacizumab-the median overall survival for patients receiving bevacizumab was 22.6 mo compared with 21.5 mo for patients treated with placebo (hazard ratio 0.91, 95% CI 0.78-1.05; stratified log-rank p=0.181).

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(study on tumor angiogenesis as elusive target in castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 425 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:882495 CAPLUS Full-text
DOCUMENT NUMBER: 159:68803
TITLE: Targeting microRNA's miR-409-5p, miR-379 and miR-154* to treat prostate cancer bone metastasis and drug resistant lung cancer
INVENTOR(S): Chung, Leland W. K.; Josson, Sajni; Gururajan, Murali; Jain, Anjali
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 79pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013082499	A1	20130606	WO 2012-US67403	20121130
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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AU 2012345666	A1	20140619	AU 2012-345666	20121130

CN 104080461	A	20141001	CN 2012-80067969		20121130
EP 2785355	A1	20141008	EP 2012-854115		20121130
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JP 2015504847	T	20150216	JP 2014-544946		20121130
EP 3106168	A2	20161221	EP 2016-170595		20121130
EP 3106168	A3	20170222			
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US 20140323551	A1	20141030	US 2014-14360489		20140523
US 20160017331	A1	20160121	US 2015-14863828		20150924
PRIORITY APPLN. INFO.:			US 2011-61565226	P	20111130
			EP 2012-854115	A3	20121130
			WO 2012-US67403	W	20121130
			US 2014-14360489	A2	20140523
			US 2014-62055215	P	20140925

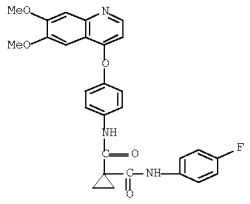
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention describes methods of treating cancer, cancer metastasis, and drug resistant cancers using miRNA inhibitors; for example, inhibitors of miR-409-5p. Also described are methods of using the miRNA as biomarkers; for example, to predict responsiveness to a cancer drug, to detect a disease state of cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting microRNA's to treat prostate cancer bone metastasis and drug resistant lung cancer and combination with other treatments and use of microRNA's as biomarkers)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 426 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:873882 CAPLUS Full-text

DOCUMENT NUMBER: 159:100783

TITLE: Medical combination containing hepatocyte growth factor receptor inhibitor and Bcl-2 inhibitor for treating cancer

INVENTOR(S): Zhao, Lei; Wang, Limei

PATENT ASSIGNEE(S): Beijing Tianhe Ruitong Technology Development Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing, 25pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

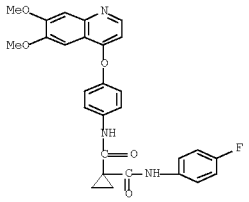
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 103127510	A	20130605	CN 2011-10389330	20111130
CN 103127510	B	20150325		
PRIORITY APPLN. INFO.:			CN 2011-10389330	20111130

AB The title medical combination comprises a hepatocyte growth factor receptor (cMet) inhibitor and a Bcl-2 inhibitor. The medical combination can be used for preparing a drug for treating colon cancer, liver cancer, lung cancer, renal cancer, gastric cancer, brain tumor, sarcoma, neurospongioma, pancreas cancer, ovarian cancer or prostatic cancer. The medical combination has the advantages of good synergistic effects, high effects, low administration dosage and low side effects.

IT 849217-68-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical combination containing hepatocyte growth factor receptor inhibitor and Bcl-2 inhibitor for treating cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 427 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:869127 CAPLUS Full-text

DOCUMENT NUMBER: 159:436784

TITLE: A Dose-Ranging Study of Cabozantinib in Men with Castration-Resistant Prostate Cancer and Bone Metastases

AUTHOR(S): Lee, Richard J.; Saylor, Philip J.; Dror Michaelson, M.; Michael Rothenberg, S.; Smas, Malgorzata E.; Miyamoto, David T.; Gurski, Carol A.; Xie, Wanling; Maheswaran, Shyamala; Haber, Daniel A.; Goldin, Jonathan G.; Smith, Matthew R.

CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Boston, MA, USA

SOURCE: Clinical Cancer Research (2013), 19(11), 3088-3094
CODEN: CCREF4; ISSN: 1078-0432

DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-13-0319

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

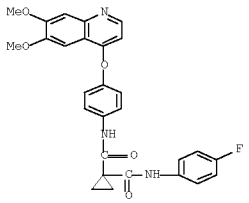
LANGUAGE: English

AB Background: Cabozantinib is an oral MET/VEGFR2 inhibitor. A recent phase II study of cabozantinib (100 mg daily) showed improved bone scans in subjects with metastatic castration-resistant prostate cancer (mCRPC), but adverse events (AE) caused frequent dose redns. This study was designed to determine the efficacy and tolerability of cabozantinib at lower starting doses. Exptl. Design: An adaptive design was used to determine the lowest active daily dose among 60, 40, and 20 mg. The primary endpoint was week 6 bone scan response, defined as ≥30% decrease in bone scan lesion area. The secondary endpoint was change in circulating tumor cells (CTC). Results: Among 11 evaluable subjects enrolled at 40 mg, there were 9 partial responses (PR), 1 complete response, and 1 stable disease (SD). Of 10 subjects subsequently enrolled at 20 mg, there were 1 PR, 5 SDs, and 4 with progressive disease. Among 13 subjects enrolled on the 40 mg expansion cohort, there were 6 PRs and 7 SDs. No subjects required dose reduction or treatment interruption at 6 or 12 wk; 3 subjects at dose level 0 discontinued due to AEs by 12 wk. At 40 mg, median treatment duration was 27 wk. 58% of subjects with ≥5 CTCs/7.5mL at baseline converted to <5. Conclusions: Cabozantinib 40 mg daily was associated with a high rate of bone scan response. Cabozantinib 40 mg daily was associated with better tolerability than previously reported for cabozantinib 100 mg daily. These observations informed the design of phase III studies of cabozantinib in mCRPC. Clin Cancer Res; 19(11); 3088-94. ©2013 AACR.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dose-ranging study of cabozantinib in men with castration-resistant prostate cancer and bone metastases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 27 THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (27 CITINGS)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 428 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:847461 CAPLUS Full-text

DOCUMENT NUMBER: 159:357745

TITLE: The antiangiogenic ceiling in hepatocellular carcinoma: does it exist and has it been reached?

AUTHOR(S): Abou-Alfa, Ghassan K.; Venook, Alan P.

CORPORATE SOURCE: Section of Gastrointestinal Oncology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

SOURCE: Lancet Oncology (2013), 14(7), e283-e288
CODEN: LOANBN; ISSN: 1470-2045

DIGITAL OBJECT ID: 10.1016/S1470-2045(13)70161-X

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; General Review; (online computer file)

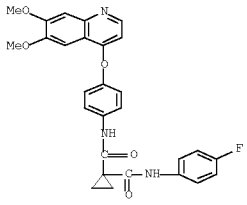
LANGUAGE: English

AB A review. The recommendation of sorafenib as std. of care in advanced hepatocellular carcinoma has lent support to the increased use of antiangiogenic therapies. However, in three phase 3 randomised trials that compared other antiangiogenics with sorafenib, results did not show superiority or non-inferiority of the new therapies. The 10-mo median overall survival shown in these studies for patients given sorafenib might be a ceiling for single-agent antiangiogenic therapy. Strategies to increase survival time include combination therapies that pair antiangiogenic treatment with biol. therapy or chemotherapy. The combination of sorafenib and erlotinib was not superior to sorafenib alone, which suggests no pos. interaction between antiangiogenics and tyrosine kinase inhibitors in the treatment of advanced hepatocellular carcinoma. A combination of sorafenib and doxorubicin is being assessed in a randomised phase 3 trial. Differences in patient outcome with sorafenib because of disease cause and the ethnic origin of patients suggest that sorafenib's multitarget capacity, including RAF kinase inhibition, might be important. MET inhibitors cabozantinib and tivantinib are drugs that might also bypass the so-called antiangiogenic ceiling and have led to selective treatment of patients that overexpress MET with these drugs. Although this intense period of research activity has not yet resulted in significant improvements

in survival for patients with advanced hepatocellular carcinoma, we are certainly closer to a customised treatment, which should increase the antiangiogenic survival ceiling.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MET inhibitors cabozantinib and tivantinib may be useful in treatment of patient with hepatocellular carcinoma)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 429 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:761990 CAPLUS Full-text
DOCUMENT NUMBER: 158:704608
TITLE: Method of quantifying cancer treatment
INVENTOR(S): Holland, Jaymes
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 50pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013070903	A1	20130516	WO 2012-US64134	20121108

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

CA 2854664	A1	20130516	CA 2012-2854664	20121108
AU 2012335750	A1	20140605	AU 2012-335750	20121108
AR 88813	A1	20140710	AR 2012-104223	20121108
CN 104039226	A	20140910	CN 2012-80066413	20121108
EP 2775921	A1	20140917	EP 2012-795939	20121108

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

JP 2015505360	T	20150219	JP 2014-541261	20121108
IN 2014CN03674	A	20150703	IN 2014-CN3674	20140515

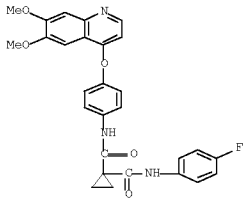
PRIORITY APPLN. INFO.: US 2011-61557362 P 20111108
WO 2012-US64134 W 20121108

OTHER SOURCE(S): CASREACT 158:704608

AB This invention is directed to a method for quantifying cancer treatment response in patients with bone metastases using computer aided bone scan assessment, comprising: (a) obtaining a bone scan image; (b) normalizing the obtained bone scan image to identify normalized bone scan lesions; and (c) quant. assessing the normalized bone scan lesions using bone scan lesion area, bone scan intensity, or bone scan lesion count.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(quantifying cancer treatment)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

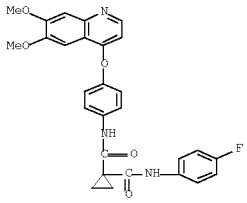


IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quantifying cancer treatment)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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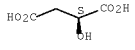
CRN 849217-68-1
CMF C28 H24 F N3 O5



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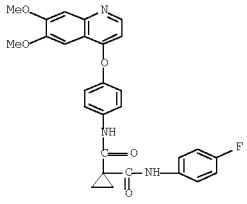
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quantifying cancer treatment)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 430 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:761969 CAPLUS Full-text
DOCUMENT NUMBER: 158:704607
TITLE: Dual inhibitor of Met and VEGF for treating cancer
INVENTOR(S): Aftab, Dana T.; Schimmoller, Frauke
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 56pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013070890	A1	20130516	WO 2012-US64116	20121108

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

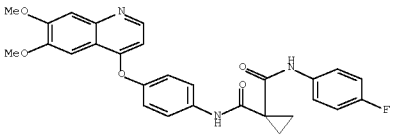
CA 2854336	A1	20130516	CA 2012-2854336	20121108
AU 2012335737	A1	20140605	AU 2012-335737	20121108
IL 232421	A	20140630	IL 2012-232421	20121108
KR 2014088610	A	20140710	KR 2014-7015127	20121108
EP 2776033	A1	20140917	EP 2012-787328	20121108

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME

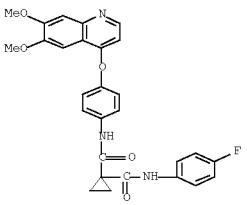
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JP 2014532766	T	20141208	JP 2014-541256		20121108
MX 2014005458	A	20150416	MX 2014-5458		20140506
US 20140323522	A1	20141030	US 2014-14356927		20140508
ZA 2014003331	A	20151223	ZA 2014-3331		20140508
IN 2014CN04067	A	20151023	IN 2014-CN4067		20140530
PRIORITY APPLN. INFO.:			US 2011-61557358	P	20111108
			WO 2012-US64116	W	20121108

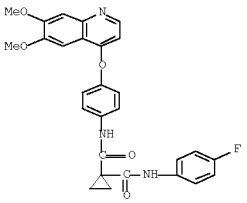
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:704607; MARPAT 158:704607
GI



AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and bone metastases, with a dual inhibitor of MET and VEGF.
IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



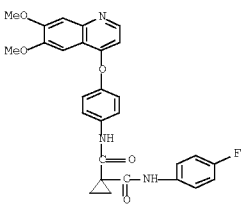
IT 1140909-48-3P



RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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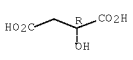
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

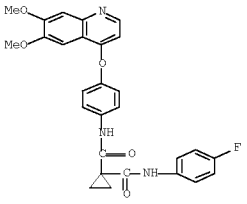
Absolute stereochemistry. Rotation (+).



RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

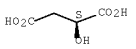
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1, Cabozantinib 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual inhibitor of Met and VEGF for treating cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 431 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:729332 CAPLUS Full-text
DOCUMENT NUMBER: 158:676742
TITLE: Fusion proteins with a C-terminal domain of the gene ret receptor and their use in cancer diagnosis
INVENTOR(S): Ju, Young-Seok; Seo, Jeong-Sun; Kim, Kun-Hee
PATENT ASSIGNEE(S): Macrogen Inc., S. Korea
SOURCE: U.S. Pat. Appl. Publ., 61pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20130116280	A1	20130509	US 2012-13663565	20121030
WO 2013066047	A1	20130510	WO 2012-KR9056	20121031
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
KR 2014092846	A	20140724	KR 2014-7013826	20121031
KR 1625139	B1	20160531		
EP 2773673	A1	20140910	EP 2012-845116	20121031
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2015504299	T	20150212	JP 2014-538724	20121031
KR 2016052751	A	20160512	KR 2016-7010433	20121031
KR 1660235	B1	20160927		

PRIORITY APPLN. INFO.:	US 2011-61553483	P 20111031
	US 2012-13663565	A 20121030
	KR 2014-7013826	A3 20121031
	WO 2012-KR9056	W 20121031

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB A fusion protein including N-terminal domain of a fusion partner at N-terminal and C-terminal domain of RET protein at C-terminal and the gene encoding are identified as diagnostic markers for cancers, especially lung cancers. The somatic mutation forming the chimeric gene was identified in a poorly differentiated lung adenocarcinoma. The adenocarcinoma did not show any of the most common lung cancer-associated mutations, but several discordant reads, indicating transposition events, were identified. Expression of the chimeric KIF5B-RET gene in NIH-3T3 resulted in a neoplastic

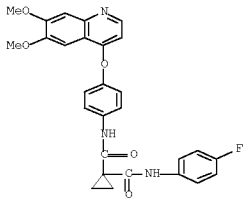
phenotype. Growth of these cells could be inhibited by the ret kinase inhibitor cabozantinib.

IT 849217-68-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as inhibitor of ret receptor fusion protein in cancer therapy; fusion proteins with C-terminal domain of gene ret receptor and their use in cancer diagnosis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 432 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:728614 CAPLUS Full-text

DOCUMENT NUMBER: 158:672026

TITLE: Methods using heteroaryl compounds for treatment of disorders involving androgen-, estrogen- and progesterone-receptors

INVENTOR(S): Protter, Andrew A.; Hung, David T.; Chakravarty, Sarvajit; Bernales, Sebastian

PATENT ASSIGNEE(S): Medivation Technologies, Inc., USA

SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013067131	A1	20130510	WO 2012-US62980	20121101

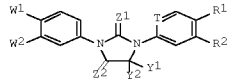
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2011-61554919 P 20111102

OTHER SOURCE(S): MARPAT 158:672026

GI



I

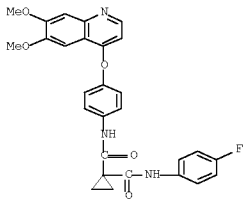
AB The disclosure describes compds. of formula I [W1 = CN, NO2, SO2R4; W2 = alkyl, alkenyl, alkynyl, halo; Z1 = S, O; Z2 = S, O, NR4; R4 = independently H, alkyl, aryl; Y1, Y2 = independently H, alkyl, alkenyl, aryl, arylalkyl, heterocyclic etc.; R1 = alkyl, cycloalkyl, heterocyclic etc.; R2 = independently H, halo, CN, alkyl etc.], or pharmaceutically acceptable salts thereof, useful for treating disorders involving androgen, estrogen, and/or progesterone receptors. In another embodiment of the invention the disorder is selected from the group consisting of neurodegenerative disorders, cancer, polyglutamate disease, rheumatoid arthritis, systemic hyperandrogenism, seborrhea, hirsutism, precocious puberty, polycystic ovary syndrome, acne, alopecia, benign prostatic hyperplasia, intrauterine fibroids, endometriosis, glaucoma, meningiomas, Kennedy's disease (KD) or X-linked spinal and bulbar muscular atrophy.

IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods using heteroaryl compds. for treatment of disorders involving androgen-, estrogen- and progesterone-receptors)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 433 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:725439 CAPLUS Full-text

DOCUMENT NUMBER: 158:676739

TITLE: Fusion proteins with a C-terminal domain of the gene ret receptor and their use in cancer diagnosis

INVENTOR(S): Ju, Young-Seok; Seo, Jeong-Sun; Kim, Eun-Hee

PATENT ASSIGNEE(S): Macrogen Inc., S. Korea

SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013066047	A1	20130510	WO 2012-KR9056	20121031

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM

US 20130116280	A1	20130509	US 2012-13663565	20121030
KR 2014092846	A	20140724	KR 2014-7013826	20121031
KR 1625139	B1	20160531		
EP 2773673	A1	20140910	EP 2012-845116	20121031

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2015504299	T	20150212	JP 2014-538724	20121031
KR 2016052751	A	20160512	KR 2016-7010433	20121031
KR 1660235	B1	20160927		

PRIORITY APPLN. INFO.:

US 2011-61553483	P	20111031
US 2012-13663565	A	20121030
KR 2014-7013826	A3	20121031
WO 2012-KR9056	W	20121031

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

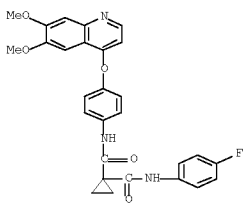
AB A fusion protein including N-terminal domain of a fusion partner at N-terminal and C-terminal domain of RET protein at C-terminal and the gene encoding are identified as diagnostic markers for cancers, especially lung cancers. The somatic mutation forming the chimeric gene was identified in a poorly differentiated lung adenocarcinoma. The adenocarcinoma did not show any of the most common lung cancer-associated mutations, but several discordant reads, indicating transposition events, were identified. Expression of the chimeric KIF5B-RET gene in NIH-3T3 resulted in a neoplastic phenotype. Growth of these cells could be inhibited by the ret kinase inhibitor cabozantinib.

IT 849217-68-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as inhibitor of ret receptor fusion protein in cancer therapy; fusion proteins with C-terminal domain of gene ret receptor and their use in cancer diagnosis)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 434 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2013:684015 CAPLUS full-text

DOCUMENT NUMBER: 158:649640

TITLE: Free prostate specific antigen (PSA) antibodies as diagnostics, prognostics and therapeutics for prostate cancer

INVENTOR(S): Sawyers, Charles; Ulmert, David; Lewis, Jason; Evans, Michael; Lija, Hans

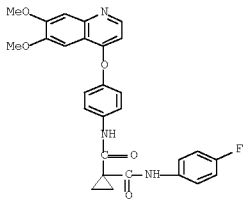
PATENT ASSIGNEE(S): Memorial Sloan-Kettering Cancer Center, USA
SOURCE: PCT Int. Appl., 103pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013063312	A1	20130502	WO 2012-US61982	20121025
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2853705	A1	20130502	CA 2012-2853705	20121025
AU 2012328679	A1	20140612	AU 2012-328679	20121025
EP 2771688	A1	20140903	EP 2012-844178	20121025
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
CN 104040341	A	20140910	CN 2012-80063852	20121025
CN 104040341	B	20161228		
JP 2015502339	T	20150122	JP 2014-539018	20121025
US 20140308204	A1	20141016	US 2014-14353989	20140424
JP 2017043634	A	20170302	JP 2016-231469	20161129

PRIORITY APPLN. INFO.: US 2011-61551195 P 20111025
JP 2014-539018 A3 20121025
WO 2012-US61982 W 20121025
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The authors disclose the use of antibodies to free prostate-specific antigen (fPSA) in the diagnosis, prognosis, and therapeutic monitoring of prostate cancer. In one example, tumor localization of labeled anti-fPSA antibody is shown to be reduced by the antiandrogen MDV3100.

IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibodies to free PSA antigen therapy monitoring of)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

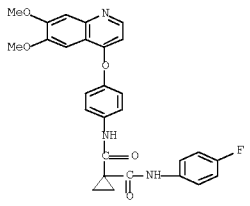


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 435 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:647172 CAPLUS Full-text
DOCUMENT NUMBER: 159:188392
TITLE: Emerging targeted therapies for castration-resistant prostate cancer
AUTHOR(S): Adamo, Vincenzo; Noto, Laura; Franchina, Tindara; Chiofalo, Giuseppe; Picciotto, Maria; Toscano, Giuseppe; Caristi, Nicola
CORPORATE SOURCE: Integrated Therapies in Oncology Unit, Department of Human Pathology, University of Messina, Messina, 98125, Italy
SOURCE: Frontiers in Cancer Endocrinology (2012), 3(May), 73
CODEN: FCERD9
DIGITAL OBJECT ID: 10.3389/fendo.2012.00073
PUBLISHER: Frontiers Media S.A.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Until recently, few therapeutic options were available for patients with castration-resistant prostate cancer (CRPC). Since 2010, four new mols. with a demonstrated benefit (sipuleucel-T, cabazitaxel, abiraterone and denosumab) have been approved in this setting and to-date several other agents are under investigation in clin. trials. The purpose of this review is to present an update of targeted therapies for CRPC. Presented data are obtained from literature and congress reports updated until Dec. 2011. Targeted therapies in advanced phases of clin. development include novel androgen signaling inhibitors, inhibitors of alternative signaling pathways, anti-angiogenic agents, inhibitors that target the bone microenvironment and immunotherapeutic agents. Radium-223 and MDV3100 demonstrated a survival advantage in phase III trials and the road for their introduction in clin. practice is rapidly ongoing. Results are also awaited for phase III studies currently underway or planned with new drugs given as monotherapy (TAK-700, cabozantinib, tasquinimod, PROSTVAC-VF, ipilimumab) or in combination with docetaxel (custirsen, aflibercept, dasatinib, zibotentan). The optimal timing, combination and sequencing of emerging therapies remain unknown and require further investigation. Addnl., the identification of novel markers of response and resistance to these therapies may better individualize treatment for patients with CRPC.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emerging targeted therapies for castration-resistance prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

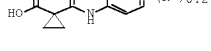


OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

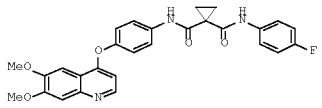
L4 ANSWER 436 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:644308 CAPLUS Full-text
DOCUMENT NUMBER: 158:620790
TITLE: Process for preparing quinoline derivatives
INVENTOR(S): Wilson, Jo Ann; Naganathan, Sriram; Pfeiffer, Matthew; Andersen, Neil G.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013059788	A1	20130425	WO 2012-US61320	20121022
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2852771	A1	20130425	CA 2012-2852771	20121022
AU 2012325768	A1	20140522	AU 2012-325768	20121022
IL 232139	A	20140528	IL 2012-232139	20121022
AR 88483	A1	20140611	AR 2012-103944	20121022
KR 2014088874	A	20140711	KR 2014-7012435	20121022
EP 2768796	A1	20140827	EP 2012-783763	20121022
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JP 2014530880	T	20141120	JP 2014-537359	20121022
CN 104395284	A	20150304	CN 2012-80054241	20121022
NZ 624328	A	20161028	NZ 2012-624328	20121022
ZA 2014002579	A	20150325	ZA 2014-2579	20140409
MX 2014004583	A	20141006	MX 2014-4583	20140415
US 20140256938	A1	20140911	US 2014-14353251	20140421
US 9365516	B2	20160614		
IN 2014CN02971	A	20150703	IN 2014-CN2971	20140421
US 20160229805	A1	20160811	US 2016-15133708	20160420

PRIORITY APPLN. INFO.: US 2011-61549312 P 20111020
WO 2012-US61320 W 20121022
US 2014-14353251 A1 20140421
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:620790; MARPAT 158:620790
GI



I



II

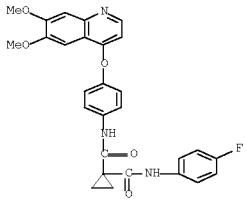
AB The invention is directed to processes for prepg. compds. of formula I (R2 is H, F, Cl and Br) by activation of 1,1-cyclopropanedicarboxylic acid with thionyl chloride followed by amidation with substituted aniline derivative Example compound II L-malate was prepared by chlorination of 6,7-dimethoxyquinolin-4-ol followed by etherification of 4-chloro-6,7-dimethoxyquinoline with 4-aminophenol; the resulting 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine underwent acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropanecarbonyl chloride to give

compound II, which underwent addition of L-malic acid to give the desired product.

IT 1140909-48-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing quinoline derivs.)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

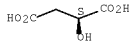
CRN 849217-68-1
CMF C28 H24 F N3 O5



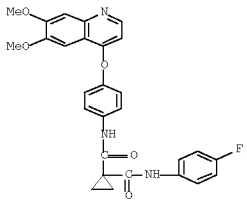
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



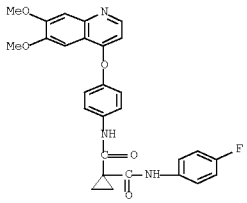
IT 849217-68-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing quinoline derivs.)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

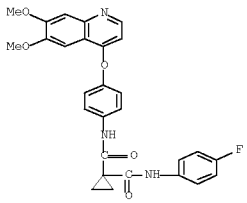
L4 ANSWER 437 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:564369 CAPLUS Full-text
DOCUMENT NUMBER: 159:419448
TITLE: Lessons learned and questions unanswered from use of multitargeted kinase inhibitors in medullary thyroid cancer
AUTHOR(S): Sherman, Steven I.
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders, University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Oral Oncology (2013), 49(7), 707-710
CODEN: EJCCER; ISSN: 1368-8375
DIGITAL OBJECT ID: 10.1016/j.oraloncology.2013.03.442
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB To review studies of novel multitargeted kinase inhibitors studied in patients with medullary thyroid cancer (MTC). Search of relevant refs. in PubMed and Google Scholar on "chemotherapy" and "medullary thyroid cancer". Multitargeted kinase inhibitors have revolutionized the role of chemotherapy for progressive MTC, providing for the first time tolerable therapeutic options that can improve outcomes in patients with progressive disease. Drugs thought to inhibit the RET kinase have advanced the furthest for this disease, but these agents also target the VEGF receptor along with other kinases that may be relevant to both beneficial and adverse effects. Vandetanib improved progression-free survival from 19.3 to 30.5 mo compared with placebo in patients with metastatic disease, whereas cabozantinib improved progression-free survival from 4.0 mo to 11.2 mo in a population with more aggressive disease. However, "cure" remains elusive, adverse events frequent, and exactly how such "targeted" agents actually function within MTC remains unclear. New approaches to clin. trial design and the preclin. development of targeted agents may be required to optimize the combination of maximum efficacy with minimal toxicity for patients with metastatic MTC.
IT 849217-68-1, Cabozantinib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of multitargeted kinase inhibitors in medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 438 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:522453 CAPLUS Full-text
DOCUMENT NUMBER: 159:125821
TITLE: Emerging therapies in metastatic castration-sensitive and castration-resistant prostate cancer
AUTHOR(S): MacVicar, Gary R.; Hussain, Maha H.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Internal Medicine, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
SOURCE: Current Opinion in Oncology (2013), 25(3), 252-260
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e32835ff161
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB Purpose of review: Therapeutic options for men with metastatic prostate cancer are expanding. Here we discuss the scientific progress in this disease that led to approval of several agents in the last decade and highlight ongoing clin. investigation. Recent findings: In androgen-sensitive disease, trials are evaluating the role of intermittent androgen-deprivation therapy, early chemotherapy, and novel targeted and hormonal therapies. For chemotherapy-naive, metastatic castration-resistant prostate cancer (mCRPC), abiraterone is effective. Trials with addnl. agents targeting androgen receptor (AR) signaling, such as TAK-700 and enzalutamide, are ongoing. Other agents in development target the endothelin pathway, angiogenesis, AR chaperones, and immune mechanisms. Docetaxel with prednisone remains the standard first-line chemotherapeutic regimen as trials incorporating novel agents with docetaxel have been neg. Postdocetaxel, enzalutamide improves survival. Early results with cabozantinib are encouraging, and phase III studies are ongoing. Denosumab and radium-223 reduce the risk of skeletal-related events (SREs), but only radium-223 improves survival. Summary: Progress in understanding the disease biol. and mechanisms of castration resistance led to significant therapeutic advancements, particularly in the setting of mCRPC in which several phase III trials, each incorporating agents with different mechanisms of action, have improved survival. As a result, new options exist, and the standard of care has changed significantly. Further advances are anticipated.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emerging therapies in metastatic castration-sensitive and castration-resistant prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

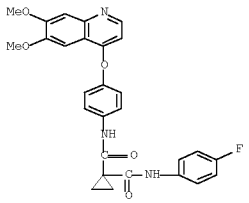
L4 ANSWER 439 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:522113 CAPLUS Full-text
DOCUMENT NUMBER: 159:125816
TITLE: From Bevacizumab to Tasquinimod: Angiogenesis as a Therapeutic Target in Prostate Cancer
AUTHOR(S): Schweizer, Michael T.; Carducci, Michael A.
CORPORATE SOURCE: Prostate Cancer Research Program, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins, Baltimore, MD, USA
SOURCE: Cancer Journal (Philadelphia, PA, United States) (2013), 19(1), 99-106
CODEN: CAJOCB; ISSN: 1528-9117
DIGITAL OBJECT ID: 10.1097/PPO.0b013e31827e0b86

PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. It was first posited in the 1970s that angiogenesis may prove to be a useful target for anticancer therapies. Since then, a number of agents have been developed and tested across a range of tumor types; however, to date, there have unfortunately been more failures than successes. Prostate cancer (PCa) is no exception in this regard, and despite a strong preclin. rationale for targeting angiogenesis in men with PCa, there has yet to be an antiangiogenic therapy proven to prolong survival in this group of patients. Drugs have been developed to target a host of angiogenesis mediators. These include vascular endothelial growth factor (VEGF), the VEGF receptors, antiangiogenic factors (e.g., thrombospondin-1), and downstream mediators of angiogenesis (e.g., hypoxia-inducible factor-1α and MET). At present, there are 2 drugs being tested in the phase III setting for men with PCa: cabozantinib and tasquinimod. Cabozantinib, a dual VEGF receptor-2/MET inhibitor, has shown dramatic beneficial effects on radiog. evident bone metastases and pain in the phase II setting. There are currently 2 large phase III trials underway to further investigate cabozantinib's role in treating men with PCa. Both trials randomize subjects to cabozantinib vs. mitoxantrone: one is designed to evaluate overall survival, and the other, pain response durability. The other drug, tasquinimod, has a somewhat poorly understood mechanism of action. It is thought to exert an antiangiogenic effect through the inhibition of myeloid-derived suppressor cells, key to the support of an angiogenic environment, and down-regulation of hypoxia-inducible factor-1α. A phase II trial randomizing men to tasquinimod vs. placebo revealed a median progression-free survival advantage in the exptl. arm (7.6 vs. 3.3 mo with placebo; P = 0.0042). Based on these encouraging phase II results, a randomized, double-blind, placebo-controlled trial in men with metastatic castration-resistant PCa was launched. That trial is powered for a primary endpoint of progression-free survival and is expected to enroll 1200 men.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiogenesis as therapeutic target in prostate cancer and the role of various angiogenesis targeting drugs including bevacizumab and tasquinimod)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



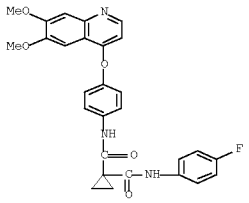
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 440 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:522110 CAPLUS Full-text
DOCUMENT NUMBER: 159:125815
TITLE: Targeting MET and Vascular Endothelial Growth Factor Receptor Signaling in Castration-Resistant Prostate Cancer
AUTHOR(S): Lee, Richard J.; Smith, Matthew R.
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA
SOURCE: Cancer Journal (Philadelphia, PA, United States) (2013), 19(1), 90-98
CODEN: CAJOCB; ISSN: 1528-9117
DIGITAL OBJECT ID: 10.1097/PPO.0b013e318281e280
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Effective management of bone metastases in men with castration-resistant prostate cancer (CRPC) remains an important unmet medical need. MET and vascular endothelial growth factor receptor (VEGFR) are rational targets for intervention in CRPC. Clin. trials involving agents that inhibit one but not both pathways have reported modest activity and no improvement in overall survival. Cabozantinib is an oral multitargeted tyrosine kinase inhibitor that inhibits both MET and VEGFR-2. A phase II randomized discontinuation study involving subjects with CRPC demonstrated that cabozantinib therapy is associated with improvement in bone scans, bone turnover markers, and pain response, but with significant adverse events leading to dose reduction and treatment discontinuation. Lower doses of cabozantinib retain high levels of activity with less toxicity. Ongoing phase III clin. trials will define the role of cabozantinib in CRPC. We summarize the rationale for targeting MET and VEGFR pathways in CRPC and the clin. data available to date.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting MET and vascular endothelial growth factor receptor signaling in castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 441 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:470327 CAPLUS Full-text
DOCUMENT NUMBER: 158:493976
TITLE: Combinations comprising c-Met antagonists and B-raf antagonists for treatment of cancer
INVENTOR(S): Wilson, Timothy R.; Koeppen, Hartmut; Merchant, Mark; Settleman, Jeffrey
PATENT ASSIGNEE(S): Genentech, Inc., USA; F. Hoffmann-La Roche AG
SOURCE: PCT Int. Appl., 148pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

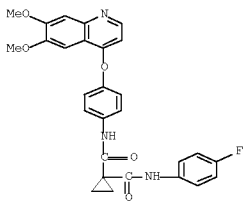
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013043715	A1	20130328	WO 2012-US56106	20120919
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
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US 20130078252	A1	20130328	US 2012-13622878	20120919
AU 2012312515	A1	20140313	AU 2012-312515	20120919
IL 231056	A	20140331	IL 2012-231056	20120919
AR 87918	A1	20140423	AR 2012-103446	20120919
KR 2014064971	A	20140528	KR 2014-7010162	20120919
CN 103930111	A	20140716	CN 2012-80055708	20120919
EP 2758055	A1	20140730	EP 2012-768982	20120919
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2014534949	T	20141225	JP 2014-530956	20120919
ZA 2014001370	A	20150930	ZA 2014-1370	20120919
MX 2014002990	A	20140521	MX 2014-2990	20140313
US 20150125452	A1	20150507	US 2014-14535071	20141106
PRIORITY APPLN. INFO.:			US 2011-61536436 P	20110919
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			US 2012-61598783 P	20120214
			US 2012-61641139 P	20120501
			US 2012-13622878 B1	20120919
			WO 2012-US56106 W	20120919

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides combination therapies for treating a pathol. condition, such as cancer, wherein a c-met antagonist (e.g. crizotinib, tivantinib, anti-HGF antibody, onartuzumab) is combined with a B-raf antagonist (e.g. vemurafenib), thereby providing significant antitumor activity. C-met expression was inversely correlated with sensitivity to vemurafenib treatment. In one aspect, provided are methods for treating a cancer patient who has increased likelihood of developing resistance to B-raf antagonist comprising administering an effective amount (in combination) of B-raf antagonist and c-met antagonist. In addition, patients with B-raf mutant melanoma who had higher levels of circulating hepatocyte growth factor (HGF) showed substantially reduced progression free survival and overall survival when treated with B-raf antagonist, relative to patients with lower circulating HGF levels treated with B-raf antagonist.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations comprising c-Met antagonists and B-raf antagonists for treatment of cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

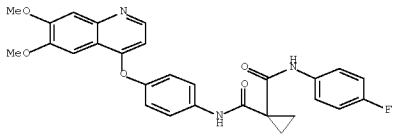


OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 442 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:466384 CAPLUS Full-text
DOCUMENT NUMBER: 158:494085
TITLE: Method for treating osteoporosis
INVENTOR(S): Aftab, Dana T.; Clary, Douglas
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 73pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2013043840	A1	20130328	WO 2012-US56281	20120920
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
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AU 2012312364	A1	20140410	AU 2012-312364	20120920
IL 231495	A	20140430	IL 2012-231495	20120920
KR 2014069133	A	20140609	KR 2014-7009534	20120920
CN 103957915	A	20140730	CN 2012-80051094	20120920
EP 2758057	A1	20140730	EP 2012-770368	20120920
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
JP 2014527984	T	20141023	JP 2014-531955	20120920
NZ 622722	A	20160930	NZ 2012-622722	20120920
AR 87995	A1	20140430	AR 2012-103501	20120921
ZA 2014001728	A	20160127	ZA 2014-1728	20140310
MX 2014003027	A	20141024	MX 2014-3027	20140313
IN 2014CN02093	A	20141010	IN 2014-CN2093	20140319
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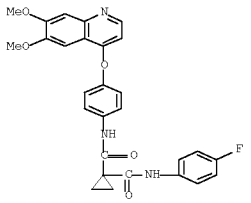
PRIORITY APPLN. INFO.: US 2011-61538039 P 20110922
WO 2012-US56281 W 20120920
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 158:494085; MARPAT 158:494085
GI



AB This invention is directed to the treatment of osteoporosis using N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide.
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for treating osteoporosis)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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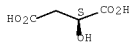
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CM 2

CRN 97-67-6
CMF C4 H6 O5

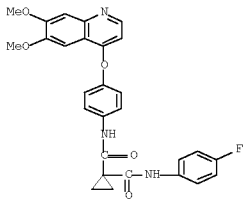
Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treating osteoporosis)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

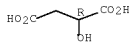
CRN 849217-68-1
CMF C28 H24 F N3 O5



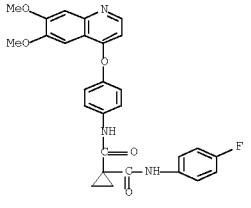
CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

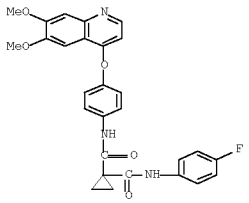


IT 849217-68-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for treating osteoporosis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 443 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:417299 CAPLUS Full-text
DOCUMENT NUMBER: 159:86304
TITLE: Pharmacokinetic evaluation of
AUTHOR(S): Karras, Spyridon; Pontikides, Nikolaos; Krassas, Gerasimos E.
CORPORATE SOURCE: Department of Endocrinology, Diabetes and Metabolism, Panagia General Hospital, Thessaloniki, Greece
SOURCE: Expert Opinion on Drug Metabolism & Toxicology (2013), 9(4), 507-515
CODEN: EODMAP; ISSN: 1742-5255
DIGITAL OBJECT ID: 10.1517/17425255.2013.780028
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Introduction: Conventional treatment modalities for thyroid cancer lead to complete remission in only one-third of patients with distant metastases. On the other hand, medullary thyroid cancer (MTC) and anaplastic thyroid cancer (ATC), although rare, are responsible for a significant percentage of thyroid cancer-related deaths. New treatments are needed to treat such patientsAreas covered: The aim of this review is to provide the latest information on , a new tyrosine kinase inhibitor (TKI) that is currently used mainly as a treatment of MTC. The authors collated data that were retrieved from a PubMed literature search.Expert opinion: CBZ targets multiple cell-signaling pathways involved in the mol. pathogenesis of thyroid cancer. These are namely VEGF receptor-2, hepatocyte growth factor receptor and rearranged during transfection receptor. Furthermore, it is a drug which may be used in cases where conventional therapies (mainly for MTC) are proved ineffective or have shown poor results with a good outcome. CBZ may also be administered alone or in combination with other drugs of the same family.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(understanding pharmacokinetics of cabozantinib may be useful in treatment of patient with medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

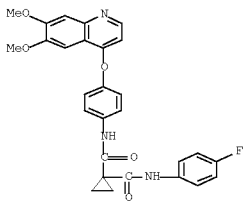


OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 444 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:414621 CAPLUS Full-text
DOCUMENT NUMBER: 159:53852
TITLE: Effects of dual targeting of tumor cells and stroma in human glioblastoma xenografts with a tyrosine kinase inhibitor against c-MET and VEGFR2
AUTHOR(S): Navis, Anna C.; Bourgonje, Annika; Wesseling, Pieter; Wright, Alan; Hendriks, Wiljan; Verrijp, Kiek; van der Laak, Jeroen A. W. M.; Heerschap, Arend; Leenders, William P. J.
CORPORATE SOURCE: Department of Pathology, Radboud University Nijmegen Medical Centre, Nijmegen, Neth.
SOURCE: PLoS One (2013), 8(3), e58262
CODEN: POLNCL; ISSN: 1932-6203
DIGITAL OBJECT ID: 10.1371/journal.pone.0058262
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Anti-angiogenic treatment of glioblastoma with Vascular Endothelial Growth Factor (VEGF)- or VEGF Receptor 2 (VEGFR2) inhibitors normalizes tumor vessels, resulting in a profound radiol. response and improved quality of life. This approach however does not halt tumor progression by diffuse infiltration, as this phenotype is less angiogenesis dependent. Combined inhibition of angiogenesis and diffuse infiltrative growth would therefore be a more effective treatment approach in these tumors. The HGF/c-MET axis is important in both angiogenesis and cell migration in several tumor types including glioma. We therefore analyzed the effects of the c-MET- and VEGFR2 tyrosine kinase inhibitor cabozantinib (XL184, Exelixis) on c-MET pos. orthotopic E98 glioblastoma xenografts, which routinely present with angiogenesis-dependent areas of tumor growth, as well as diffuse infiltrative growth. In in vitro cultures of E98 cells, cabozantinib effectively inhibited c-MET phosphorylation, concomitant with inhibitory effects on AKT and ERK1/2 phosphorylation, and cell proliferation and migration. VEGFR2 activation in endothelial cells was also effectively inhibited in vitro. Treatment of BALB/c nu/nu mice carrying orthotopic E98 xenografts resulted in a significant increase in overall survival. Cabozantinib effectively inhibited angiogenesis, resulting in increased hypoxia in angiogenesis-dependent tumor areas, and induced vessel normalization. Yet, tumors ultimately escaped cabozantinib therapy by diffuse infiltrative outgrowth via vessel co-option. Of importance, in contrast to the results from in vitro expts., in vivo blockade of c-MET activation was incomplete, possibly due to multiple factors including restoration of the blood-brain barrier resulting from cabozantinib-induced VEGFR2 inhibition. In conclusion, cabozantinib is a promising therapy for c-MET pos. glioma, but improving delivery of the drug to the tumor and/or the surrounding tissue may be needed for full activity.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of dual targeting of tumor cells and stroma in human glioblastoma xenografts with tyrosine kinase inhibitor against c-MET and VEGFR2)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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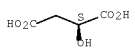
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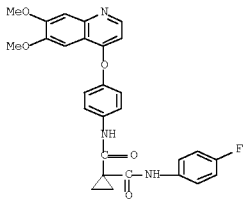
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CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



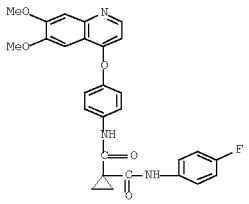
OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 445 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:378985 CAPLUS Full-text
DOCUMENT NUMBER: 159:193339
TITLE: Cellular signaling pathway alterations and potential targeted therapies for medullary thyroid carcinoma
AUTHOR(S): Giunti, Serena; Antonelli, Alessandro; Amorosi, Andrea; Santarpia, Libero
CORPORATE SOURCE: Department of Pathology, Centro Oncologico Fiorentino, Sesto Fiorentino, 50019, Italy
SOURCE: International Journal of Endocrinology (2013) 803171, 16 pp.
CODEN: IJENIG; ISSN: 1687-8345
DIGITAL OBJECT ID: 10.1155/2013/803171
PUBLISHER: Hindawi Publishing Corp.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Parafollicular C-cell-derived medullary thyroid cancer (MTC) comprises 3% to 4% of all thyroid cancers. While cytotoxic treatments have been shown to have limited efficacy, targeted mol. therapies that inhibit rearranged during transfection (RET) and other tyrosine kinase receptors that are mainly involved in angiogenesis have shown great promise in the treatment of metastatic or locally advanced MTC. Multi-tyrosine kinase inhibitors such as vandetanib, which is already approved for the treatment of progressive MTC, and cabozantinib have shown distinct advantages with regard to rates of disease response and control. However, these types of tyrosine kinase inhibitor compds. are able to concurrently block several types of targets, which limits the understanding of RET as a specific target. Moreover, important resistances to tyrosine kinase inhibitors can occur, which limit the long-term efficacy of these treatments. Deregulated cellular signaling pathways and genetic alterations in MTC, particularly the activationof the RAS/mammalian target of rapamycin (mTOR) cascades and RET crosstalk signaling, are now emerging as novel and potentially promising therapeutic treatments for aggressive MTC.
IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cellular signaling pathway alterations and potential targeted therapies for medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 446 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:377358 CAPLUS Full-text
DOCUMENT NUMBER: 159:86211
TITLE: Cabozantinib as a Novel Therapy for Renal Cell Carcinoma
AUTHOR(S): Vaishampayan, Ulka
CORPORATE SOURCE: Wayne State University, Detroit, MI, 48201, USA
SOURCE: Current Oncology Reports (2013), 15(2), 76-82
CODEN: CORUAT; ISSN: 1534-6269
DIGITAL OBJECT ID: 10.1007/s11912-012-0289-x
PUBLISHER: Springer
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Cabozantinib/XL184 (Exelexis, Inc.) has demonstrated remarkable responses in kidney cancer. Preclin. results revealed VEGF, KIT and MET inhibition in a variety of solid tumors such as thyroid, ovarian, renal, lung, liver and prostate cancers. A phase II trial demonstrated efficacy in renal cancer with a 28 % objective response rate, stable disease rate of 62 % and median progression free survival of 14.7 mo. Predominant toxicities of fatigue and diarrhea were noted. Dramatic responses in bone metastases (three of four patients) make the agent especially valuable for palliation in a disease, where presence of bone metastases is a predictor of worse survival. Cabozantinib is an emerging novel agent with promising activity in advanced kidney cancer. Randomized trials are planned in comparison with standard VEGF inhibitor therapy. Defining the role of MET overexpression would help patient selection and enrich and enhance the future evaluation of this targeted novel agent.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib as novel therapy may be useful for treatment of patient with renal cell carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

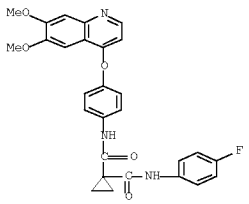


OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 447 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:359822 CAPLUS full-text
DOCUMENT NUMBER: 159:33929
TITLE: Treatment directed to signalling molecules in patients with advanced differentiated thyroid cancer
AUTHOR(S): Saez, Jose M. G.
CORPORATE SOURCE: Endocrinology and Nutrition Service, L'Hospitalet of Llobregat, Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (CIBERDEM), University Hospital of Bellvitge, Barcelona, Spain
SOURCE: Anti-Cancer Agents in Medicinal Chemistry (2013), 13(3), 483-495
CODEN: AAMCE4; ISSN: 1871-5206
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Mutation detection in samples from thyroid cancer with the addition of BRAF mutation, and also the detection of RAS, RET/PTC, and PAX8/PPARγ mutations, may also contribute to cancer diagnosis. On the other hand, the MAPK/ERK (mitogen-activated protein kinase/extracellular signal-regulated kinase signaling pathway) and PI3K/Akt (lipid kinase phoshoinositid-3-kinase signaling pathway) play an important role in the transmission of cell signals. The genes, coding the signaling cascade proteins (RET, RAS, BRAF, PI3K, PTEN, AKT), are mutated or aberrantly expressed in thyroid cancer derived from follicular thyroid cells. Genetic and epigenetic alternations, concerning MAPK/ERK and PI3K/Akt signaling pathways, contribute to their activation and interaction as a consequence of malignant follicular cell transformation. The understanding of this mol. mechanism provides access to novel mol. prognostic and therapeutic strategies for inhibiting the oncogenic activity of the signaling pathways. This ability to investigate tumor biol. allows for the selection of different drugs. Nowadays the most relevant are treatments directed to tyrosine kinase receptors that bind for a wide variety of ligands and are frequently mutated and induce a constitutive activation such that a chimerical protein expression takes place in follicular cells in the domain of RET, as well as in other receptors. Many mols. such as: motesanib, sorafenib, vandetanib, sunitinib, XL-184, imatinib, axitinib, pazopanib, lenvatinib, combretastatin, gefitinib, cetuximab, bortezomib and thiazoldonedione have been developed. Some of them also can act in receptors of vascular endothelial growth factor and epidermal growth factor receptors. Information obtained through cytol. or biopsy samples permits the study of complex metabolic or genetic pathways, thus providing researchers with a high throughput tool for elucidating changes in the global expression patterns seen in tumor cells and allowing for different therapeutic strategies in thyroid cancer which take into account the predominant altered pathways observed in these samples.
IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment directed to signaling mols. in patients with advanced differentiated thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

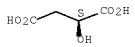
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CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



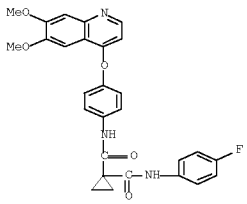
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L4 ANSWER 448 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:260769 CAPLUS full-text
DOCUMENT NUMBER: 158:690611
TITLE: Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial
AUTHOR(S): Smith, David C.; Smith, Matthew R.; Sweeney, Christopher; Elfiky, Aymen A.; Logothetis, Christopher; Corn, Paul G.; Vogelzang, Nicholas J.; Small, Eric J.; Harzstark, Andrea L.; Gordon, Michael S.; Vaishampayan, Ulka N.; Haas, Naomi B.; Spira, Alexander I.; Lara, Primo N., Jr.; Lin, Chia-Chi; Srinivas, Sandy; Sella, Avishay; Schoffski, Patrick; Scheffold, Christian; Weitzman, Aaron L.; Hussain, Maha
CORPORATE SOURCE: University of Michigan, Ann Arbor, USA
SOURCE: Journal of Clinical Oncology (2013), 31(4), 412-419
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.45.0494
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Cabozantinib (XL 184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. Patients and Methods: Patients received 100 mg of cabozantinib daily. Those with stable disease per RECIST at 12 wk were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 wk and progression-free survival (PFS) after random assignment. Results: One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 wk was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 wk (95% CI, 10.7 to 62.4 wk) with cabozantinib and 5.9 wk (95% CI, 5.4 to 6.6 wk) with placebo (hazard ratio, 0.12; P < .001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by ≥ 50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot

syndrome (8%). Conclusion: Cabozantinib has clin. activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and redns. in bone turnover markers, pain, and narcotic use.

IT 849217-68-1, Cabozantinib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib improved progression-free survival, reduced soft tissue lesions, bone turnover markers, pain and narcotic use in patient with castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



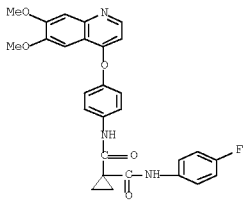
OS.CITING REF COUNT: 147 THERE ARE 147 CAPLUS RECORDS THAT CITE THIS RECORD (147 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 449 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:260767 CAPLUS Full-text
DOCUMENT NUMBER: 160:42366
TITLE: Cabozantinib in prostate cancer: the beginning of a precision paradigm?
AUTHOR(S): Goodin, Susan; DiPaola, Robert S.
CORPORATE SOURCE: The Cancer Institute of New Jersey, University of Medicine and Dentistry of New Jersey Robert Wood Johnson Medical School, New Brunswick, NJ, USA
SOURCE: Journal of Clinical Oncology (2013), 31(4), 401-403
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2012.46.6185
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The research of Smith et al. (2013) entitled, 'Cabozantinib in patients with advanced prostate cancer: Results of a phase II randomized discontinuation trial' is reviewed with commentary and refs. The authors presented data on a novel orally bioavailable tyrosine kinase inhibitor (TKI), cabozantinib, with activity against multiple targets including mesenchymal-epithelial transition factor (MET), also known as hepatocyte growth factor receptor, and the vascular endothelial growth factor receptor 2 (VEGFR2). They reported a reduction in uptake on bone scan with improvement in 68% of men (79 of 116) with bone metastasis and complete resolution in 14 patients.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib in prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



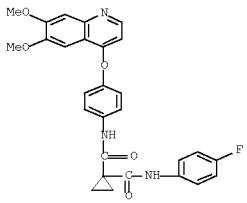
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REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 450 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2013:187940 CAPLUS Full-text
DOCUMENT NUMBER: 159:33573
TITLE: Profile of cabozantinib and its potential in the treatment of advanced medullary thyroid cancer
AUTHOR(S): Hart, Christopher D.; De Boer, Richard H.
CORPORATE SOURCE: Department of Oncology, Royal Melbourne Hospital, Parkville, Victoria, 3050, Australia
SOURCE: OncoTargets and Therapy (2013), 6, 1-7
CODEN: OTNHAZ; ISSN: 1178-6930
DIGITAL OBJECT ID: 10.2147/OTT.S27671
PUBLISHER: Dove Medical Press Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Medullary thyroid cancer is an uncommon malignancy for which until recently little effective treatment existed. It is often characterized by mutation and overexpression of the receptor tyrosine kinases RET (rearranged during transfection), VEGFR2 (vascular endothelial growth factor receptor 2) and MET (mesenchymal-epithelial transition factor), which make attractive targets for drug development. Cabozantinib is an orally bioavailable tyrosine kinase inhibitor which blocks MET, VEGRF2 and RET, and has shown considerable activity in medullary thyroid cancer in a Phase III trial, including in heavily pretreated patients. Its novel combination of vascular endothelial growth factor and MET inhibition is believed to address the MET escape pathway, which is thought to be the cause of nonsustained tumor responses resulting from inhibition of vascular endothelial growth factor alone.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(profile of cabozantinib and potential in treatment of advanced medullary thyroid cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 451 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1893113 CAPLUS Full-text
DOCUMENT NUMBER: 158:123654
TITLE: Methods of treating cancer using a chemotherapeutic agent with an agent that blocks the activity of hepatocyte growth factor or its cognate receptor c-MET.
INVENTOR(S): Golub, Todd; Straussman, Ravid
PATENT ASSIGNEE(S): The Broad Institute, Inc., USA; Dana-Farber Cancer Institute, Inc.
SOURCE: PCT Int. Appl., 104pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

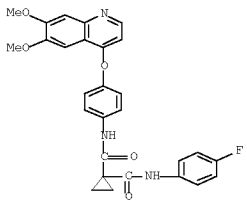
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US 20140348819	A1	20141127	US 2014-14128916	20140819
PRIORITY APPLN. INFO.:			US 2011-61501091 P1	20110624
			WO 2012-US43788 W	20120622

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides methods of treating cancer by preventing or reducing chemoresistance in a tumor by administering a chemotherapeutic agent together with another agent that blocks the activity of hepatocyte growth factor or its cognate receptor c-MET.

IT 849217-68-1, Cabozantinib 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer treatment using a chemotherapeutic agent with an agent that blocks the activity of HGF or its cognate receptor c-MET)

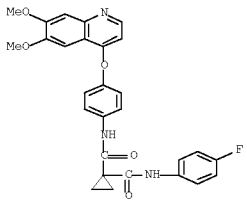
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

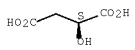
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

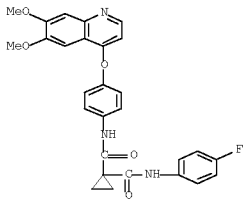
CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



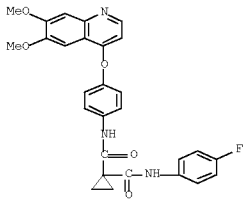
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 452 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1845709 CAPLUS Full-text
DOCUMENT NUMBER: 158:644003
TITLE: New agents in metastatic prostate cancer
AUTHOR(S): Choudhury, Atish D.; Kantoff, Philip W.
CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE: Journal of the National Comprehensive Cancer Network (2012), 10(11), 1403-1409
CODEN: JNCCA4; ISSN: 1540-1405
DIGITAL OBJECT ID: 10.6004/jnccn.2012.0145
PUBLISHER: Harborside Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Discoveries of mol. mechanisms and therapeutic targets in metastatic castration-resistant prostate cancer (CRPC) have led to significant advancements in the development of effective agents in this setting, with diverse mechanisms of action. Within the past 2 years, 5 agents have been approved for the treatment of patients with metastatic CRPC (cabazitaxel, abiraterone, sipuleucel-T, denosumab, and enzalutamide), and another (Alpharadin) has shown overall survival benefit in a phase III trial. This article summarizes the phase III data showing clin. benefit from these agents, highlights other promising therapies in phase III studies as single agents (PROSTVAC-VF, ipilimumab, cabozantinib), discusses important unanswered questions regarding these therapies, and provides a schema for their use based on current regulatory approval and how this is likely to evolve as data from ongoing studies are reported. Although curative interventions in metastatic CRPC still do not exist, the hope is that optimization of therapeutic strategies can reduce the morbidity and mortality associated with this disease.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new agents in metastatic prostate cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 453 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1765841 CAPLUS Full-text
DOCUMENT NUMBER: 158:670189
TITLE: Cabozantinib for the Treatment of Advanced Medullary Thyroid Cancer
AUTHOR(S): Nagilla, Madhavi; Brown, Rebecca L.; Cohen, Ezra E. W.
CORPORATE SOURCE: Section of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Chicago, Chicago, IL, 60645, USA
SOURCE: Advances in Therapy (2012), 29(11), 925-934
CODEN: ADTHE7; ISSN: 0741-238X
DIGITAL OBJECT ID: 10.1007/s12325-012-0060-6
PUBLISHER: Springer Healthcare Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Introduction Patients with advanced medullary thyroid cancer (MTC) have poor prognoses and limited treatment options. Improved knowledge about mol. aberrations associated with MTC and the availability of novel targeted tyrosine kinase inhibitors (TKIs) have led to new potential treatment modalities. Cabozantinib is an oral multitargeted TKI with activity against multiple receptors including RET, vascular endothelial growth factor receptor type 2 (VEGFR2), and MET that has been evaluated in MTC in the preclin. and clin. arenas. Methods This article reviews unmet clin. needs in advanced MTC. The authors consider novel agents that have been studied in MTC, with a focus on the investigational agent cabozantinib. Up-to-date clin. data of cabozantinib in MTC are discussed. Results Recent clin. evaluation suggests that cabozantinib is the first agent to prolong progression-free survival in patients with progressive MTC. These findings indicate that cabozantinib may be an effective therapy in advanced MTC. No improvement in overall survival has been demonstrated but data are not mature. Conclusion Cabozantinib may be an effective treatment option for patients with advanced MTC and is worthy of further evaluation.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib for the treatment of advanced medullary thyroid cancer)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)

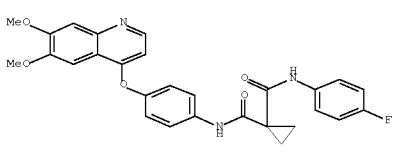


OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 454 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1630842 CAPLUS Full-text
DOCUMENT NUMBER: 157:699601
TITLE: Method of treating cancer and bone cancer pain
INVENTOR(S): Schwab, Gisela; Aftab, Dana T.
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 52pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012151326	A1	20121108	WO 2012-US36191	20120502
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, RU, TJ, TM				
CA 2834778	A1	20121108	CA 2012-2834778	20120502
AR 86242	A1	20131127	AR 2012-101544	20120502
AU 2012250759	A1	20131128	AU 2012-250759	20120502
IL 229094	A	20131231	IL 2012-229094	20120502
KR 2014025496	A	20140304	KR 2013-7031635	20120502
EP 2704717	A1	20140312	EP 2012-720754	20120502
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 103717221	A	20140409	CN 2012-80026424	20120502
JP 2014513129	T	20140529	JP 2014-509417	20120502
BR 212013028314	U2	20151103	BR 2013-212013028314	20120502
NZ 617508	A	20160429	NZ 2012-617508	20120502
MX 2013012695	A	20140327	MX 2013-12695	20131030
ZA 2013008206	A	20140730	ZA 2013-8206	20131101
IN 2013KN03259	A	20140221	IN 2013-KN3259	20131105
US 20140179736	A1	20140626	US 2014-14115236	20140228

PRIORITY APPLN. INFO.: US 2011-61481682 P 20110502
US 2011-61557366 P 20111108
WO 2012-US36191 W 20120502
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:699601; MARPAT 157:699601
GI

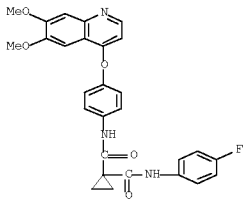


AB This invention is directed to the treatment of cancer, particularly lung cancer, breast cancer, melanoma, renal cell carcinoma, thyroid cancer that has metastasized to the bone. The invention is also directed to a method for treating bone cancer pain in an individual in need of such treatment comprising administering to the individual an effective amount of a compound of Formula I.

IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(method of treating cancer and bone cancer pain)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



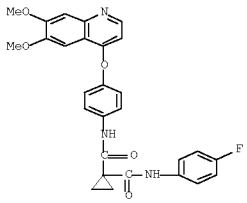
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cancer and bone cancer pain)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

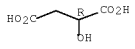
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 455 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2012:1563334 CAPLUS Full-text

DOCUMENT NUMBER: 158:492390

TITLE: New developments in castrate-resistant prostate cancer

AUTHOR(S): Shore, N.; Mason, M.; de Reijke, Th. M.

CORPORATE SOURCE: Carolina Urologic Research Center, Atlantic Urology Clinics, Myrtle Beach, SC, USA

SOURCE: BJU International (2012), 109(Suppl. 6), 22-32
CODEN: BJINFO; ISSN: 1464-4096

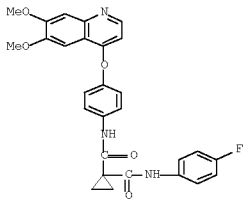
DIGITAL OBJECT ID: 10.1111/j.1464-410X.2012.11217.x

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

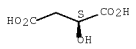
AB A review. Castrate-resistant prostate cancer (CRPC) occurs when disease progresses in the presence of castrate levels of androgens and remains sensitive to further hormonal manipulation. For many years the treatment of CRPC was limited to the use of docetaxel for metastatic disease. However, this has recently changed with the approval of several new agents. Sipuleucel-T, an immunotherapeutic vaccine, is now available in the US for patients with non-metastatic CRPC and abiraterone, an oral enzyme inhibitor of androgen biosynthesis, as well as cabazitaxel, a cytotoxic



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cancer and bone cancer pain)

RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

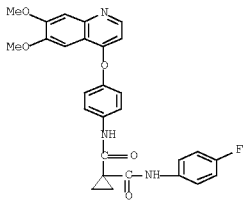
CRN 849217-68-1
CMF C28 H24 F N3 O5

chemotherapeutic, have been approved for the treatment of metastatic CRPC. Also, denosumab, a s.c. antibody, is now an option for the treatment of patients with CRPC with bone metastases, in addition to zoledronic acid, an i.v. bisphosphonate. Further treatment advances for metastatic CRPC therapeutics are in late stage phase III development. These include therapies affecting the androgen receptor (MDV3100) as well as addnl. immune-based therapeutics, PROSTVAC and ipilimumab. A broad range of agents is also emerging under the term targeted therapies. The endothelin-A receptor antagonist zibotentan, the tyrosine kinase inhibitors dasatinib, sorafenib and cabozantinib, the anti-angiogenic agent aflibercept, and the clusterin inhibitor custirsen, are all currently being tested for efficacy in metastatic CRPC. The mechanism of action of these and other promising agents are discussed alongside current therapeutic options and their potential place in the treatment landscape for CRPC is considered.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new developments in castrate-resistant prostate cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 456 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2012:1483426 CAPLUS Full-text

DOCUMENT NUMBER: 157:573884

TITLE: Methods for predicting and improving the survival of gastric cancer patients

INVENTOR(S): Kim, Phillip; Singh, Sharat

PATENT ASSIGNEE(S): Nestec SA, Switz.

SOURCE: PCT Int. Appl., 147pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012138785	A1	20121011	WO 2012-US32206	20120404
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2831468	A1	20121011	CA 2012-2831468	20120404
AU 2012240242	A1	20131010	AU 2012-240242	20120404
IL 228579	A	20131128	IL 2012-228579	20120404
EP 2694972	A1	20140212	EP 2012-716858	20120404
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
KR 2014020318	A	20140218	KR 2013-7029113	20120404
CN 103597354	A	20140219	CN 2012-80027365	20120404
CN 103597354	B	20160420		
JP 2014517259	T	20140717	JP 2014-503964	20120404
NZ 615738	A	20151127	NZ 2012-615738	20120404
SG 10201601301	A1	20160330	SG 2016-10201601301	20120404
MX 2013011431	A	20140606	MX 2013-11431	20130930
US 20140099300	A1	20140410	US 2013-14044792	20131002
IN 2013DN08648	A	20160603	IN 2013-DN8648	20131004

PRIORITY APPLN. INFO.: US 2011-61471678 P 20110404
US 2012-61590787 P 20120125
WO 2012-US32206 W 20120404

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides assays and methods for predicting the post-operative survival of a subject having an early stage gastric cancer after tumor surgery. The present invention also provides methods for treating a subject having an early stage gastric cancer by administering a combination therapy tailored to the signal transduction biomarkers that are activated in the cancer. In particular embodiments, the methods of the invention rely on the detection of the activation state or level of a specific combination of signal transducer analytes in a cancer cell obtained from the subject. Thus, the methods of the invention are particularly useful for predicting the survival or prognosis of a subject having an early stage gastric cancer and for guiding both pre- and post-operative treatment decisions by identifying subjects who would benefit from combination therapy as opposed to monotherapy.

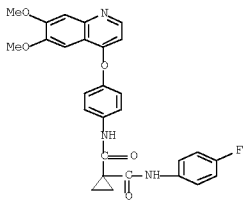
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cMET and HER as markers and drug targets for predicting survival of a subject having type I or II gastric cancer after tumor surgery)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

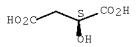
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 457 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1450760 CAPLUS Full-text
DOCUMENT NUMBER: 157:567006
TITLE: Method of treating cancer
INVENTOR(S): Aftab, Dana T.; Schimmoller, Frauke
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 17pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120252840	A1	20121004	US 2012-13438964	20120404
US 20150196545	A1	20150716	US 2015-14668312	20150325
US 20160051532	A1	20160225	US 2015-14933801	20151105

PRIORITY APPLN. INFO.: US 2011-61471367 P 20110404
US 2012-13438964 A1 20120404
US 2015-14668312 A1 20150325

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

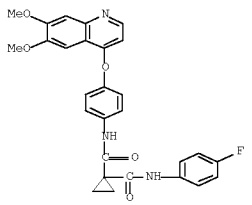
OTHER SOURCE(S): CASREACT 157:567006

AB This invention is directed to the treatment of cancer, particularly ocular melanoma, with a dual inhibitor of MET and VEGF such as Compound 1.

IT 849217-68-1
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(method of treating cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



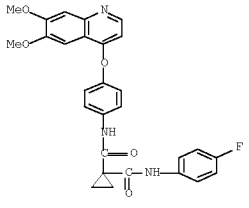
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

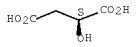
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



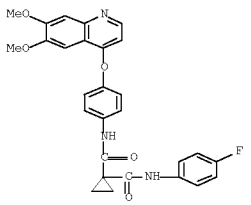
IT 1365530-43-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cancer)

RN 1365530-43-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

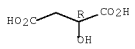
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 458 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1270117 CAPLUS Full-text
DOCUMENT NUMBER: 157:438359
TITLE: Preparation of substituted quinoline compounds as protein tyrosine kinase modulators
INVENTOR(S): Xi, Ning
PATENT ASSIGNEE(S): Sunshine Lake Pharma Co., Ltd., USA; Calitor Sciences, LLC
SOURCE: U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120219522	A1	20120830	US 2012-13400586	20120221
US 9133162	B2	20150915		
CA 2820709	A1	20120907	CA 2012-2820709	20120221
CA 2820709	C	20160216		
WO 2012118632	A1	20120907	WO 2012-US25834	20120221

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

KR 2013095806	A	20130828	KR 2013-7015842	20120221
KR 1546693	B1	20150824		
EP 2680886	A1	20140108	EP 2012-752321	20120221
EP 2680886	B1	20160810		

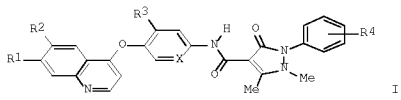
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2014506925	T	20140320	JP 2013-556713	20120221
JP 5707518	B2	20150430		
ZA 2013003793	A	20140730	ZA 2013-3793	20120221
AU 2012223639	B2	20150319	AU 2012-223639	20120221
RU 2568258	C2	20151120	RU 2013-135662	20120221
BR 112013014708	A2	20161004	BR 2013-112013014708	20120221
ES 2590778	T3	20161123	ES 2012-752321	20120221
IN 2013DN04974	A	20160520	IN 2013-DN4974	20130604
MX 2013007278	A	20130913	MX 2013-7278	20130621
HK 1187259	A1	20170428	HK 2014-100267	20140109
US 20150342945	A1	20151203	US 2015-14824096	20150812
US 9598400	B2	20170321		

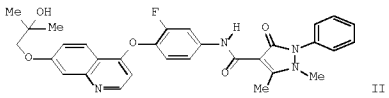
PRIORITY APPLN. INFO.:

US 2011-61447104	P	20110228
US 2012-13400586	A3	20120221
WO 2012-US25834	W	20120221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:438359; MARPAT 157:438359
GI

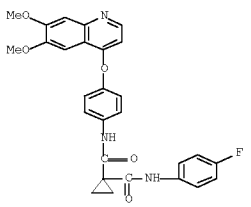


I



II

AB The present invention provides novel substituted quinoline compds. I [R1, R2 = H, alkoxy, hydroxyalkoxy; R3 = H, F; R4 = H, F, Cl, Br, I, etc.; X = CH or N, wherein at least one of R1 and R2 = hydroxyalkoxy], pharmaceutical acceptable salts and formulations thereof useful in modulating the protein tyrosine kinase activity, and in modulating cellular activities such as proliferation, differentiation, apoptosis, migration and invasion. Syntheses of exemplified compds. I were described. E.g., a multi-step synthesis of the pyrazolecarboxamide II, starting from 3-benzyloxybenzenamine, was provided. Exemplified compds. I were tested for their efficacy as inhibitors of receptor tyrosine kinases such as c-Met, VEGFR and Axl, and as antitumor agents (data given). The invention also provides pharmaceutically acceptable compns. comprising compds. I and methods of using the compns. in the treatment of hyperproliferative disorders in mammals, especially humans.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of substituted quinoline compds. as protein tyrosine kinase modulators)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 459 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1269771 CAPLUS Full-text
DOCUMENT NUMBER: 157:431629
TITLE: Methods for detecting cancer and/or determining response to therapeutic agent, and numerous circulating markers (including proteins, nucleic acids and vesicles) used in said methods
INVENTOR(S): Spetzler, David; Holterman, Daniel A.; Pawlowski, Traci; Tasinato, Andrea
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, S.A.R.L., Luxembourg
SOURCE: PCT Int. Appl., 695pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012115885	A1	20120830	WO 2012-US25741	20120217

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2827894	A1	20120830	CA 2012-2827894	20120217
AU 2012220872	A1	20130912	AU 2012-220872	20120217
CN 103492590	A	20140101	CN 2012-80019718	20120217
EP 2678448	A1	20140101	EP 2012-749642	20120217

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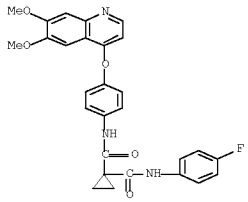
JP 2014507160	T	20140327	JP 2013-555467	20120217
US 20140141986	A1	20140522	US 2014-14001016	20140207
AU 2015268602	A1	20160107	AU 2015-268602	20151209

PRIORITY APPLN. INFO.:

US 2011-61445273	P	20110222
US 2011-61446313	P	20110224
US 2011-61471417	P	20110404
US 2011-61501680	P	20110627
US 2011-61523763	P	20110815
AU 2011-291599	A3	20110818
WO 2012-US25741	W	20120217

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The invention provides methods for detecting cancer, for detg. whether a cancer is responding to treatment, and /or for determining whether a cancer is likely to respond to treatment that involve detecting of circulating biomarkers. The invention relates that said circulating biomarkers can includie nucleic acids, proteins, vesicles and/or microRNAs. The invention also relates that said biol. samples used in the disclosed methods include isolated extracellular microvesicle populations. The invention also provides kits comprising all reagents used in the disclosed methods. In the examples, the invention disclosed that specific biomarkers are elevated in specific types of cancer, which can used in diagnosis and in determining treatments.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for detecting cancer and/or determining response to therapeutic agent, and numerous circulating markers (including proteins, nucleic acids and vesicles) used in said methods)
RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



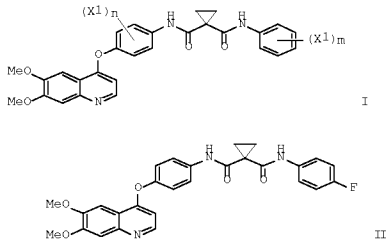
OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 460 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1201570 CAPLUS Full-text
DOCUMENT NUMBER: 157:382704
TITLE: Processes for preparing quinoline compounds and pharmaceutical compositions containing such compounds
INVENTOR(S): Wilson, Jo Ann
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012109510	A1	20120816	WO 2012-US24591	20120210
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2826751	A1	20120816	CA 2012-2826751	20120210
AU 2012214322	A1	20130829	AU 2012-214322	20120210
AU 2012214322	B2	20170427		
AR 85155	A1	20130911	AR 2012-100446	20120210
IL 227848	A	20130930	IL 2012-227848	20120210
CN 103459373	A	20131218	CN 2012-80017723	20120210
EP 2673262	A1	20131218	EP 2012-704492	20120210
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JP 2014505109	T	20140227	JP 2013-553580	20120210
KR 2014044782	A	20140415	KR 2013-7023174	20120210
NZ 614130	A	20151030	NZ 2012-614130	20120210
NZ 712808	A	20170331	NZ 2012-712808	20120210
MX 2013009116	A	20140131	MX 2013-9116	20130807
ZA 2013006072	A	20140430	ZA 2013-6072	20130813
IN 2013KN02666	A	20140103	IN 2013-KN2666	20130903
US 20140200242	A1	20140717	US 2014-13984559	20140320
JP 2016188216	A	20161104	JP 2016-94411	20160510
US 20170057921	A1	20170302	US 2016-15348716	20161110

PRIORITY APPLN. INFO.:
US 2011-61441520 P 20110210
US 2011-61441527 P 20110210
JP 2013-553580 A3 20120210
NZ 2012-614130 A3 20120210
WO 2012-US24591 W 20120210
US 2014-13984559 A1 20140320

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 157:382704; MARPAT 157:382704
GI

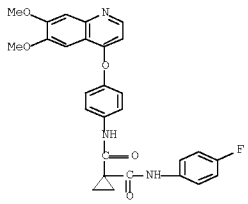


I

II

AB The invention is directed to processes for prepg. quinoline compds. of formula I wherein X1 is H, Br, Cl and F; X2 is H, Br, Cl and F; n is 1-2 and m is 1-2; and pharmaceutically acceptable salts thereof. Example compound II L-malate was prepared by chlorination of 6,7-dimethoxyquinolin-4-ol followed by etherification of 4-chloro-6,7-dimethoxyquinoline with 4-aminophenol; the resulting 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine underwent acylation with 1-[(4-fluorophenyl)carbamoyl]cyclopropanecarbonyl chloride to give compound II, which underwent addition of L-malic acid to give the desired product.

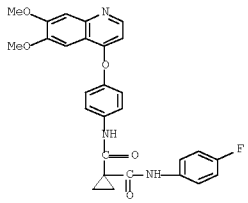
IT 849217-68-1P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for preparing quinoline derivs. and pharmaceutical compns. thereof)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparing quinoline derivs. and pharmaceutical compns. thereof)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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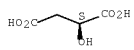
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 461 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:1051547 CAPLUS Full-text
DOCUMENT NUMBER: 157:218520
TITLE: Molecular diagnostic methods for predicting brain metastasis of breast cancer
INVENTOR(S): Wong, Stephen T. C.; Zhao, Hong
PATENT ASSIGNEE(S): The Methodist Hospital Research Institute, USA
SOURCE: U.S. Pat. Appl. Publ., 53pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120184560	A1	20120719	US 2011-13245706	20110926
US 9651554	B2	20170516		

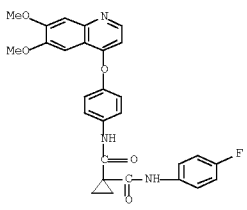
PRIORITY APPLN. INFO.: US 2010-61386186 P 20100924
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Disclosed are mol. diagnostic compns. and methods for predicting brain metastasis of breast cancer, as well as methods for drug repositioning to

identify existing and new therapeutics for use in developing individualized, patient-specific treatment regimens for improving diagnoses and patient outcomes in individuals at risk for brain metastasis of breast cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. diagnostic methods for predicting brain metastasis of breast cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 462 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2012:1042874 CAPLUS Full-text

DOCUMENT NUMBER: 157:221701

TITLE: Bcl-2-like protein 11 (BIM) SRM/MRM assay

INVENTOR(S): Krizman, David B.; Hembrough, Todd; Thyparambil, Sheeno; Liao, Wei-Li

PATENT ASSIGNEE(S): Expression Pathology, Inc., USA

SOURCE: PCT Int. Appl., 28pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012097276	A2	20120719	WO 2012-US21283	20120113
WO 2012097276	A3	20121129		

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2824752	A1	20120719	CA 2012-2824752	20120113
AU 2012205337	A1	20130801	AU 2012-205337	20120113
AU 2012205337	B2	20170413		
IL 227471	A	20130829	IL 2012-227471	20120113
EP 2663863	A2	20131120	EP 2012-734572	20120113

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2014505251	T	20140227	JP 2013-549580	20120113
JP 6046053	B2	20161214		
US 20130302334	A1	20131114	US 2013-13942574	20130715
US 9551719	B2	20170124		
US 20160377633	A1	20161229	US 2016-15262736	20160912

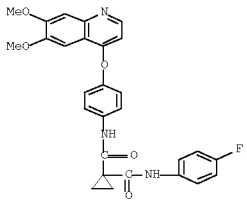
PRIORITY APPLN. INFO.: US 2011-61432462 P 20110113
WO 2012-US21283 W 20120113
US 2013-13942574 A1 20130715

AB Specific peptides, and derived ionization characteristics of those peptides, from the Bcl-2-like protein 11 (BIM) are provided that are particularly advantageous for quantifying the BIM protein directly in biol. samples that have been fixed in formalin by the method of Selected Reaction Monitoring (SRM) mass spectrometry, or what can also be termed as Multiple Reaction Monitoring (MRM). Such biol. samples are chemical preserved and fixed where the biol. sample is selected from tissues and cells treated with formaldehyde containing agents/fixatives including formalin-fixed tissue/cells, formalin- fixed/paraffin embedded (FFPE) tissue/cells, FFPE tissue blocks and cells from those blocks, and tissue culture cells that have been formalin fixed and or paraffin embedded. A protein sample is prepared from the biol. sample using the Liquid Tissue reagents and protocol, and the BIM protein is quantitated in the Liquid Tissue sample by the method of SRM/MRM mass spectrometry by quantitating in the protein sample at least one or more of the peptides described. These peptides can be quantitated if they reside in a modified or an unmodified form. An example of a modified form of a BIM peptide is phosphorylation of a tyrosine, threonine, serine, and/or other amino acid residues within the peptide sequence. Samples were prepared with Liquid Tissue and digested with trypsin. Three peptides from BIM were found to be suitable for SRM/MRM assay.

IT 849217-68-1, Cabozantinib
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(determination of cancer resistance to; BIM protein determination by determining BIM peptides
by SRM/MRM mass spectrometry)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



L4 ANSWER 463 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2012:924299 CAPLUS Full-text

DOCUMENT NUMBER: 157:122897

TITLE: Drug selection for therapy for malignancies involving c-Met signaling using antibody-based arrays

INVENTOR(S): Singh, Sharat; Hoe, Nicholas; Princen, Fred; Liu, Xinjun

PATENT ASSIGNEE(S): Prometheus Laboratories Inc., USA

SOURCE: PCT Int. Appl., 140pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012088337	A1	20120628	WO 2011-US66624	20111221

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2822283	A1	20120628	CA 2011-2822283	20111221
AU 2011348256	A1	20130711	AU 2011-348256	20111221
IL 227009	A	20130829	IL 2011-227009	20111221
EP 2656077	A1	20131030	EP 2011-805738	20111221

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CN 103384828	A	20131106	CN 2011-80068269	20111221
KR 2014002711	A	20140108	KR 2013-7019356	20111221
JP 2014503821	T	20140213	JP 2013-546392	20111221
NZ 612483	A	20150327	NZ 2011-612483	20111221
SG 10201510086	A1	20160128	SG 2015-10201510086	20111221
US 20140024548	A1	20140123	US 2013-13923316	20130620
MX 2013007429	A	20140131	MX 2013-7429	20130621

PRIORITY APPLN. INFO.: US 2010-61426948 P 20101223
US 2011-61438904 P 20110202
WO 2011-US66624 W 20111221

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods for selecting a suitable anticancer drug therapy, and for identifying and predicting response, for the treatment of a malignant cancer involving aberrant c-Met signaling. The present invention also provides methods for monitoring the status of a malignant cancer involving aberrant c-Met signaling and monitoring how a patient with the malignant cancer is responding to anticancer drug therapy. Information on the expression and/or activation states of components of signal transduction pathways (e.g., HER3 and/or c-Met signal transduction pathway components) derived from practice of the present invention can be used for malignant cancer diagnosis, prognosis, and in the design of cancer treatments for malignancies involving aberrant c-Met signaling. Certain embodiments comprise administering a cMet inhibitor alone or a cMet inhibitor in combination with a pathway-directed therapy based upon the differences between the expression and/or activation levels of cMet protein and/or HER3 protein in the sample compared to the control protein and/or control sample.

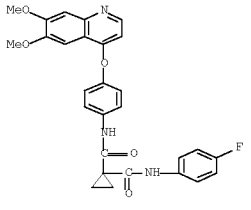
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for therapy for malignancies involving aberrant c-Met signaling using antibody-based arrays)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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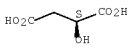
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 464 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:706472 CAPLUS Full-text
DOCUMENT NUMBER: 156:628365
TITLE: Cancer cell-derived receptor activator of the NF-KB ligand drives bone and soft tissue metastases
INVENTOR(S): Chu, Gina C. Y.; Chung, Leland W. K.; Zhau, Haiyen E.; Wang, Ruoxiang
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

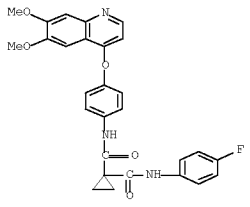
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012064967	A2	20120518	WO 2011-US60204	20111110
WO 2012064967	A3	20120705		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20130263297	A1	20131003	US 2013-13889135	20130507

PRIORITY APPLN. INFO.: US 2010-61412360 P 20101110
US 2011-61442679 P 20110214
WO 2011-US60204 A2 20111110
US 2012-61718626 P 20121025
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to metastases. More specifically, the invention relates to compns. and methods for the inhibition of metastases of cancer cells, such as prostate cancer cells, to bones and soft tissue. The present invention also relates to the treatment of cancer, including but not limited to prostate cancer. Also provided are animal models for studying cancer metastasis; particularly, prostate cancer metastasis.
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer cell-derived receptor activator of the NF-KB ligand drives bone and soft tissue metastases)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

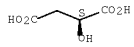
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

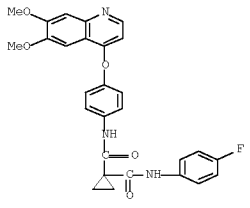
Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 465 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2012:560657 CAPLUS Full-text
DOCUMENT NUMBER: 158:122090
TITLE: Recent advances in the molecular pathogenesis and targeted therapies of medullary thyroid carcinoma
AUTHOR(S): Almeida, Madson Q.; Hoff, Ana O.
CORPORATE SOURCE: Instituto do Cancer da Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil
SOURCE: Current Opinion in Oncology (2012), 24(3), 229-234
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e328351c71a
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: This review will focus on the recent advances in mol. pathogenesis and targeted therapies for medullary thyroid carcinoma (MTC). Unlike hereditary MTC in which rearranged during transfection (RET) mutations are the most important precipitating events, in sporadic MTC the genetic or mol. biomarkers are yet to be established. Recent findings: Targeted mol. therapies that inhibit RET and other tyrosine kinase receptors involved in angiogenesis have shown great promise in the treatment of metastatic or locally advanced MTC and are under investigation. In addition, the recent findings of H-RAS mutations in 56% of RET-neg. sporadic MTC and the activation of the mammalian target of rapamycin (mTOR) intracellular signaling pathway in hereditary MTC suggests that addnl. or alternative genetic events are important for MTC pathogenesis. Summary: Recently, vandetanib (ZD6474), an inhibitor of vascular endothelial growth factor receptor (VEGFR) 2 and VEGFR 3, RET, and epidermal growth factor receptor (EGFR), was approved for the treatment of adults with symptomatic or progressive MTC. Significant advantages for vandetanib over placebo were seen in terms of response rate, disease control rate, and biochem. response in a phase III study. Furthermore, cabozantinib (XL184), an inhibitor of VEGFR 1 and VEGFR 2, hepatocyte growth factor receptor (MET), and RET, was associated with partial response and stable disease in 29 and 41%, resp.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vandetanib and cabozantinib was effective in treatment of patient with medullary thyroid carcinoma)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



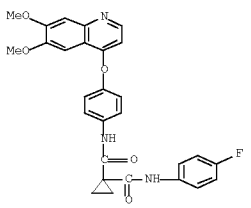
OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 466 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:508891 CAPLUS Full-text
DOCUMENT NUMBER: 158:93453
TITLE: Novel Molecular Targets for the Therapy of Castration-Resistant Prostate Cancer
AUTHOR(S): Agarwal, Neeraj; Sonpavde, Guru; Sternberg, Cora N.
CORPORATE SOURCE: Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA
SOURCE: European Urology (2012), 61(5), 950-960
CODEN: EUURAV; ISSN: 0302-2838
DIGITAL OBJECT ID: 10.1016/j.eururo.2011.12.028
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Improved understanding of mechanisms underlying metastatic castration-resistant prostate cancer (mCRPC) progression has led to the recognition of multiple mol. targets and advances in the therapeutic landscape. The addition of abiraterone acetate, sipuleucel-T, cabazitaxel, and denosumab to the therapeutic armamentarium and the impending addition of MDV-3100 and radium-223 underscore the importance of androgen pathway inhibition, immunotherapy, tubulin antagonism, and pathophysiol. of bone metastasis. Review the next generation of mol. targets in mCRPC. Medline databases were searched for >100 original articles published as of Oct. 18, 2011, with the search terms metastatic castration-resistant prostate cancer, targeted therapy, biol. agents, and immunotherapy. Proceedings from the last 5 yr of conferences of the American Society of Clin. Oncol., American Urol. Association, European Society of Medical Oncol., and the European Association of Urol. were also searched. We included novel and promising drugs that have reached clin. trial evaluation. The major findings were addressed in an evidence-based fashion. Prospective trials and important preclin. data were analyzed.mCRPC is a disease with multiple mol. drivers. Mol. pathways being targeted in ongoing phase 3 trials are androgen signaling (MDV3100, TAK700), immunoregulatory pathways (ipilimumab, Prostvac-VF-TRICOM), Src (dasatinib), Met (cabozantinib), clusterin (custirsen), and angiogenesis (aflibercept, tasquinimod). The strides made

in identifying multiple other novel mol. targets offer potential opportunities for further improving outcomes.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(knowledge on novel mol. targets like Met signaling pathway using drugs like cabozantinib could be more beneficial in patient with metastatic castration-resistant prostate cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



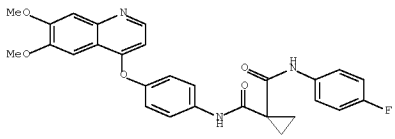
OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 467 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:495814 CAPLUS Full-text
DOCUMENT NUMBER: 156:469436
TITLE: Dual inhibitors of Met and VEGF for the treatment of castration- resistant prostate cancer and osteoblastic bone metastases
INVENTOR(S): Smith, David; Hussain, Maha
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012044572	A1	20120405	WO 2011-US53233	20110926
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
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CA 2812750	A1	20120405	CA 2011-2812750	20110926
AU 2011307304	A1	20130502	AU 2011-307304	20110926
AU 2011307304	B2	20160414		
IL 225507	A	20130530	IL 2011-225507	20110926
EP 2621481	A1	20130807	EP 2011-764655	20110926
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CN 103402505	A	20131120	CN 2011-80056580	20110926
KR 2014025304	A	20140304	KR 2013-7010372	20110926
NZ 707930	A	20160930	NZ 2011-707930	20110926
MX 2013003594	A	20130801	MX 2013-3594	20130327
ZA 2013002422	A	20131223	ZA 2013-2422	20130404
IN 2013KN00998	A	20130906	IN 2013-KN998	20130409
US 20140057943	A1	20140227	US 2013-13876290	20131105
US 20160220554	A1	20160804	US 2015-14843480	20150902
AU 2016204747	A1	20160728	AU 2016-204747	20160708

PRIORITY APPLN. INFO.:
US 2010-61386959 P 20100927
US 2011-61481671 P 20110502
AU 2011-307304 A3 20110926
NZ 2011-609212 A3 20110926
WO 2011-US53233 W 20110926
US 2013-13876290 B1 20131105

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:469436; MARPAT 156:469436
GI

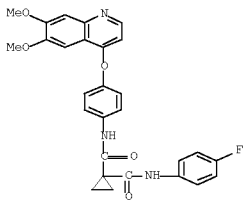


AB This invention is directed to the treatment of cancer, particularly castration-resistant prostate cancer and osteoblastic bone metastases, with a dual inhibitor of MET and VEGF.

IT 849217-68-1

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



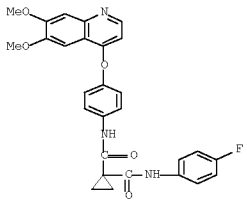
IT 1140909-48-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

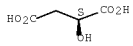
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



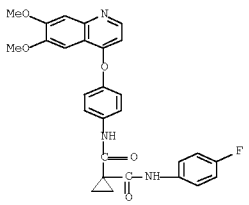
IT 1365530-43-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)

RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

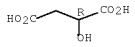
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 468 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:495788 CAPLUS Full-text
DOCUMENT NUMBER: 156:469435
TITLE: Dual inhibitors of Met and VEGF for the treatment of castration resistant prostate cancer and osteoblastic bone metastases
INVENTOR(S): Smith, David; Hussain, Maha
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012044577	A1	20120405	WO 2011-US53245	20110926

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2812744	A1	20120405	CA 2011-2812744	20110926
AU 2011307309	A1	20130502	AU 2011-307309	20110926
EP 2621483	A1	20130807	EP 2011-764657	20110926

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

JP 2013537918	T	20131007	JP 2013-530392	20110926
CN 103391773	A	20131113	CN 2011-80056999	20110926
US 20140057908	A1	20140227	US 2013-13876306	20131108

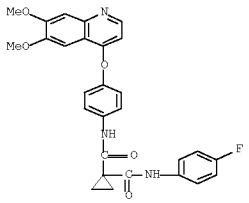
PRIORITY APPLN. INFO.:

US 2010-61386971	P	20100927
US 2010-61386983	P	20100927
US 2010-61386993	P	20100927
WO 2011-US53245	W	20110926

OTHER SOURCE(S): CASREACT 156:469435; MARPAT 156:469435
AB This invention discloses compds. directed at the treatment of cancer, particularly castration- resistant prostate cancer and osteoblastic bone metastases, with a dual inhibitor of MET and VEGF.
IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

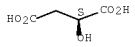
CRN 849217-68-1
CMF C28 H24 F N3 O5



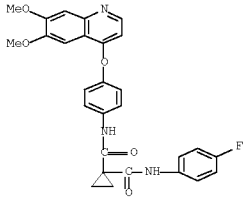
CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



IT 849217-68-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(dual inhibitors of Met and VEGF for treatment of castration resistant prostate cancer and osteoblastic bone metastases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

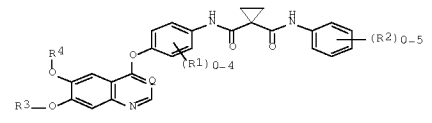
L4 ANSWER 469 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:425741 CAPLUS Full-text
DOCUMENT NUMBER: 156:412018
TITLE: Methods of using C-met modulators as Anticancer agents
INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-Ming; Forsyth, Timothy Patrick; Khoury, Richard George; Leahy, James William; Mac, Morrison B.; Mann, Larry W.; Nuss, John M.; Parks, Jason Jevious; Wang, Yong; Xu, Wei; Simeone, Diane
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 25pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20120070368	A1	20120322	US 2011-13087094	20110414
US 20150202196	A1	20150723	US 2014-14518733	20141020

PRIORITY APPLN. INFO.:

US 2010-61325095	P	20100416
US 2011-13087094	B1	20110414

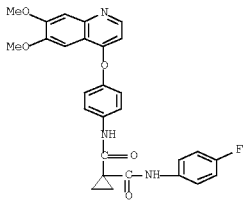
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:412018; MARPAT 156:412018
GI



I

AB Disclosed are methods of treating cancer by administering a compd. of Formula I (wherein R1, R2 = independently, halo; R3, R4 = independently, (C1-C6)-alkyl; Q = CH, N) in combination with gemcitabine (GEM).
IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(c-met modulators as antitumor agents)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-

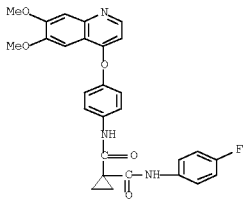
quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1365530-43-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(c-met modulators as antitumor agents)
RN 1365530-43-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

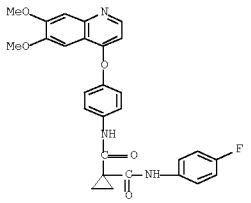
CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

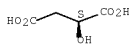
CRN 636-61-3



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 471 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:345887 CAPLUS Full-text
DOCUMENT NUMBER: 156:388076
TITLE: C-met biomarker in treatment efficacy and prognosis
INVENTOR(S): Patel, Premal; Peterson, Amy C.; Yauch, Robert L.; Zha, Jiping
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 134pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012031027	A1	20120308	WO 2011-US50069	20110831

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2808236	A1	20120308	CA 2011-2808236	20110831
US 20120089541	A1	20120412	US 2011-13223173	20110831
AU 2011295919	A1	20130307	AU 2011-295919	20110831
IL 224962	A	20130430	IL 2011-224962	20110831
EP 2612151	A1	20130710	EP 2011-754597	20110831
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
CN 103221825	A	20130724	CN 2011-80051781	20110831
KR 2013103734	A	20130924	KR 2013-7008025	20110831
JP 2013537966	T	20131007	JP 2013-526209	20110831
ZA 2013001175	A	20140430	ZA 2013-1175	20110831
SG 10201408229	A1	20150227	SG 2014-10201408229	20110831
BR 112013004673	A2	20160802	BR 2013-112013004673	20110831
IL 248530	A	20161229	IL 2011-248530	20110831
MX 2013002084	A	20130509	MX 2013-2084	20130221
IN 2013DN01711	A	20141024	IN 2013-DN1711	20130225
AU 2013202759	A1	20130502	AU 2013-202759	20130406
US 20140037625	A1	20140206	US 2013-14046867	20131004
JP 2016105096	A	20160609	JP 2015-253669	20151225
AU 2016200630	A1	20160218	AU 2016-200630	20160202

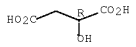
PRIORITY APPLN. INFO.:

US 2010-61378911	P	20100831
US 2010-61389922	P	20101005
US 2010-61390995	P	20101007
US 2010-61420703	P	20101207
US 2011-61487527	P	20110518
US 2011-61492338	P	20110601
US 2011-61503489	P	20110630
AU 2011-295919	A3	20110831
IL 2011-224962	A3	20110831
JP 2013-526209	A3	20110831
US 2011-13223173	B1	20110831
WO 2011-US50069	W	20110831
AU 2013-202759	A3	20130406

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The authors disclose the use of c-met as a biomarker for patient selection and patient prognosis in cancer. In a clin. trial, combination treatment with MetMAb (onartuzumab) and erlotinib provided a clin. meaningful benefit to patients with non-small cell lung cancer (NSCLC) that expressed high levels of c-met biomarker. The results showed that the efficacy, as evaluated by progression free survival (PFS) and overall survival (OS), was pos. especially when compared to PFS and OS data for erlotinib treatment alone. The addition of MetMAb to erlotinib nearly doubled the progression free and overall survival in patients with NSCLC that expressed high levels of c-met biomarker. The clin. trial data also showed that treatment with MetMAb in combination with erlotinib increased the risk of progression and death in patients with NSCLC that expressed low levels of c-met biomarker.
IT 849217-68-1, Cabozantinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



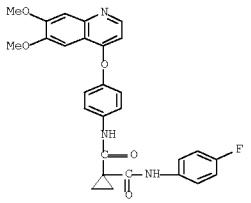
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 470 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:373163 CAPLUS Full-text
DOCUMENT NUMBER: 157:622817
TITLE: Multi-targeted tyrosine kinase inhibitors in clinical development: focus on XL-184 (cabozantinib)
AUTHOR(S): Bowles, D. W.; Kessler, E. R.; Jimeno, A.
CORPORATE SOURCE: Division of Medical Oncology, University of Colorado Denver, Aurora, CO, USA
SOURCE: Drugs of Today (2011), 47(11), 857-868
CODEN: MDACAP; ISSN: 1699-3993
DIGITAL OBJECT ID: 10.1358/dot.2011.47.11.1688487
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. XL-184 (cabozantinib) is a novel, small-mol., multi-targeted receptor tyrosine kinase inhibitor with particular activity against hepatocyte growth factor receptor (tyrosine-protein kinase Met), vascular endothelial growth factor receptor 2 (VEGFR-2) and proto-oncogene tyrosine-protein kinase receptor Ret. There is ample evidence of Met, VEGFR-2 and Ret signaling in several tumor types. Preclin. data suggest that XL-184 has activity in tumors derived from both epithelial and mesenchymal origins. Phase I and II clin. studies support significant antitumor activity, particularly in medullary thyroid cancer and cancers metastatic to the bone. This review will evaluate XL-184's preclin. pharmacol., pharmacokinetics, drug interactions and clin. activity in phase I through phase III studies.
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(focus on XL-184 (cabozantinib) is a novel multi-targeted tyrosine kinase inhibitors in clin. development)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

(Met receptor as biomarker for combination therapy efficacy and cancer prognosis)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

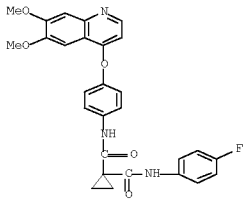
L4 ANSWER 472 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:340365 CAPLUS Full-text
DOCUMENT NUMBER: 156:380310
TITLE: Synergistic drug combination for the treatment of cancer
INVENTOR(S): Gusenbauer, Simone; Ullrich, Axel
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 111pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 2425830	A1	20120307	EP 2010-75382	20100903
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BA, ME, RS				
PRIORITY APPLN. INFO.:			EP 2010-75382	20100903

AB The invention relates to synergistic drug combinations and the use of said drug combinations for the treatment of proliferative diseases such as cancer. Combination of drugs include e.g. chlorethamine, cyclophosphamide, trofosfamide, daunorubicin, doxorubicin, mitomycin C.
IT 1140909-48-3, Xl184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic drug combination for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

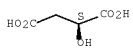
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

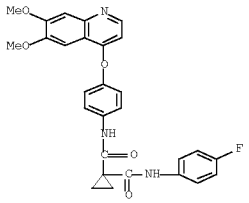


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 473 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:265414 CAPLUS Full-text
DOCUMENT NUMBER: 156:357951
TITLE: Circulating biomarkers for disease
INVENTOR(S): Spetzler, David; Holterman, Daniel; Pawlowski, Traci; Kuslich, Christine
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, Luxembourg
SOURCE: PCT Int. Appl., 639pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012024543	A1	20120223	WO 2011-US48327	20110818
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2808417	A1	20120223	CA 2011-2808417	20110818
AU 2011291599	A1	20130307	AU 2011-291599	20110818
AU 2011291599	B2	20150910		
EP 2606353	A1	20130626	EP 2011-818814	20110818
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2013540995	T	20131107	JP 2013-526012	20110818
US 20140148350	A1	20140529	US 2013-13817383	20130520
US 20150301055	A1	20151022	US 2015-14789729	20150701
AU 2015268602	A1	20160107	AU 2015-268602	20151209
PRIORITY APPLN. INFO.:			US 2010-61374951	P 20100818
			US 2010-61379670	P 20100902
			US 2010-61381305	P 20100909
			US 2010-61383305	P 20100915
			US 2010-61391504	P 20101008
			US 2010-61393823	P 20101015
			US 2010-61411890	P 20101109
			US 2010-61413377	P 20101112
			US 2010-61414870	P 20101117
			US 2010-61416560	P 20101123
			US 2010-61421851	P 20101210
			US 2010-61423557	P 20101215
			US 2010-61428196	P 20101229
			US 2011-61471417	P 20110404
			US 2010-61321392	P 20100406
			US 2010-61321407	P 20100406
			US 2010-61322690	P 20100409
			US 2010-61332174	P 20100506
			US 2010-61334547	P 20100513
			US 2010-61348214	P 20100525
			US 2010-61348685	P 20100526
			US 2010-61354125	P 20100611
			US 2010-61355387	P 20100616
			US 2010-61356974	P 20100621
			US 2010-61357517	P 20100622
			US 2010-61362674	P 20100708
			US 2010-61364785	P 20100715
			US 2010-61370088	P 20100802
			WO 2011-US31479	A 20110406
			AU 2011-291599	A3 20110818
			WO 2011-US48327	W 20110818
			US 2013-13639756	A2 20130424
			US 2013-13817383	A1 20130520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Biomarkers can be assessed for diagnostic, therapy-related or prognostic methods to identify phenotypes, such as a condition or disease, or the stage or progression of a disease. Circulating biomarkers from a bodily fluid can be used in profiling of physiol. states or determining phenotypes. These include nucleic acids, protein, and circulating structures such as vesicles. Biomarkers can be used for theranostic purposes to select candidate treatment regimens for diseases, conditions, disease stages, and stages of a condition, and can also be used to determine treatment efficacy. The biomarkers can be circulating biomarkers, including vesicles and microRNA. Various anti-DLL4 antibodies were tethered to beads and used to capture vesicles in blood samples from subjects with breast cancer, colorectal cancer or normal subjects. The bead captured vesicles were detected with fluorescently-labeled antibodies against the tetraspanins CD9, CD63, and CD81. The median fluorescence intensity of the captured and labeled vesicles was measured using laser detection. There were noticeable differences both among normals and breast cancer plasma as well as between the avs. of normals and cancer patients.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DLL4, vesicle, and microRNA circulating biomarkers for disease diagnosis, therapy, prognosis, or theranostics)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

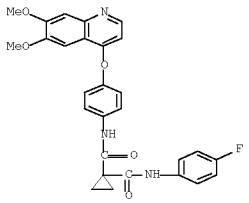
L4 ANSWER 474 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:155432 CAPLUS Full-text

DOCUMENT NUMBER: 157:565304
TITLE: Drug development to overcome resistance to EGFR inhibitors in lung and colorectal cancer
AUTHOR(S): Dienstmann, Rodrigo; De Dosso, Sara; Felip, Enriqueta; Tabernero, Josep
CORPORATE SOURCE: Medical Oncology Department, Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, 08035, Spain
SOURCE: Molecular Oncology (2012), 6(1), 15-26
CODEN: MOONC3; ISSN: 1574-7891
DIGITAL OBJECT ID: 10.1016/j.molonc.2011.11.009
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. Epidermal growth factor receptor (EGFR) is a validated target in different human malignancies. EGFR tyrosine kinase inhibitors (TKIs) are known to contribute considerably to the extension of progression-free survival in EGFR-mutant non-small cell lung cancer and monoclonal antibodies (mAbs) targeting EGFR have also improved the efficacy outcomes in KRAS wild-type colorectal cancer. Nevertheless, a significant percentage of lung and colorectal cancer patients do not respond to anti-EGFR agents and secondary resistance after initial benefit is a challenging reality faced by clinicians. Extensive preclin. work on the potential mechanisms of resistance to EGFR inhibitors in different disease settings has guided the development of second-generation irreversible EGFR TKIs, more efficient anti-EGFR mAbs, and combination strategies with agents targeting other receptors and downstream effectors. In order to elucidate the role of the multiple therapeutic strategies under investigation to overcome EGFR inhibitors-resistance, rational drug development based on stringent preclin. data, biomarker validation and proper selection of patients in the ongoing clin. trials are of paramount importance. Preliminary results of clin. trials evaluating these approaches will be discussed in this manuscript, with emphasis on TKIs in lung cancer and mAbs in advanced colorectal cancer.

IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug development to overcome resistance to EGFR inhibitors in lung and colorectal cancer)

RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 475 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:99813 CAPLUS Full-text
DOCUMENT NUMBER: 157:249246
TITLE: HGF/c-MET targeted therapeutics: novel strategies for cancer medicine
AUTHOR(S): Yap, Timothy A.; Sandhu, Shahneen K.; Alam, Salma M.; de Bono, Johann S.
CORPORATE SOURCE: The Royal Marsden NHS Foundation Trust, Sutton, Surrey, SM2 5PT, UK
SOURCE: Current Drug Targets (2011), 12(14), 2045-2058
CODEN: CDTUAU; ISSN: 1389-4501
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

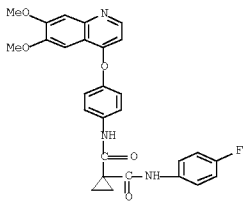
AB A review. The hepatocyte growth factor/mesenchymal-epithelial transition factor (HGF/c-MET) receptor tyrosine kinase (RTK) pathway plays a pleotropic role in cell proliferation, migration, invasion, angiogenesis and survival. Although it has critical physiol. functions in embryonic development and tissue repair, this signaling cascade is frequently deregulated in a wide range of tumors. Aberrant HGF/c-MET signaling, driven by various mechanisms, including constitutive activation and over-expression, has multifunctional effects in oncogenesis and is implicated in the acquisition of an aggressive phenotype with metastatic potential. The central role of c-MET activity in cancer progression, as well as disparities between quiescent HGF/c-MET signaling in normal tissue and overexpression in tumor may provide a degree of tumor selectivity for therapeutic intervention, making HGF or c-MET inhibition an attractive proposition in oncol. This review focuses on the underlying oncogenic role of aberrant HGF/c-MET signaling in malignant progression, as well as recent preclin. and clin. data on the different strategies employed in inhibiting HGF/c-MET function.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapies targeting hepatocyte growth factor/mesenchymal-epithelial transition factor signaling involved in cell proliferation, migration, invasion, angiogenesis and survival may be useful for treatment of patient with cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

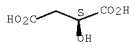
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 134 THERE ARE 134 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 476 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:94602 CAPLUS Full-text
DOCUMENT NUMBER: 156:167648
TITLE: Administration of hypoxia activated prodrugs and antiangiogenic agents for the treatment of cancer
INVENTOR(S): Hart, Charles; Curd, John; Kroll, Stewart; Sun, Jessica
PATENT ASSIGNEE(S): Threshold Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012009288	A2	20120119	WO 2011-US43594	20110711
WO 2012009288	A9	20120419		
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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
CA 2803675	A1	20120119	CA 2011-2803675	20110711
KR 2013045341	A	20130503	KR 2013-7002206	20110711
EP 2593139	A2	20130522	EP 2011-807356	20110711
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR				
JP 2013531038	T	20130801	JP 2013-519747	20110711
JP 6066421	B2	20170125		
RU 2597844	C2	20160920	RU 2013-103027	20110711
MX 2012014428	A	20130305	MX 2012-14428	20121210
ZA 2013000692	A	20130925	ZA 2013-692	20130125
US 20140010805	A1	20140109	US 2013-13809135	20130724

PRIORITY APPLN. INFO.:

US 2010-61363610	P	20100712
US 2011-61470412	P	20110331
US 2011-61470812	P	20110401
WO 2011-US43594	W	20110711

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

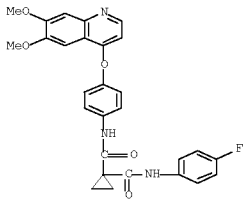
AB Administration of a hypoxia activated prodrug in combination with an antiangiogenic agent is useful for treating cancer. Hypoxia activated prodrug is selected from the group consisting of TH-281, TH-302, and TH-308. The antiangiogenic agent is selected from the group consisting of an anti-VEGF antibody, a VEGF-trap, an anti-VEGFR antibody, a VEGFR inhibitor, thalidomide etc.

IT 1140909-48-3, XL-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of hypoxia activated prodrugs and antiangiogenic agents for treatment of cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

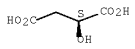
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L4 ANSWER 477 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:90800 CAPLUS full-text
DOCUMENT NUMBER: 156:186804
TITLE: C-met modulator pharmaceutical compositions comprising N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide
INVENTOR(S): Wilson, Jo Ann
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 40pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2012009722	A1	20120119	WO 2011-US44378	20110718

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

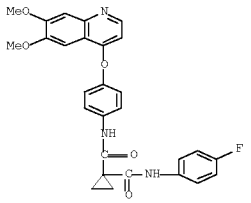
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AR 82252	A1	20121121	AR 2011-102584	20110718
AU 2011278950	A1	20130307	AU 2011-278950	20110718
AU 2011278950	B2	20160721		
IL 224189	A	20130324	IL 2011-224189	20110718
EP 2593090	A1	20130522	EP 2011-740764	20110718
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BA, ME				
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JP 2013531045	T	20130801	JP 2013-519870	20110718
JP 5934204	B2	20160615		
KR 2013137586	A	20131217	KR 2013-7003043	20110718
NZ 607118	A	20150529	NZ 2011-607118	20110718
TW I516477	B	20160111	TW 2011-125336	20110718
SG 10201609324	A1	20170127	SG 2016-10201609324	20110718
CN 106420743	A	20170222	CN 2016-10157218	20110718
IN 2013KN00112	A	20130705	IN 2013-KN112	20130114
MX 2013000567	A	20130501	MX 2013-567	20130115
ZA 2013000458	A	20130925	ZA 2013-458	20130117
US 20130337015	A1	20131219	US 2013-13810537	20130826
JP 2016188215	A	20161104	JP 2016-93433	20160506
AU 2016247044	A1	20161103	AU 2016-247044	20161018

PRIORITY APPLN. INFO.:

US 2010-61365253	P	20100716
US 2010-61370843	P	20100805
AU 2011-278950	A3	20110718
CN 2011-80044602	A3	20110718
JP 2013-519870	A3	20110718
WO 2011-US44378	W	20110718

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 156:186804
AB Pharmaceutical compns. and unit dosage forms comprising N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (I) are disclosed. Thus, 6,7-dimethoxyquinolin-4-ol was converted to 4-chloro-6.7-dimethoxyquinoline followed by reaction with 4-aminphenol to give 4-(6,7-dimethoxy-quinolin-4-yloxy)-phenylamine. This was further allowed to react with 1-(4-fluorophenylcarbamoyl)cyclopropanecarbonyl chloride to give I. A tablet composition comprised 31.68% along with excipients such as microcryst. cellulose 38.85, lactose, HPC, and Croscarmellose sodium.
IT 849217-68-1P 1140909-48-3P, Cabozantinib S-malate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-met modulator pharmaceutical compns. comprising dimethoxyquinolinyloxyphenyl(fluorophenyl)cyclopropanedicarboxamide)

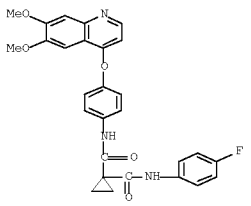
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

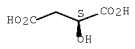
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CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

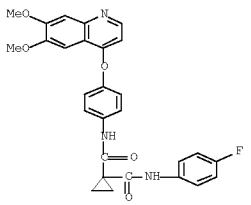
Absolute stereochemistry. Rotation (-).



IT 1235470-36-6 1235470-38-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C-met modulator pharmaceutical compns. comprising dimethoxyquinolinyloxyphenyl(fluorophenyl)cyclopropanedicarboxamide)
RN 1235470-36-6 CAPLUS
CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

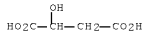
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CMF C28 H24 F N3 O5



CM 2

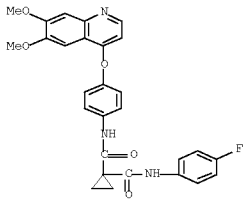
CRN 6915-15-7
CMF C4 H6 O5



RN 1235470-38-8 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

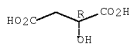
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

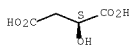
CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 478 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2012:10093 CAPLUS Full-text
DOCUMENT NUMBER: 157:152076
TITLE: In the clinic: ongoing clinical trials evaluating c-MET-inhibiting drugs
AUTHOR(S): Sharma, Neelesh; Adjei, Alex A.
CORPORATE SOURCE: Department of Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA
SOURCE: Therapeutic Advances in Medical Oncology (2011), 3(Suppl. 1), S37-S50
CODEN: TAMOB8; ISSN: 1758-8340
DIGITAL OBJECT ID: 10.1177/1758834011423403
PUBLISHER: Sage Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

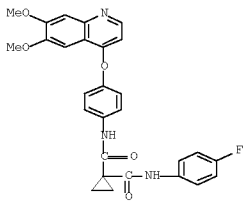
L4 ANSWER 479 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:1586879 CAPLUS Full-text
DOCUMENT NUMBER: 156:655505
TITLE: Cabozantinib (XL184), a Novel MET and VEGFR2 Inhibitor, Simultaneously Suppresses Metastasis, Angiogenesis, and Tumor Growth
AUTHOR(S): Yakes, F. Michael; Chen, Jason; Tan, Jenny; Yamaguchi, Kyoko; Shi, Yongchang; Yu, Peiwen; Qian, Fawn; Chu, Felix; Bentzien, Frauke; Cancilla, Belinda; Orf, Jessica; You, Andrew; Laird, A. Douglas; Engst, Stefan; Lee, Lillian; Lesch, Justin; Chou, Yu-Chien; Joly, Alison H.
CORPORATE SOURCE: Exelixis, Inc., South San Francisco, CA, 94083, USA
SOURCE: Molecular Cancer Therapeutics (2011), 10(12), 2298-2308
CODEN: MCTOCF; ISSN: 1535-7163
DIGITAL OBJECT ID: 10.1158/1535-7163.MCT-11-0264
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The signaling pathway of the receptor tyrosine kinase MET and its ligand hepatocyte growth factor (HGF) is important for cell growth, survival, and motility and is functionally linked to the signaling pathway of VEGF, which is widely recognized as a key effector in angiogenesis and cancer progression. Dysregulation of the MET/VEGF axis is found in a number of human malignancies and has been associated with tumorigenesis. Cabozantinib (XL184) is a small-mol. kinase inhibitor with potent activity toward MET and VEGF receptor 2 (VEGFR2), as well as a number of other receptor tyrosine kinases that have also been implicated in tumor pathobiol., including RET, KIT, AXL, and FLT3. Treatment with cabozantinib inhibited MET and VEGFR2 phosphorylation in vitro and in tumor models in vivo and led to significant redns. in cell invasion in vitro. In mouse models, cabozantinib dramatically altered tumor pathol., resulting in decreased tumor and endothelial cell proliferation coupled with increased apoptosis and dose-dependent inhibition of tumor growth in breast, lung, and glioma tumor models. Importantly, treatment with cabozantinib did not increase lung tumor burden in an exptl. model of metastasis, which has been observed with inhibitors of VEGF signaling that do not target MET. Collectively, these data suggest that cabozantinib is a promising agent for inhibiting tumor angiogenesis and metastasis in cancers with dysregulated MET and VEGFR signaling. Mol Cancer Ther; 10(12); 2298-308.
IT 849217-68-1, Cabozantinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cabozantinib inhibited proliferation of human, mouse and rat cancer

AB A review. The c-MET (mesenchymal-epithelial transition factor) pathway is dysregulated in many human cancers and promotes tumor growth, invasion and dissemination. The c-MET receptor tyrosine kinase can be activated via gene mutation, gene amplification, protein overexpression and/or a Ligand-dependent autocrine/paracrine loop. Abnormalities in c-MET signaling have been reported to correlate with poor clin. outcomes and drug resistance in patients with cancer. Significant progress has been made in advancement of c-MET pathway inhibitors through to clin. trials. A robust pipeline of high-quality inhibitors targeting different aspects of c-MET activation is currently being explored in phase I, II and III clin. trials across multiple tumor types. Preliminary data demonstrate promising clin. activity with these agents, along with an acceptable toxicity profile. In this manuscript, the pharmacol. profile of drugs targeting the c-MET pathway and available data from ongoing clin. trials of these drugs are discussed.
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ongoing clin. trials evaluating mesenchymal-epithelial transition factor-inhibiting drugs)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

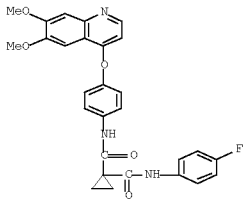
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 248 THERE ARE 248 CAPLUS RECORDS THAT CITE THIS RECORD (249 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 480 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:1503311 CAPLUS Full-text
DOCUMENT NUMBER: 155:694113
TITLE: Replication-competent retroviral vectors carrying expression cassettes for cytosine deaminase variants
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas J.; Perez, Omar D.; Logg, Christopher R.
PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 207pp., Cont.-in-part of Appl. No. PCT/US2009/058512.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20110287020	A1	20111124	US 2011-13072704	20110326
US 8829173	B2	20140909		
WO 2010036986	A2	20100401	WO 2009-US58512	20090926
WO 2010036986	A3	20100701		

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SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

CN 105274125	A	20160127	CN 2015-10505943		20090926
CN 105624193	A	20160601	CN 2015-10624987		20090926
WO 2011126864	A2	20111013	WO 2011-US30402		20110329
WO 2011126864	A3	20120419			

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EP 2547353	A2	20130123	EP 2011-766479		20110329

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JP 2013523754	T	20130617	JP 2013-502771		20110329
JP 6014020	B2	20161025			
US 20130130986	A1	20130523	US 2013-13638490		20130116
AU 2013205006	A1	20130516	AU 2013-205006		20130413
AU 2013205006	B2	20160218			
US 20160053232	A1	20160225	US 2014-14477741		20140904
JP 2015119712	A	20150702	JP 2015-4923		20150114
JP 5992548	B2	20160914			
JP 2015186479	A	20151029	JP 2015-97980		20150513
JP 6062485	B2	20170118			
JP 2016153403	A	20160825	JP 2016-35272		20160226
JP 2017018121	A	20170126	JP 2016-159893		20160817

PRIORITY APPLN. INFO.:

US 2008-61100666	P	20080926
US 2008-61120618	P	20081208
US 2009-61186823	P	20090613
WO 2009-US58512	A2	20090926
US 2010-61318728	P	20100329
AU 2009-303690	A3	20090926
CN 2009-80147509	A3	20090926
CN 2009-80147515	A3	20090926
JP 2011-529291	A3	20090926
JP 2011-529292	A3	20090926
US 2011-13072704	A1	20110326
JP 2013-502771	A3	20110329
WO 2011-US30402	W	20110329
JP 2015-4923	A3	20150114

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Methods of delivering cytosine deaminase variants for prodrug activation using retroviral expression vectors are described. The vector includes the viral gag, pol, and env genes with the cytosine deaminase gene being coexpressed using an internal ribosome entry site. Vectors were derived from the prior art pACE-GFPemd vector. The envelope protein of the virus is amphotropic and excess viral sequences outside the long terminal repeats were removed. The resulting vector was named pACE-emdGFP. The vector was stable in storage and replicated efficiently in mammalian cells and could be used to deliver a range of therapeutic genes. The Saccharomyces cerevisiae cytosine deaminase gene was modified to give a codon usage suitable for mammalian cells and to improve thermostability of the enzyme. Use of these vectors results in high intracellular copy nos. for the therapeutic gene and these cells can be superinfected by the vector.

IT 1140909-48-3

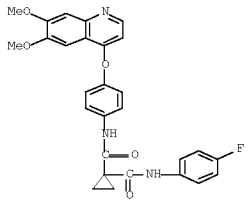
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (in cancer therapy with retroviral gene therapy vectors; replication-competent retroviral vectors carrying expression cassettes for cytosine deaminase variants)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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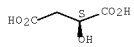
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 0 THERE ARE 0 CAPLUS RECORDS THAT CITE THIS RECORD (0 CITINGS)

L4 ANSWER 481 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2011:1304241 CAPLUS Full-text
DOCUMENT NUMBER: 155:559702
TITLE: Detection of circulating mRNA, microRNA, protein and vesicle markers in disease diagnosis and selection of therapies
INVENTOR(S): Kuslich, Christine; Poste, George; Klass, Michael; Spetzler, David; Pawlowski, Traci
PATENT ASSIGNEE(S): Caris Life Sciences Luxembourg Holdings, Luxembourg
SOURCE: PCT Int. Appl., 584pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011127219	A1	20111013	WO 2011-US31479	20110406

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RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2795776	A1	20111013	CA 2011-2795776	20110406
AU 2011237669	A1	20121101	AU 2011-237669	20110406
AU 2011237669	B2	20160908		
IL 222232	A	20121129	IL 2011-222232	20110406
EP 2556172	A1	20130213	EP 2011-766687	20110406

R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

CN 103025890	A	20130403	CN 2011-80027541	20110406
CN 103025890	B	20161214		
KR 2013043104	A	20130429	KR 2012-7028831	20110406
JP 2013526852	T	20130627	JP 2013-503934	20110406
IN 2012DN09454	A	20160101	IN 2012-DN9454	20121101
US 20140162888	A1	20140612	US 2013-13639756	20130424
US 9469876	B2	20161018		
US 20150301055	A1	20151022	US 2015-14789729	20150701
JP 2016028584	A	20160303	JP 2015-176236	20150908
AU 2015268602	A1	20160107	AU 2015-268602	20151209

PRIORITY APPLN. INFO.:

US 2010-61321392	P	20100406
US 2010-61321407	P	20100406
US 2010-61322690	P	20100409
US 2010-61332174	P	20100506
US 2010-61334547	P	20100513
US 2010-61348214	P	20100525
US 2010-61348685	P	20100526
US 2010-61354125	P	20100611
US 2010-61355387	P	20100616
US 2010-61356974	P	20100621
US 2010-61357517	P	20100622
US 2010-61362674	P	20100708
US 2010-61364785	P	20100715
US 2010-61370088	P	20100802
US 2010-61379670	P	20100902
US 2010-61381305	P	20100909
US 2010-61383305	P	20100915
US 2010-61391504	P	20101008
US 2010-61393823	P	20101015
US 2010-61411890	P	20101109
US 2010-61413377	P	20101112
US 2010-61416560	P	20101123
US 2010-61274124	P	20100301
US 2010-61374951	P	20100818
US 2010-61414870	P	20101117
US 2010-61421851	P	20101210
US 2010-61423557	P	20101215
US 2010-61428196	P	20101229
JP 2012-556185	A3	20110301
US 2011-61471417	P	20110404
WO 2011-US31479	W	20110406
AU 2011-291599	A3	20110818
WO 2011-US48327	A	20110818
US 2013-13639756	A2	20130424
US 2013-13817383	A1	20130520

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Biomarkers can be assessed for diagnostic, therapy-related or prognostic methods to identify phenotypes, such as a condition or disease, or the stage or progression of a disease. Circulating biomarkers from a bodily fluid can be used in profiling of physiol. states or determining phenotypes. These include nucleic acids, protein, and circulating structures such as vesicles. Biomarkers can be used for theranostic purposes to select candidate treatment regimens for diseases, conditions, disease stages, and stages of a condition, and can also be used to determine treatment efficacy. The biomarkers can be circulating biomarkers, including microvesicles and their protein content and microRNAs.

IT 1140909-48-3, XL184

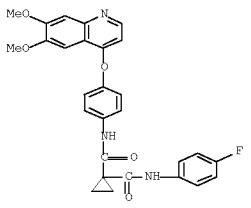
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (selection for cancer therapy; detection of circulating mRNA, microRNA, protein and vesicle markers in disease diagnosis)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

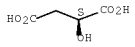
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

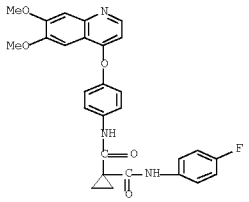


OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 482 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:1016190 CAPLUS Full-text
DOCUMENT NUMBER: 156:353197
TITLE: Biologically targeted therapies for thyroid cancers
AUTHOR(S): Sherman, Steven I.
CORPORATE SOURCE: Department of Endocrine Neoplasia and Hormonal Disorders Division of Internal Medicine, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Thyroid Cancer (2011), 329-349. Editor(s): Carpi, Angelo; Mechanick, Jeffrey I. CRC Press: Boca Raton, Fla.
CODEN: 69OKVM; ISBN: 978-1-4398-6221-6
DIGITAL OBJECT ID: 10.1201/b10945-21
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review. Systemic chemotherapies for advanced or metastatic thyroid carcinomas have been of only limited effectiveness. For patients with differentiated thyroid epithelial or medullary thyroid carcinomas unresponsive to conventional treatments, novel therapies are needed to improve disease outcomes. Multiple novel therapies primarily targeting angiogenesis have entered clin. trials for metastatic thyroid carcinoma. Partial response rates up to 30% have been reported in single agent studies, but prolonged disease stabilization is more commonly seen. The most successful agents target the vascular endothelial growth factor receptors, with potential targets including the mutant kinases associated with papillary and medullary oncogenesis. Two drugs approved for other malignancies, sorafenib and sunitinib, have had promising preliminary results reported, and are being used selectively for patients who do not qualify for clin. trials. Addnl. agents targeting tumor vasculature, nuclear receptors, epigenetic abnormalities, and the immune response to neoplasia have also been investigated. Randomized trials for several agents are under way that may lead to eventual drug approval for thyroid cancer. Treatment for patients with metastatic or advanced thyroid carcinoma now emphasizes clin. trial opportunities for novel agents with considerable promise. Alternative options now exist for use of these mol. targeted therapies, especially tyrosine kinase inhibitors, which are well tolerated and may prove worthy of regulatory approval for this disease.
IT 1140909-48-3, XL 184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. targeted therapies for thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

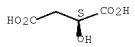
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

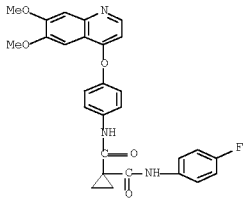


REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 483 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:991678 CAPLUS Full-text
DOCUMENT NUMBER: 156:440657
TITLE: Activity of XL184 (cabozantinib), an oral tyrosine kinase inhibitor, in patients with medullary thyroid cancer
AUTHOR(S): Kurzrock, Razelle; Sherman, Steven I.; Ball, Douglas W.; Forastiere, Arlene A.; Cohen, Roger B.; Mehra, Ranee; Pfister, David G.; Cohen, Ezra E. W.; Janisch, Linda; Nauling, Forlisa; Hong, David S.; Ng, Chaan S.; Ye, Lei; Gagel, Robert F.; Frye, John; Muller, Thomas; Ratain, Mark J.; Salgia, Ravi
CORPORATE SOURCE: The University of Texas MD Anderson Cancer Center, Houston, USA
SOURCE: Journal of Clinical Oncology (2011), 29(19), 2660-2666
CODEN: JCONDN; ISSN: 0732-183X
DIGITAL OBJECT ID: 10.1200/JCO.2010.32.4145
PUBLISHER: American Society of Clinical Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: XL184 (cabozantinib) is a potent inhibitor of MET, vascular endothelial growth factor receptor 2 (VEGFR2), and RET, with robust antiangiogenic, antitumor, and anti-invasive effects in preclin. models. Early observations of clin. benefit in a phase I study of cabozantinib, which included patients with medullary thyroid cancer (MTC), led to expansion of an MTC-enriched cohort, which is the focus of this article. Patients and Methods: A phase I dose-escalation study of oral cabozantinib was conducted in patients with advanced solid tumors. Primary end points included evaluation of safety, pharmacokinetics, and maximum-tolerated dose (MTD) determination Addnl. end points included RECIST (Response Evaluation Criteria in Solid Tumors) response, pharmacodynamics, RET mutational status, and biomarker analyses. Results: Eighty-five patients were enrolled, including 37 with MTC. The MTD was 175 mg daily. Dose-limiting toxicities were grade 3 palmar plantar erythrodysesthesia (PPE), mucositis, and AST, ALT, and lipase elevations and grade 2 mucositis that resulted in dose interruption and reduction Ten (29%) of 35 patients with MTC with measurable disease had a confirmed partial response. Overall, 18 patients experienced tumor shrinkage of 30% or more, including 17 (49%) of 35 patients with MTC with measurable disease. Addnl., 15 (41%) of 37 patients with MTC had stable disease (SD) for at least 6 mo, resulting in SD for 6 mo or longer or confirmed partial response in 68% of patients with MTC. Conclusion: Cabozantinib has an acceptable safety profile and is active in MTC. Cabozantinib may provide clin. benefit by simultaneously targeting multiple pathways of importance in MTC, including MET, VEGFR2, and RET. A global phase III pivotal study in MTC is ongoing (ClinicalTrials.gov number NCT00215605).
IT 1140909-48-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activity of cabozantinib, an oral tyrosine kinase inhibitor, in patients with medullary thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

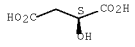
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CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



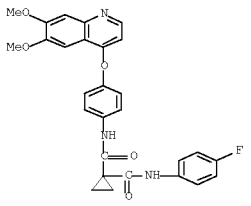
OS.CITING REF COUNT: 185 THERE ARE 185 CAPLUS RECORDS THAT CITE THIS RECORD (186 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 484 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:945715 CAPLUS Full-text
DOCUMENT NUMBER: 156:301829
TITLE: Current status of molecularly targeted drugs for the treatment of advanced thyroid cancer
AUTHOR(S): Takami, Hiroshi E.

CORPORATE SOURCE: Department of Surgery, Teikyo University School of Medicine, Tokyo, 173-8605, Japan
SOURCE: Endocrine Journal (Kyoto, Japan) (2011), 58(3), 151-153
CODEN: ENJOEO; ISSN: 0918-8959
DIGITAL OBJECT ID: 10.1507/endocrj.K11E-076
PUBLISHER: Japan Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The prognosis of almost all thyroid cancers is good, but some patients have indications for these molecularly targeted drugs. Some of these drugs, i.e., vandetanib, XL-184, sorafenib, motesanib, axitinib, and pazopanib, are clearly useful clin.
IT 1140909-48-3, XL-184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(current status of molecularly targeted drugs for the treatment of advanced thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

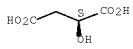
CRN 849217-68-1
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



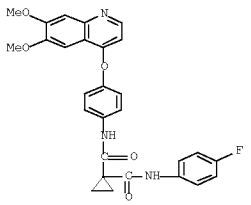
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 485 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:724271 CAPLUS Full-text
DOCUMENT NUMBER: 155:290943
TITLE: The effects of four different tyrosine kinase inhibitors on medullary and papillary thyroid cancer cells
AUTHOR(S): Verbeek, Hans H. G.; Alves, Maria M.; de Groot, Jan-Willem B.; Osinga, Jan; Plukker, John T. M.; Links, Thera P.; Hofstra, Robert M. W.
CORPORATE SOURCE: Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, 9700 RB, Neth.
SOURCE: Journal of Clinical Endocrinology and Metabolism (2011), 96(6), E991-E995
CODEN: JCEMAZ; ISSN: 0021-972X
DIGITAL OBJECT ID: 10.1210/jc.2010-2381
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Medullary and papillary thyroid carcinoma (MTC and PTC) are 2 types of thyroid cancer that can originate from activating mutations or rearrangements in the RET gene. Therapeutic options are limited in recurrent disease, but because RET is a tyrosine kinase (TK) receptor involved in cellular growth and proliferation, treatment with a TK inhibitor might be promising. Several TK inhibitors were tested in clin. trials, but it is unknown which inhibitor is most effective and whether there is any specificity for particular RET mutations. We aimed to compare the effect of 4 TK inhibitors (axitinib, sunitinib, vandetanib, and XL184) on cell proliferation, RET expression and autophosphorylation, and ERK activation in cell lines expressing a MEN2A (MTC-TT), a MEN2B (MZ-CRC-1) mutation, and a RET/PTC (TPC-1) rearrangement. The 3 cell lines were cultured and treated with the 4 TK inhibitors. Effects on cell proliferation and RET and ERK expression and activation were determined XL184 and vandetanib most effectively inhibited cell proliferation, RET autophosphorylation in combination with a reduction of RET expression, and ERK phosphorylation in MTC-TT and MZ-CRC-1, resp. TPC-1 cells showed a decrease in RET autophosphorylation after treatment with XL184, but no effect was observed on ERK activation. There is indeed specificity for different RET mutations, with XL184 being the most potent inhibitor in MEN2A and PTC and vandetanib the most effective in MEN2B in vitro. No TK inhibitor was superior for all the cell lines tested, indicating that mutation-specific therapies could be beneficial in treating MTC and PTC.
IT 1140909-48-3, XL184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Tyr kinase inhibitors effect on medullary and papillary thyroid cancer related to RET mutation, rearrangement, and ERK)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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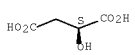
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CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

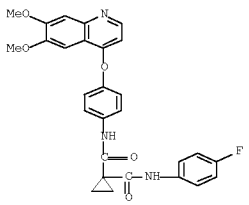


OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 486 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:461207 CAPLUS Full-text
DOCUMENT NUMBER: 156:46100
TITLE: Novel agents and new therapeutics in castration-resistant prostate cancer
AUTHOR(S): Wu, Yichao; Rosenberg, Jonathan E.; Taplin, Mary-Ellen
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
SOURCE: Current Opinion in Oncology (2011), 23(3), 290-296
CODEN: CUOOE8; ISSN: 1040-8746
DIGITAL OBJECT ID: 10.1097/CCO.0b013e3283449400
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: This review highlights recent therapeutic advances in systemic therapies for prostate cancer (PCa). Recent findings: Progress in PCa therapeutics has been made during the past year with the approval of a vaccine therapy, second-line chemotherapy, and reported survival advantage for a CYP (17,20) lyase inhibitor in castration-resistant prostate cancer (CRPC). This report will summarize the recently reported and expected data for PCa trials including an evaluation of intermittent vs. continuous androgen deprivation therapy. Denosumab is shown to support bone mineral d. in hormonal sensitive PCa patients. Targeting of androgen-dependent pathways in CRPC postchemotherapy has been shown to improve survival with the lyase inhibitor abiraterone, and lead to prostate-specific antigen and objective responses with an androgen receptor antagonist (MDV3100). However, the addition of bevacizumab to docetaxel/prednisone in treating metastatic CRPC failed to provide a survival benefit. Cabazitaxel in metastatic CRPC postdocetaxel did demonstrate a survival benefit. Provenge, an autologous dendritic cell-based vaccine, demonstrated a reduction in the risk of death in metastatic CRPC. Other immunotherapy agents, including Prostvac and ipilimumab are under investigation. We also discuss the receptor tyrosine kinase inhibitor XL184 and poly (ADP-ribose) polymerase inhibitors which are in early clin. trials. Summary: Recent advances in androgen targeting, chemotherapy, immunotherapy, and other targeted therapies have led to significant improvements in the care of CRPC patients.
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel agents and new therapeutics in castration-resistant prostate cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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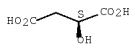
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CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

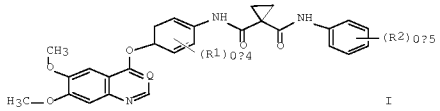
L4 ANSWER 487 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:174316 CAPLUS Full-text
DOCUMENT NUMBER: 154:225400
TITLE: C-met modulators as antitumor agents
INVENTOR(S): Aftab, Dana T.; Mueller, Thomas; Weitzman, Aaron; Holland, Jaymes
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011017639	A1	20110210	WO 2010-US44749	20100806
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
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AU 2010279234	A1	20120301	AU 2010-279234	20100806
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KR 2012059540	A	20120608	KR 2012-7006111	20100806
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CN 102647985	A	20120822	CN 2010-80045677	20100806
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NZ 598055	A	20140530	NZ 2010-598055	20100806
IL 238849	A	20150630	IL 2010-238849	20100806
NZ 624643	A	20151127	NZ 2010-624643	20100806
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IN 2012MN00278	A	20120824	IN 2012-MN278	20120203
ZA 2012000842	A	20121128	ZA 2012-842	20120203
MX 2012001654	A	20120314	MX 2012-1654	20120207
US 20120282179	A1	20121108	US 2012-13389266	20120712
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PRIORITY APPLN. INFO.:

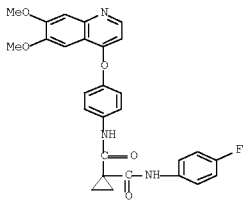
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AU 2010-279234	A3	20100806
IL 2010-217889	A3	20100806
JP 2012-523982	A3	20100806
NZ 2010-598055	A3	20100806
WO 2010-US44749	W	20100806
US 2012-13389266	B1	20120712
JP 2016-45205	A3	20160309

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 154:225400; MARPAT 154:225400
GI



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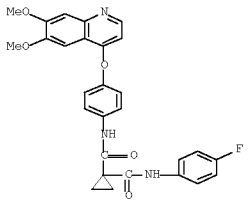
AB Methods of treating cancer by administering a compd. of Formula I (wherein R1 = halo; R2 = halo; Q = CH, N; n = 0-4; m = 0-5) or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments are described.
IT 849217-68-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(methods of using c-met modulators)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



IT 1140909-48-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of using c-met modulators)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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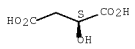
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 488 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:111410 CAPLUS Full-text
DOCUMENT NUMBER: 155:346258
TITLE: Antiangiogenic agents in the treatment of recurrent or newly diagnosed glioblastoma: analysis of single-agent and combined modality approaches
AUTHOR(S): Beal, Kathryn; Abrey, Lauren E.; Gutin, Philip H.
CORPORATE SOURCE: Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Radiation Oncology (2011), 6, 2
CODEN: ROANCM; ISSN: 1748-717X
URL: http://www.ro-journal.com/content/pdf/1748-717X-6-2.pdf

DIGITAL OBJECT ID: 10.1186/1748-717X-6-2
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. Surgical resection followed by radiotherapy and temozolomide in newly diagnosed glioblastoma can prolong survival, but it is not curative.

For patients with disease progression after frontline therapy, there is no standard of care, although further surgery, chemotherapy, and radiotherapy may be used. Antiangiogenic therapies may be appropriate for treating glioblastomas because angiogenesis is critical to tumor growth. In a large, noncomparative phase II trial, bevacizumab was evaluated alone and with irinotecan in patients with recurrent glioblastoma; combination treatment was associated with an estimated 6-mo progression-free survival (PFS) rate of 50.3%, a median overall survival of 8.9 mo, and a response rate of 37.8%. Single-agent bevacizumab also exceeded the predetd. threshold of activity for salvage chemotherapy (6-mo PFS rate, 15%), achieving a 6-mo PFS rate of 42.6% ($p<0.0001$). On the basis of these results and those from another phase II trial, the US Food and Drug Administration granted accelerated approval of single-agent bevacizumab for the treatment of glioblastoma that has progressed following prior therapy. Potential antiangiogenic agents - such as cilengitide and XL184 - also show evidence of single-agent activity in recurrent glioblastoma. Moreover, the use of antiangiogenic agents with radiation at disease progression may improve the therapeutic ratio of single-modality approaches. Overall, these agents appear to be well tolerated, with adverse event profiles similar to those reported in studies of other solid tumors. Further research is needed to determine the role of antiangiogenic therapy in frontline treatment and to identify the optimal schedule and partnering agents for use in combination therapy.

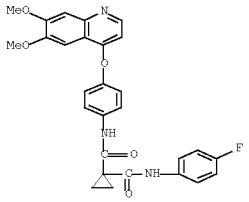
IT 1140909-48-3, XL184
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiangiogenic agents in the treatment of recurrent or newly diagnosed glioblastoma)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

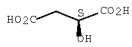
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CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 34 THERE ARE 34 CAPLUS RECORDS THAT CITE THIS RECORD (34 CITINGS)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 489 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2011:80577 CAPLUS Full-text
DOCUMENT NUMBER: 154:174225
TITLE: Drug selection for gastric cancer therapy using antibody-based arrays
INVENTOR(S): Singh, Sharat; Kim, Phillip; Liu, Xinjun; Ybarrondo, Belen
PATENT ASSIGNEE(S): Prometheus Laboratories Inc., USA
SOURCE: PCT Int. Appl., 189pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2011008990	A1	20110120	WO 2010-US42182	20100715
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2768013	A1	20110120	CA 2010-2768013	20100715
AU 2010273319	A1	20120223	AU 2010-273319	20100715
AU 2010273319	B2	20150122		
EP 2454598	A1	20120523	EP 2010-800567	20100715
EP 2454598	B1	20170322		
R: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BA, ME, RS				
JP 2012533738	T	20121227	JP 2012-520794	20100715
JP 5795311	B2	20151014		
US 20110281748	A1	20111117	US 2011-13014674	20110126
US 20130237436	A9	20130912		
US 20120270745	A1	20121025	US 2012-13354257	20120119
AU 2013202682	A1	20130502	AU 2013-202682	20130405
AU 2013202682	B2	20150716		
JP 2016001187	A	20160107	JP 2015-159663	20150812

PRIORITY APPLN. INFO.:

US 2009-61225866	P	20090715
US 2009-61265218	P	20091130
US 2010-61325000	P	20100416
US 2006-61007527	P	20060921
US 2007-60913087	P	20070420
AU 2007-299774	A3	20070920
WO 2007-US79002	A1	20070920
US 2008-46381	A2	20080311
JP 2012-520794	A3	20100715
WO 2010-US42182	W	20100715
US 2011-13014674	A2	20110126
US 2011-61436945	P	20110127
US 2011-61467950	P	20110325

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides methods for selecting a suitable anticancer therapy, and for identifying and predicting response for the treatment of a gastric cancer. The present invention provides compns. and methods for detecting the status (e.g., expression and/or activation levels) of components of signal transduction pathways in tumor cells (e.g., gastric tumor cells). Information on the expression and/or activation states of components of signal transduction pathways (e.g., HER2 and/or c-Met signal transduction pathway components) derived from practice of the present invention can be used for gastric cancer diagnosis, prognosis, and in the design of gastric cancer treatments. The compns. and methods of the present invention advantageously provide accurate prediction, selection, and monitoring of cancer patients (e.g., gastric cancer patients) most likely to benefit from targeted therapy by performing pathway profiling on easily accessible tumor cells using multiplexed, antibody-based proximity assays.

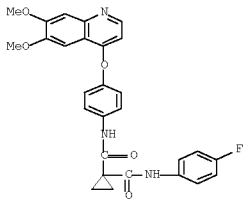
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug selection for gastric cancer therapy using antibody-based arrays for detecting the status of signal transduction pathways)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

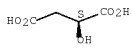
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 490 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:1570396 CAPLUS Full-text
DOCUMENT NUMBER: 155:177406
TITLE: Targeting RET Receptor Tyrosine Kinase Activation in Cancer
AUTHOR(S): Phay, John E.; Shah, Manisha H.
CORPORATE SOURCE: Department of Surgery, Division of Surgical Oncology, Department of Internal Medicine, and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA
SOURCE: Clinical Cancer Research (2010), 16(24), 5936-5941
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-09-0786
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. After ligand binding induces dimerization, the RET receptor tyrosine kinase activates multiple signal transduction pathways. Constitutively activating mutations and chromosomal rearrangements are the primary oncogenic event in a significant number of medullary thyroid cancers (MTC) and papillary thyroid cancers (PTC), resp. When specific germline

mutations in RET are identified early, prophylactic thyroidectomy can be timed to remove at-risk tissue in patients with multiple endocrine neoplasia 2 (MEN2) syndromes who would otherwise develop MTC. Conventional therapy for progressive metastatic MTC is limited. Small-mol. tyrosine kinase inhibitors can target multiple kinases at nanomolar concns., including RET, and have shown efficacy against a variety of malignancies. Initial clin. evidence suggests that several of these inhibitors, including sorafenib, vandetanib, motesanib, sunitinib, and XL-184, may have some benefit in treating progressive MTC. Although initial success seen in these trials seems to be modest, it represents a major breakthrough in the treatment of patients with widespread metastatic MTC. Clin Cancer Res; 16(24); 5936-41.

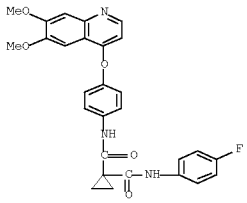
IT 1140909-48-3, XL-184,
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(role of RET receptor tyrosine kinase activation in cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

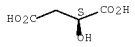
CRN 849217-68-1
CMF C28 H24 F N3 O5

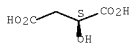


CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).





REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 492 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:1003327 CAPLUS Full-text
DOCUMENT NUMBER: 153:278035
TITLE: Treatment of lung cancer with a PARP inhibitor in combination with a growth factor inhibitor
INVENTOR(S): Sherman, Barry M.; Bradley, Charles; Ossovskaya, Valeria S.
PATENT ASSIGNEE(S): BiPar Sciences, Inc., USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010091140	A1	20100812	WO 2010-US23137	20100204
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2751397	A1	20100812	CA 2010-2751397	20100204
AR 75239	A1	20110316	AR 2010-100305	20100204
AU 2010210636	A1	20110922	AU 2010-210636	20100204
KR 2011113648	A	20111017	KR 2011-7020246	20100204
EP 2393364	A1	20111214	EP 2010-739097	20100204
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CN 102307475	A	20120104	CN 2010-80006536	20100204
JP 2012516895	T	20120726	JP 2011-549246	20100204
IL 214366	A	20130131	IL 2010-214366	20100204
MX 2011008221	A	20110817	MX 2011-8221	20110804
IN 2011CN06195	A	20121012	IN 2011-CN6195	20110829
US 20120130144	A1	20120524	US 2011-13146865	20111222
PRIORITY APPLN. INFO.:			US 2009-61149977 P	20090204
			WO 2010-US23137 W	20100204

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OS.CITING REF COUNT: 53 THERE ARE 53 CAPLUS RECORDS THAT CITE THIS RECORD (53 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

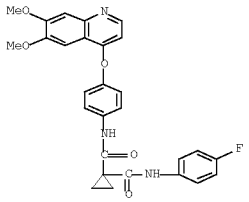
L4 ANSWER 491 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:1240526 CAPLUS Full-text
DOCUMENT NUMBER: 153:595314
TITLE: Tyrosine kinase inhibitors in thyroid cancer
AUTHOR(S): Illouz, Frederic
CORPORATE SOURCE: Service EDN, Centre de reference des pathologies de la receptivite hormonale, CHU d'Angers, Fr.
SOURCE: Correspondances en Metabolismes, Hormones, Diabetes et Nutrition (2010), 14(7), 210-214
CODEN: CMHDBH; ISSN: 2100-9619
PUBLISHER: Edimark SAS
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French
AB A review.
IT 1140909-48-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitors in thyroid cancer therapy)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 849217-68-1
CMF C28 H24 F N3 O5

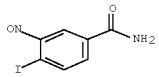


CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

OTHER SOURCE(S): MARPAT 153:278035
GI



AB In one aspect, the present invention provides a method of treating lung cancer, comprising administering to a subject at least one PARP inhibitor in combination with at least one growth factor inhibitor. In another aspect, the present invention provides a method of treating non-small cell lung cancer comprising administering to a subject at least one PARP inhibitor in combination with at least one growth factor inhibitor.

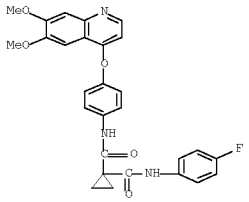
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of lung cancer with a PARP inhibitor in combination with a growth factor inhibitor)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

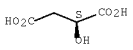
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

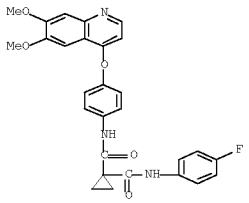
L4 ANSWER 493 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:944155 CAPLUS Full-text
DOCUMENT NUMBER: 155:230334
TITLE: Patients with advanced head and neck cancers have similar progression-free survival on phase I trials and their last food and drug administration-approved treatment
AUTHOR(S): Garrido-Laguna, Ignacio; Janku, Filip; Falchook, Gerald S.; Fu, Siqing; Hong, David S.; Naing, Aung; Aaron, Joanne; Wang, Xuemei; Kies, Merrill; Kurzrock, Razelle
CORPORATE SOURCE: Departments of Investigational Cancer Therapeutics (Phase I Clinical Trials Program), The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Clinical Cancer Research (2010), 16(15), 4031-4037
CODEN: CCREF4; ISSN: 1078-0432
DIGITAL OBJECT ID: 10.1158/1078-0432.CCR-10-0672
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: To compare clin. outcomes of metastatic head and neck cancer patients treated in phase I clin. trials with clin. outcomes of those patients who had their last Food and Drug Administration (FDA)-approved therapy in the setting of metastatic disease. Exptl. Design: We retrospectively reviewed the outcomes of 61 consecutive patients with head and neck tumors treated in 36 phase I trials at The University of Texas M.D. Anderson Cancer Center between July 2004 and Sept. 2009. Results: The most common histol. was head and neck squamous cell carcinoma (62%). Median age was 55 years (range, 26-80). Eastern Cooperative Oncol. Group performance status was 0 to 1 for 95% of patients. Fifty-nine patients had received FDA-approved drugs as the backbone of their last systemic therapy before inclusion in phase I trials (median, 2 systemic therapies). Progression-free survival (PFS) on phase I trials was not inferior to PFS on their last FDA-approved therapies (12 vs. 10.7 wk, log-rank P = 0.87). Fifty-three patients were evaluable for response by Response Evaluation Criteria in Solid Tumors criteria. Four (7%) had partial responses and 16 (26%) had stable disease for ≥4 mo. In univariate anal., number of metastatic sites, lactate dehydrogenase (LDH) levels at baseline, and Royal Marsden Hospital prognosis scores were significant predictors of survival. Only LDH was significant in multivariate anal. (hazard ratio, 6.35; P ≤ 0.0001). Conclusions: For patients with heavily pretreated advanced head and neck tumors, PFS on phase I trials is not inferior to PFS with their last FDA-approved therapy. The only significant predictor of survival in the multivariate anal. was baseline LDH.

IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(patients with advanced head and neck cancers have similar progression-free survival on phase I trials and their last food and drug administration-approved treatment)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

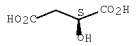
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
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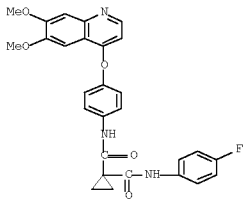
L4 ANSWER 494 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:928655 CAPLUS Full-text
DOCUMENT NUMBER: 154:425137
TITLE: XL-184, a MET, VEGFR-2 and RET kinase inhibitor for the treatment of thyroid cancer, glioblastoma multiforme and NSCLC
AUTHOR(S): Zhang, Ying; Guessous, Fadila; Kofman, Alex; Schiff, David; Abounader, Roger
CORPORATE SOURCE: Department of Microbiology, University of Virginia, Charlottesville, VA, 22903, USA
SOURCE: IDrugs (2010), 13(2), 112-121
CODEN: IDRUFN; ISSN: 2040-3410
URL: http://www.biomedcentral.com/content/pdf/cd-1071541.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English

AB A review. XL-184 (BMS-907351), under development by Exelixis Inc and Bristol-Myers Squibb Co, is a pan-tyrosine kinase inhibitor for the potential oral treatment of medullary thyroid cancer, glioblastoma multiforme and NSCLC. The prinicipal targets of XL-184 are MET, VEGFR-2 and RET, but the drug is also reported to display inhibitory activity against KIT, FLT3 and TEK. Preclin. studies demonstrated that XL-184 potently inhibited multiple receptor tyrosine kinases in various cancer cell lines and animal xenograft models, and that the drug exhibited significant oral bioavailability and blood-brain barrier penetration. A phase I clin. trial in patients with advanced solid malignancies indicated that XL-184 accumulated dose-dependently in the plasma and had a long terminal half-life. A phase II trial in patients with progressive or recurrent glioblastoma revealed modest but promising median progression-free survival. Toxicity and side effects for the drug have generally been of low-to-moderate severity. At the time of publication, three addnl. trials of XL-184 were recruiting patients, including a phase I trial in combination with standard of care in patients with glioblastoma, a phase I/II trial in combination with erlotinib in patients with NSCLC, and a phase III trial in patients with medullary thyroid cancer.

IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL-184, a MET, VEGFR-2 and RET kinase inhibitor for the treatment of thyroid cancer, glioblastoma multiforme and NSCLC)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

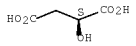
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 51 THERE ARE 51 CAPLUS RECORDS THAT CITE THIS RECORD (51 CITINGS)
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 495 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:912816 CAPLUS Full-text
DOCUMENT NUMBER: 153:204211
TITLE: Preparation of malate salts of N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide and crystalline forms thereof for the treatment of cancer.
INVENTOR(S): St Clair Brown, Adrian; Lamb, Peter; Gallagher, William P.
PATENT ASSIGNEE(S): Exelixis, Inc., USA; Bristol-Meyers Squibb Company
SOURCE: PCT Int. Appl., 72pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010083414	A1	20100722	WO 2010-US21194	20100115
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,				

CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2758030	A1	20100722	CA 2010-2758030	20100115
AR 75025	A1	20110302	AR 2010-100098	20100115
AU 2010204619	A1	20110901	AU 2010-204619	20100115
AU 2010204619	B2	20160811		
EP 2387563	A1	20111123	EP 2010-701175	20100115
EP 2387563	B1	20130306		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
KR 2012013301	A	20120214	KR 2011-7018924	20100115
KR 1733773	B1	20170510		
CN 102388024	A	20120321	CN 2010-80012656	20100115
JP 2012515220	T	20120705	JP 2011-546390	20100115
JP 5677318	B2	20150225		
IL 214086	A	20130131	IL 2010-214086	20100115
PT 2387563	E	20130325	PT 2010-701175	20100115
ES 2402524	T3	20130506	ES 2010-701175	20100115
NZ 594594	A	20131129	NZ 2010-594594	20100115
EA 19959	B1	20140730	EA 2011-70941	20100115
TW I447108	B	20140801	TW 2010-101140	20100115
IL 234097	A	20140930	IL 2010-234097	20100115
NZ 618004	A	20150626	NZ 2010-618004	20100115
TW I511956	B	20151211	TW 2014-115685	20100115
CN 106083714	A	20161109	CN 2016-10140984	20100115
KR 2017052702	A	20170512	KR 2017-7011913	20100115
ZA 2011005167	A	20120328	ZA 2011-5167	20110713
MX 2011007620	A	20111104	MX 2011-7620	20110715
IN 2011KN03402	A	20121102	IN 2011-KN3402	20110811
US 8877776	B2	20141104	US 2011-13145054	20111020
US 20120035212	A1	20120209		
HK 1164305	A1	20131108	HK 2012-104893	20120518
AU 2013203780	A1	20130502	AU 2013-203780	20130411
AU 2013203780	B2	20160901		
JP 2015096543	A	20150521	JP 2014-264071	20141226
JP 5980894	B2	20160831		
JP 2017014232	A	20170119	JP 2016-146934	20160727
AU 2016262732	A1	20161215	AU 2016-262732	20161124

PRIORITY APPLN. INFO.:

US 2009-61145421	P	20090116
AU 2010-204619	A3	20100115
CN 2010-80012656	A3	20100115
IL 2010-214086	A3	20100115
JP 2011-546390	A3	20100115
KR 2011-7018924	A3	20100115
NZ 2010-594594	A3	20100115
WO 2010-US21194	W	20100115
AU 2013-203780	A3	20130411

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 153:204211

AB N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide malate salts were prepared Thus, 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid (preparation given) was stirred with (COCl)2 in THF/DMF at ≤30° and the mixture was added to 4-(6,7-dimethoxyquinolin-4-yloxy)phenylamine (preparation given) and K2CO3 in THF/H2O followed by addition of H2O and stirring for 10 h to give N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide. The latter in EtOH was treated with malic acid in H2O followed by addition of C, thiol silica, heating to 78°, and addition of H2O followed by filtration, addition of Me2CHOH, cooling, and filtration to give N-[4-[[6,7-bis(methyloxy)quinolin-4-yl]oxy]phenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide malate.

IT 1235470-36-6P

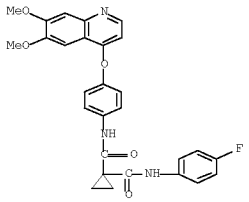
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)

RN 1235470-36-6 CAPLUS

CN Butanedioic acid, 2-hydroxy-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

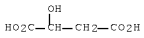
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CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 6915-15-7
CMF C4 H6 O5



IT 1235470-37-7P 1235470-38-8P

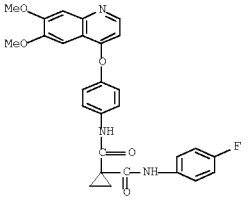
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)

RN 1235470-37-7 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

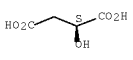
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

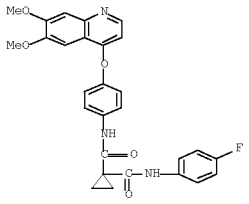


RN 1235470-38-8 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2R)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:?) (CA INDEX NAME)

CM 1

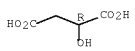
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CMF C28 H24 F N3 O5



CM 2

CRN 636-61-3
CMF C4 H6 O5

Absolute stereochemistry. Rotation (+).

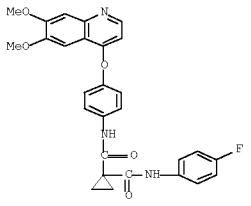


IT 849217-68-1

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of malate salts of bismethoxyquinolinyloxyphenylfluorophenylcyclopropanedicarboxamide and crystalline forms thereof for the treatment of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



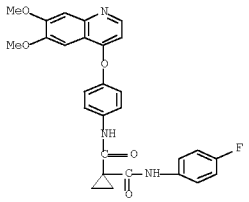
OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 496 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:726266 CAPLUS Full-text
DOCUMENT NUMBER: 153:633557
TITLE: Targeted therapy for thyroid cancer: an updated review of investigational agents
AUTHOR(S): Deshpande, Hari A.; Gettinger, Scott N.; Sosa, Julie A.
CORPORATE SOURCE: Yale Cancer Center, New Haven, CT, 06520, USA
SOURCE: Current Opinion in Investigational Drugs (BioMed Central) (2010), 11(6), 661-668
CODEN: COIDAZ; ISSN: 2040-3429
URL: http://www.biomedcentral.com/content/pdf/cd-1102161.pdf

PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
AB A review. The treatment of thyroid cancer is evolving. The mol. mechanisms of carcinogenesis for many thyroid cancers have been investigated, and have yielded targets for potential therapies. These targets include VEGFR in the treatment of all thyroid cancers, BRAF in the treatment of papillary thyroid cancer, and RET in the treatment of medullary thyroid cancer (MTC). Many promising drugs that target one or more of these proteins are currently being evaluated, including sorafenib and sunitinib, both of which are still under development for the treatment of thyroid cancer but which have been approved for use in other malignancies. In addition, compds. such as vandetanib (AstraZeneca plc) and XL-184 (Bristol-Myers Squibb Co/Exelixis Inc) have demonstrated activity in early-phase clin. trials of MTC and are being tested further in randomized trials.
IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XL-184 targeting vascular endothelial growth factor receptor, RET and BRAF protein may be effective in patient with thyroid cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

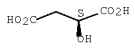
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



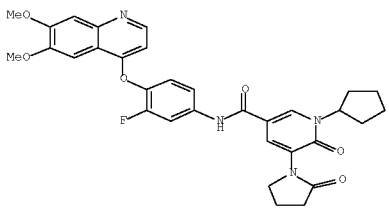
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 497 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:439254 CAPLUS Full-text
DOCUMENT NUMBER: 152:422278
TITLE: Methods for the treatment of cancer
INVENTOR(S): Johns, Terrance
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 139pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010039248	A1	20100408	WO 2009-US5421	20090930
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2009300328	A1	20100408	AU 2009-300328	20090930
CA 2738583	A1	20100408	CA 2009-2738583	20090930
EP 2349328	A1	20110803	EP 2009-740207	20090930
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JP 2012504606	T	20120223	JP 2011-530051	20090930
MX 2011003363	A	20110427	MX 2011-3363	20110329
US 20110229469	A1	20110922	US 2011-13122106	20110613
JP 2015107974	A	20150611	JP 2014-256872	20141219
AU 2015201812	A1	20150430	AU 2015-201812	20150410
PRIORITY APPLN. INFO.:			US 2008-61101971	P 20081001
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			WO 2009-US5421	W 20090930

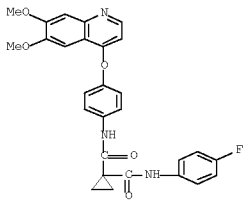
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 152:422278
GI



AB Methods for treating cancer with at least one HGF-Met inhibitor and at least one EGFR inhibitor are provided.
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treatment of cancer)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

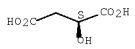
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 498 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:402977 CAPLUS Full-text
DOCUMENT NUMBER: 152:423197
TITLE: Recombinant replication-competent retroviral vectors expressing therapeutic products for treatment of proliferative disorders
INVENTOR(S): Gruber, Harry E.; Jolly, Douglas; Perez, Omar

PATENT ASSIGNEE(S): Tocagen Inc., USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010036986	A2	20100401	WO 2009-US58512	20090926
WO 2010036986	A3	20100701		
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 2344648	A2	20110720	EP 2009-816967	20090926
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CN 102227503	A	20111026	CN 2009-80147515	20090926
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CN 105274125	A	20160127	CN 2015-10505943	20090926
MY 156333	A	20160215	MY 2011-1328	20090926
CN 105624193	A	20160601	CN 2015-10624987	20090926
PH 12011500630	B1	20151211	PH 2011-12011500630	20110325
US 20110287020	A1	20111124	US 2011-13072704	20110326
US 8829173	B2	20140909		
AU 2013205006	A1	20130516	AU 2013-205006	20130413
AU 2013205006	B2	20160218		
US 20160053232	A1	20160225	US 2014-14477741	20140904
JP 2015119712	A	20150702	JP 2015-4923	20150114
JP 5992548	B2	20160914		
JP 2015186479	A	20151029	JP 2015-97980	20150513
JP 6062485	B2	20170118		
JP 2017018121	A	20170126	JP 2016-159893	20160817

PRIORITY APPLN. INFO.:

US 2008-61100666	P	20080926
US 2008-61120618	P	20081208
US 2009-61186823	P	20090613
AU 2009-303690	A3	20090926
CN 2009-80147509	A3	20090926
CN 2009-80147515	A3	20090926
JP 2011-529291	A3	20090926
JP 2011-529292	A3	20090926
WO 2009-US58512	W	20090926
US 2010-61318728	P	20100329
US 2011-13072704	A1	20110326

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

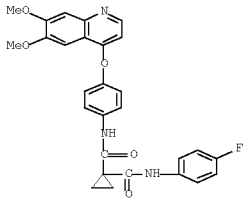
AB Recombinant replication-competent retroviral (RCR) vectors are provided comprising: a retroviral gag protein; a retroviral pol protein; a retroviral envelop, a retroviral polynucleotide comprising long terminal repeat (LTR) sequence at the 3' end of the retroviral polynucleotide sequence; a mammalian-suitable promoter sequence at the 5' end of the retroviral polynucleotide, a cassette comprising an internal ribosome entry site (IRES) operably linked to a heterologous polynucleotide; and cis-acting sequences necessary for reverse transcription, packaging and integration in a target cell. The RCR maintains higher replication competency after 6 passages compared to a pACE vector. The heterologous polynucleotide may encode modified cytosine deaminase (thermostabilized and codon optimized), single-chain antibody to CTLA-4, microRNAs miR-128-1 and miR-128-2, γ-interferon, interleukin 2, or other therapeutic proteins of interest. The disclosure further relates to cells and vector expressing or comprising such modified CDs and methods of using such modified CDs in the treatment of disease and disorders, and in particular cell proliferative disorders such as cancer.

IT 1140909-48-3, XL 184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy with; recombinant replication-competent retroviral vectors expressing therapeutic products for treatment of proliferative disorders)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

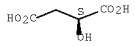
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 499 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2010:55413 CAPLUS Full-text
DOCUMENT NUMBER: 152:163651
TITLE: Methods for diagnosis, prognosis and treatment
INVENTOR(S): Fantl, Wendy J.; Rosen, David B.; Cesano, Alessandra; Putta, Santosh K.; Nolan, Garry P.; Cohen, Aileen C.; Evenson, Erik
PATENT ASSIGNEE(S): Nodality, Inc., USA
SOURCE: PCT Int. Appl., 201pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2010006291	A1	20100114	WO 2009-US50295	20090710
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2304436	A1	20110406	EP 2009-790295	20090710
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR, AL, BA, RS				
US 20150017119	A1	20150115	US 2014-14279905	20140516
US 9500655	B2	20161122		

PRIORITY APPLN. INFO.:

US 2008-61079766	P	20080710
US 2008-61085789	P	20080801
US 2008-61104666	P	20081010
US 2008-61120320	P	20081205
US 2009-460029	A3	20090710
WO 2009-US50295	W	20090710
US 2012-13473829	A1	20120517

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

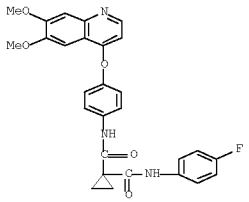
AB The present invention provides an approach for the detn. of the activation states of a plurality of proteins in single cells. This approach permits the rapid detection of heterogeneity in a complex cell population based on activation states, expression markers and other criteria, and the identification of cellular subsets that exhibit correlated changes in activation within the cell population. Moreover, this approach allows the correlation of cellular activities or properties. In addition, the use of modulators of cellular activation allows for characterization of pathways and cell populations. Several exemplary diseases that can be analyzed using the invention include AML, MDS, and MPN.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hematopoietic cell flow cytometry anal. and pathway stimulation for diagnosing, prognosing, therapy and progression of acute leukemia, myelodysplastic syndrome and myeloproliferative syndrome)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

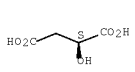
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

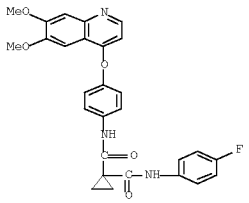
L4 ANSWER 500 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2009:1534585 CAPLUS Full-text
DOCUMENT NUMBER: 153:76060
TITLE: Antiangiogenic strategies for treatment of malignant gliomas
AUTHOR(S): Chi, Andrew S.; Norden, Andrew D.; Wen, Patrick Y.
CORPORATE SOURCE: Stephen E. and Catherine Pappas Center for Neuro-Oncology, Department of Neurology, Division of Hematology and Oncology, Dana-Farber/Harvard Cancer Center, Harvard Medical School, Massachusetts General Hospital Cancer Center, USA
SOURCE: Neurotherapeutics (2009), 6(3), 513-526
CODEN: NEURNV; ISSN: 1933-7213
DIGITAL OBJECT ID: 10.1016/j.nurt.2009.04.010
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Numerous antiangiogenic agents with diverse mechanisms of action are currently under investigation for the treatment of patients with glioblastoma (GBM), a diagnosis that continues to carry a poor prognosis despite maximal conventional therapy. Early clin. trials suggest that antiangiogenic drugs, which target the blood vessels of these highly angiogenic tumors, may have clin. benefit in GBM patients. Antiangiogenic agents have potent antiedema and steroid-sparing effects in patients, and emerging data suggest that these drugs may modestly improve progression-free survival. Although these early results are encouraging, several issues arise regarding the use and efficacy of these agents. Interpretation of the radiog. changes that occur after treatment with antiangiogenic agents presents a major challenge. Still lacking are reliable radiog. and biol. markers that can predict which patients will benefit from treatment and that accurately indicate response and progression during therapy. In addition, most patients treated with antiangiogenic drugs eventually progress, and the mechanisms by which tumors escape from therapy are only beginning to be understood. Larger prospective trials that incorporate correlative biomarker studies will be required to address these challenges. Here, we summarize the clin. experience with antiangiogenic therapy in patients with malignant gliomas (MG), review the major issues concerning the use and development of these agents, and discuss strategies that may build upon the initial gains observed with antiangiogenic agents.

IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiangiogenic agent XL 184 may show clin. utility in treatment of patient with malignant glioblastoma)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

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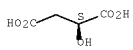
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 501 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2009:1435911 CAPLUS Full-text
DOCUMENT NUMBER: 151:565112
TITLE: Combinations VEGF(R) inhibitors and hepatocyte growth factor (c-met) inhibitors for the treatment of cancer
INVENTOR(S): Burgess, Theresa L.; Coxon, Angela; Dussault, Isabelle; Kaplan-Lefko, Paula; Polverino, Anthony J.; Beaupre, Darrin
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009140549	A1	20091119	WO 2009-US44034	20090514

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

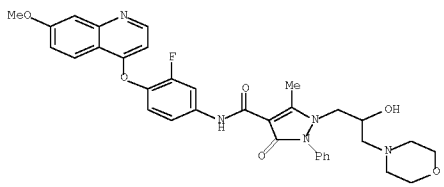
AU 2009246263	A1	20091119	AU 2009-246263	20090514
AU 2009246263	B2	20140821		
CA 2723617	A1	20091119	CA 2009-2723617	20090514
EP 2288383	A1	20110302	EP 2009-747630	20090514

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, RS

JP 2011520908	T	20110721	JP 2011-509721	20090514
JP 5699075	B2	20150408		
MX 2010012290	A	20110221	MX 2010-12290	20101110
US 20110104161	A1	20110505	US 2011-992359	20110111
US 20140243339	A1	20140828	US 2014-14194431	20140228

PRIORITY APPLN. INFO.: US 2008-61127753 P 20080514
WO 2009-US44034 W 20090514
US 2011-992359 B3 20110111

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 151:565112
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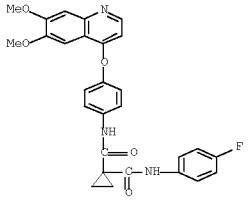


AB This invention is in the field of pharmaceutical agents and specifically relates to compds., compns., uses and methods for treating cancer, by combining VEGF(R) inhibitors and inhibitors of HGF/SF:c-Met. E.g., enhanced activity was observed when AMG 706 (Motesanib) was combined with Amgen Compound 3 [N-[4-[4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-carboxamido)-2-fluorophenoxy]pyridin-2-yl]morpholine-4-carboxamide] compared to either single agent alone when tested on human gastric adenocarcinoma cancer cells.

IT 1140909-48-3, XL 184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations VEGF(R) inhibitors and hepatocyte growth factor inhibitors for cancer treatment)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

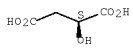
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 502 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2009:1001773 CAPLUS Full-text
DOCUMENT NUMBER: 152:349858
TITLE: Novel treatment of medullary thyroid cancer
AUTHOR(S): Sugawara, Masahiro; Geffner, David L.; Martinez, Dorothy; Hershman, Jerome M.
CORPORATE SOURCE: aEndocrinology and Diabetes Division, Veterans Affairs

Greater Los Angeles Medical Center, Department of Medicine, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA
SOURCE: Current Opinion in Endocrinology, Diabetes and Obesity (2009), 16(5), 367-372
CODEN: COEDFK; ISSN: 1752-296X
DIGITAL OBJECT ID: 10.1097/MED.0b013e3283304f0c
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

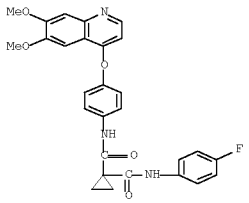
AB Purpose of review: Metastatic medullary thyroid cancer (MTC) is an incurable disease once metastasis becomes unresectable. Many therapeutic drugs and methods have been tried to circumvent this difficulty. We review currently published treatments and hope for future developments of more effective treatment methods. Recent findings: Motesanib, vandetanib, axitinib (tyrosine kinase inhibitors), and XL184 (multikinase inhibitor) have been shown to achieve partial response or stable disease state of metastatic MTC. Sunitinib and sorafenib, currently available tyrosine kinase inhibitors, can also be tried for patients with MTC. However, these medications are not curative and do not improve survival rate. Only carcinoembryonic antigen-I-iodine-based radioimmunotherapy improved survival of a subset of patients with a very aggressive type of MTC. Drugs currently available for possible use of MTC treatment include bortezomib (proteasome inhibitor), valproic acid (histone deacetylase inhibitor), capecitabine (5-fluorouracil prodrug), and indomethacin (NSAID), although clin. studies have yet to be done. Cardiac natriuretic hormones and an extract of the plant Cautleya gracilis are new agents to be studied for MTC. Summary: Kinase inhibitors are the first drugs showing some efficacy in MTC. To improve survival, unconventional drugs or other therapies with or without kinase inhibitors need to be considered.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multikinase inhibitors like XL184 was effective in patient with metastatic thyroid cancer)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

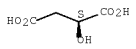
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 503 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2009:378374 CAPLUS Full-text
DOCUMENT NUMBER: 153:495871
TITLE: EGFR agonist: irreversible EGFR-TKI and c-Met inhibitors combination
AUTHOR(S): Yadoya, Takehito; Takahashi, Toshiaki; Yamamoto, Nobuyuki
CORPORATE SOURCE: Dep. of Respiratory Diseases, Shizuoka Cancer Center, Shizuoka, Japan
SOURCE: Mebio Oncology (2009), 6(1), 23-31
CODEN: MOENAJ; ISSN: 1349-2179
PUBLISHER: Mejikarubyusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

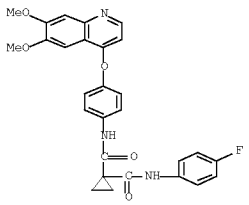
AB A review discussing (1) resistant mechanism to reversible epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), (2) irreversible EGFR-TKIs HKI-272, BIBW-2992, PF-299804 and CI-1033 and (3) c-Met inhibitors AMG-102, XL-184, XL-880 and ARQ-197.

IT 1140909-48-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epidermal growth factor receptor agonist and the combination of irreversible EGFR-TKI and c-Met inhibitors)

RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

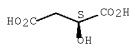
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



L4 ANSWER 504 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2009:239386 CAPLUS Full-text
DOCUMENT NUMBER: 150:275539
TITLE: Methods for diagnosis, prognosis and methods of treatment
INVENTOR(S): Fantl, Wendy J.; Putta, Santosh K.; Perez, Omar D.; Francis-Lang, Helen L.; Cohen, Aileen C.
PATENT ASSIGNEE(S): Nodality, Inc., USA
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009025847	A2	20090226	WO 2008-US9975	20080821
WO 2009025847	A3	20090611		
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
AU 2008289442	A1	20090226	AU 2008-289442	20080821
CA 2696402	A1	20090226	CA 2008-2696402	20080821
US 20090098594	A1	20090416	US 2008-229476	20080821
EP 2179037	A2	20100428	EP 2008-795509	20080821
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, AL, BA, MK, RS				
CN 101802182	A	20100811	CN 2008-80107737	20080821
JP 2010536371	T	20101202	JP 2010-521884	20080821
EP 2860247	A1	20150415	EP 2014-189449	20080821
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR				
IN 2010DN01966	A	20100820	IN 2010-DN1966	20100319
US 20120309029	A1	20121206	US 2012-13493857	20120611
US 9182385	B2	20151110		
US 20160097770	A1	20160407	US 2015-14825486	20150813

PRIORITY APPLN. INFO.:
US 2007-60957160 P 20070821
US 2008-61048920 P 20080429
EP 2008-795509 A3 20080821
US 2008-229476 A1 20080821
WO 2008-US9975 W 20080821
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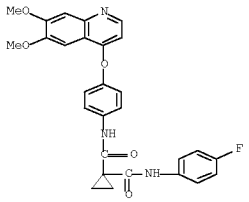
AB This invention is directed to methods and comps. for diagnosis, prognosis and for determining methods of treatment. The physiol. status of cells present in a sample (e.g. clin. sample) can be used in diagnosis or prognosis of a condition (e.g. chronic lymphocytic leukemia), in patient selection for therapy, to monitor treatment and to modify or optimize therapeutic regimens. The physiol. status of a cell can be determined by comparing the intracellular status of one or more activation elements (e.g. the phosphorylation status of a signaling mol.) in a cell (e.g. a cancer cell) to that of another cell (e.g. a normal cell). The physiol. status of a cell can be further classified by adding one or more modulators (e.g. an inhibitor or activator) to the cell in question. In some embodiments, the invention is directed to methods of determining a phenotypic profile of a population of cells.

IT 1140909-48-3, XL 184
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(methods for diagnosis, prognosis and treatment of diseases)
RN 1140909-48-3 CAPLUS
CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

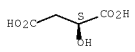
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CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).

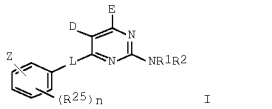


OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

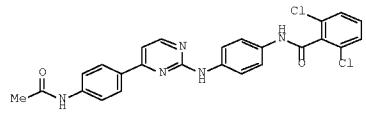
L4 ANSWER 505 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2009:140345 CAPLUS Full-text
DOCUMENT NUMBER: 150:214411
TITLE: Pyrimidine derivatives as JAK-2 inhibitors in combination with other agents and their preparation and use in the treatment of diseases
INVENTOR(S): Lamb, Peter
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 854pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009017838	A2	20090205	WO 2008-US9360	20080731
WO 2009017838	A3	20090702		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			

PRIORITY APPLN. INFO.: US 2007-60962776 P 20070801
OTHER SOURCE(S): CASREACT 150:214411; MARPAT 150:214411
GI



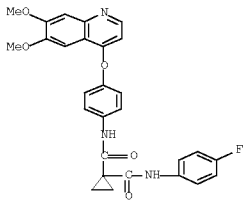
I



II

AB A method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a JAK-2 compound of formula I, or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of formula I and a pharmaceutically acceptable carrier, in combination with an active agent selected from of a Raf inhibitor, an EGFR inhibitor, a VEGFR inhibitor, a ErbB2 inhibitor, a BCR-Abl, inhibitor, a Flt3 inhibitor, a Src inhibitor, a c Kit inhibitor, an Akt inhibitor, a Ret inhibitor, an IFG1R inhibitor, an m-Tor inhibitor, a PI3K inhibitor, a PI3Kalpha inhibitor, wherein the mammal is in need of the treatment. Compds. of formula I wherein D and E are independently H, halo, CF3, heterocycloalkyl and alkyl; D and E taken together to form a 5- to 7-membered heteroaryl, and 5- to 7-membered heterocycloalkyl; L is a bond, O and NH; Z is alkoxy, cycloalkyl, and (un)substituted heteroaryl; Z and R25 taken together for form a 5- to 6-membered heterocycloalkyl, 5- to 6-membered heteroaryl, 5- to 6-membered cycloalkyl, etc.; each R25 is independently alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, etc.; R1 is H; R2 is (un)substituted aryl, (un)substituted heteroaryl, alkyl, etc.; n is 0 - 4; and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by acylation of 2-(4-aminophenylamino)-5-(4-acetylaminophenyl)pyrimidine with 2,6-dichlorobenzoyl chloride. All the invention compds. were evaluated for their JAK-2 inhibitory activity (some data given).

IT 849217-68-1
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as JAK-2 inhibitors in combination with other agents useful in treatment of diseases)
RN 849217-68-1 CAPLUS
CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L4 ANSWER 506 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2008:1282443 CAPLUS Full-text
DOCUMENT NUMBER: 149:486836
TITLE: Methods for treating cancer resistant to ErbB therapeutics
INVENTOR(S): Janne, Pasi A.; Engelman, Jeffrey; Cantley, Lewis C.
PATENT ASSIGNEE(S): Dana Farber Cancer Institute, USA; Beth Israel Deaconess Medical Center; Massachusetts General Hospital
SOURCE: PCT Int. Appl., 96pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008127710	A2	20081023	WO 2008-US4804	20080411
WO 2008127710	A3	20081204		
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
AU 2008239594	A1	20081023	AU 2008-239594	20080411
AU 2008239594	B2	20131024		
CA 2683559	A1	20081023	CA 2008-2683559	20080411
EP 2076289	A2	20090708	EP 2008-742861	20080411
EP 2076289	B1	20141112		
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JP 2010523680	T	20100715	JP 2010-503084	20080411
JP 5926487	B2	20160525		
ES 2529790	T3	20150225	ES 2008-742861	20080411
EP 2851091	A1	20150325	EP 2014-189064	20080411
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US 8715665	B2	20140506	US 2010-450826	20100318
US 20120225870	A1	20120906		
AU 2013203111	A1	20130502	AU 2013-203111	20130409
AU 2013203111	B2	20151008		
US 20140296100	A1	20141002	US 2014-14256418	20140418
JP 2014141530	A	20140807	JP 2014-97474	20140509
US 20170073760	A1	20170316	US 2015-14965923	20151211
JP 2016121176	A	20160707	JP 2016-39191	20160301

PRIORITY APPLN. INFO.: US 2007-60923384 P 20070413
AU 2008-239594 A3 20080411
EP 2008-742861 A3 20080411
JP 2010-503084 A3 20080411
WO 2008-US4804 W 20080411
US 2010-450826 A1 20100318
US 2014-14256418 A1 20140418
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Provided herein are methods for treating cancer that is resistant to treatment with an anti- ErbB therapeutic agent and which is associated with an activating MET gene mutation or a MET gene amplification. The methods involve administering to a subject a combination of an anti- ErbB therapeutic and an anti-MET therapeutic. Also provided are methods for reducing ErbB mediated signaling or PI3 kinase mediated signaling in a cancer cell.

IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

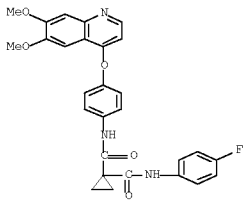
(methods for treating cancer resistant to ErbB therapeutics using combination of anti-Met receptor agent and anti-ErbB receptor agent in relation to activation mutation or gene amplification)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

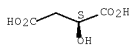
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



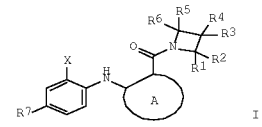
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L4 ANSWER 507 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2008:771167 CAPLUS Full-text
DOCUMENT NUMBER: 149:104583
TITLE: N-Acylazetidine derivatives as MEK inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer
INVENTOR(S): Lamb, Peter
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 534pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

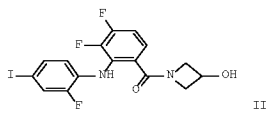
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008076415	A1	20080626	WO 2007-US25751	20071214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007334402	A1	20080626	AU 2007-334402	20071214
AU 2007334402	B2	20140213		
CA 2671982	A1	20080626	CA 2007-2671982	20071214
CA 2671982	C	20160126		
US 20080166359	A1	20080710	US 2007-2340	20071214
US 7999006	B2	20110816		
EP 2101759	A1	20090923	EP 2007-853418	20071214
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
CN 101605540	A	20091216	CN 2007-80051355	20071214
JP 2010513288	T	20100430	JP 2009-541420	20071214
JP 5311673	B2	20131009		
CN 105106199	A	20151202	CN 2015-10422958	20071214
AU 2013204026	A1	20130516	AU 2013-204026	20130411
AU 2013204026	B2	20170119		
JP 2013151569	A	20130808	JP 2013-102016	20130514

PRIORITY APPLN. INFO.:
US 2006-60875412 P 20061214
AU 2007-334402 A3 20071214
CN 2007-80051355 A3 20071214
JP 2009-541420 A3 20071214
WO 2007-US25751 W 20071214

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 149:104583; MARPAT 149:104583
GI



I



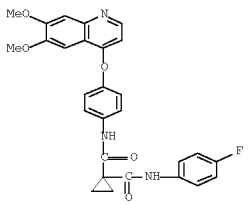
II

AB The invention provides methods of treating cancer by administering a compound of formula I, or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments. Compds. of formula I wherein ring A is (un)substituted (hetero)arylene; X is (halo)alkyl, halo and haloalkoxy; R1, R2, R3, R4, R5 and R6 are independently H, halo, NO2, NH2 and derivs., OH and derivs., NHSO2H and derivs., CN, SH and derivs., etc.; R7 is H, halo and alkyl; and their pharmaceutically acceptable salts and solvates thereof are claimed. Example compound II was prepared by amidation of 3,4-difluoro-2-[(2-fluoro-4- iodophenyl)amino]benzoic acid with azetidin-3-ol hydrochloride. All the invention compds. were evaluated for their MEK inhibitory activity (some data given).

IT 849217-68-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-acylazetidine derivs. as MEK inhibitors useful in the mono- and combination therapy of cancer)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 508 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2008:699999 CAPLUS Full-text
DOCUMENT NUMBER: 149:30417
TITLE: Antibodies and inhibitory nucleic acids for targeing HIF-1α and for diagnosing/treating tumor or metastasis
INVENTOR(S): Huang, L. Eric
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 157pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008070616	A2	20080612	WO 2007-US86264	20071203
WO 2008070616	A3	20090430		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20100074897	A1	20100325	US 2009-517132	20090710

PRIORITY APPLN. INFO.:
US 2006-60868188 P 20061201
WO 2007-US86264 W 20071203

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Disclosed are compns. and methods related to HIF-1α (hypoxia-inducible factor 1α). The compns. and methods comprise use of HIF-1α inhibitors for reducing tumor growth or metastatic tumor growth. The HIF-1α inhibitor is an antibody (including monoclonal, human and humanized antibody), small mol., siRNA, shRNA, or antisense polynucleotide.

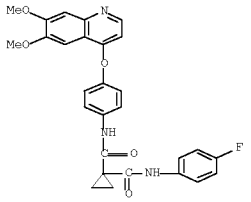
IT 1140909-48-3, XL 184
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibodies and inhibitory nucleic acids for targeing HIF-1α and for diagnosing/treating tumor or metastasis)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

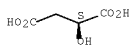
CRN 849217-68-1
CMF C28 H24 F N3 O5



CM 2

CRN 97-67-6
CMF C4 H6 O5

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 509 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN

ACCESSION NUMBER: 2007:671771 CAPLUS Full-text
DOCUMENT NUMBER: 147:93969
TITLE: Combination of anti-angiopoietin 2 human monoclonal antibody and of VEGF-A, KDR and/or FLT1 antagonist for treating cancer
INVENTOR(S): Brown, Jeffrey Lester; Emery, Stephen Charles; Blakey, David Charles
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007068895	A1	20070621	WO 2006-GB4611	20061212
WO 2007068895	A9	20080612		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2006324477	A1	20070621	AU 2006-324477	20061212
CA 2633211	A1	20070621	CA 2006-2633211	20061212
KR 2008073766	A	20080811	KR 2008-7015745	20061212
KR 1371773	B1	20140307		
EP 1962903	A1	20080903	EP 2006-820476	20061212
EP 1962903	B1	20130313		
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CN 101370519	A	20090218	CN 2006-80052740	20061212
CN 101370519	B	20130724		
JP 2009521412	T	20090604	JP 2008-545075	20061212
JP 5179373	B2	20130410		
NZ 569787	A	20110729	NZ 2006-569787	20061212
EP 2518083	A2	20121031	EP 2011-167374	20061212
EP 2518083	A3	20121205		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
ES 2411505	T3	20130705	ES 2006-820476	20061212
CN 103341168	A	20131009	CN 2013-10251494	20061212
CN 103341168	B	20161102		
BR 2006019853	A2	20160823	BR 2006-19853	20061212
EP 3168234	A1	20170517	EP 2016-199226	20061212
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AR 58359	A1	20080130	AR 2006-105550	20061215
NO 2008002448	A	20080710	NO 2008-2448	20080528
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to agents which possess anti-angiogenic activity and are accordingly useful in methods of treatment of disease states associated with angiogenesis in the animal or human body. More specifically the invention concerns a combination of a monoclonal antibody against human angiopoietin 2 (anti-Ang-2) and an antagonist of the biol. activity of VEGF-A, and/or KDR receptor, and/or FLT1, and uses of such antagonists. The nucleotide sequences and the encoded amino acid sequences of anti-Ang-2 monoclonal antibodies are disclosed.

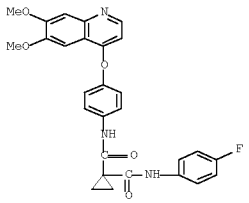
IT 1140909-48-3, XL 184
RL: PAC (Pharmacological activity); BIOL (Biological study)
(combination of anti-angiopoietin 2 human monoclonal antibody and of VEGF-A, KDR and/or FLT1 antagonist for treating cancer)

RN 1140909-48-3 CAPLUS

CN Butanedioic acid, 2-hydroxy-, (2S)-, compd. with N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(4-fluorophenyl)-1,1-cyclopropanedicarboxamide (1:1) (CA INDEX NAME)

CM 1

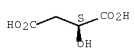
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CM 2

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Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 510 OF 510 CAPLUS COPYRIGHT 2017 ACS on STN
ACCESSION NUMBER: 2005:300201 CAPLUS Full-text
DOCUMENT NUMBER: 142:373856
TITLE: Preparation of quinolines and quinazolines as inhibitors of c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases
INVENTOR(S): Bannen, Lynne Canne; Chan, Diva Sze-ming; Chen, Jeff; Dalrymple, Lisa Esther; Forsyth, Timothy Patrick; Huynh, Tai Phat; Jammalamadaka, Vasu; Khoury, Richard George; Leahy, James William; Mac, Morrison B.; Mann, Grace; Mann, Larry W.; Nuss, John M.; Parks, Jason Jevious; Takeuchi, Craig Stacy; Wang, Yong; Xu, Wei
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 428 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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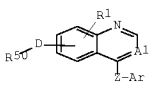
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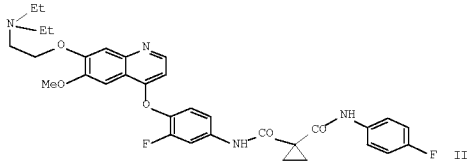
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 142:373856; MARPAT 142:373856

GI



Z-Ar I



II

AB The present invention provides compds. (shown as I; variables defined below; e.g. N-[4-[[7-[[2-(diethylamino)ethyl]oxy]-6-(methyloxy)quinolin-4-yl]oxy]-3-fluorophenyl]-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide (shown as II)) for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. More specifically, the invention provides quinazolines and quinolines which inhibit, regulate and/or modulate kinase receptors, particularly c-Met, KDR, c-Kit, flt-3 and flt-4, signal transduction pathways related to the changes in cellular activities as mentioned above, compns. which contain these compds., and methods of using them to treat kinase-dependent diseases and conditions. The present invention also provides methods for making compds. as mentioned above, and compns. which contain these compds. For I: R1 = H, halogen, OR3, NO2, NH2, NR3R4, and (un)substituted lower alkyl; A1 = :N-, :C(H)-, and :C(CN)-; Z = -S(O)0-2-, -O-, and -NR5-; Ar is aryl or heteroaryl; D = -O-, -S(O)0-2-, and -NR15-; R50 = R3 or bicyclic radical; addnl. details are given in the claims. Methods of preparation are claimed and .apprx.80 example preprns. of I and intermediates are included. For example, II was prepared (34 %) from 2-(diethylamino)ethanol and cyclopropane-1,1-dicarboxylic acid N-[3-fluoro-4-[(7-hydroxy-6-methoxyquinolin-4-yl)oxy]phenyl]amide N-(4-fluorophenyl)amide, which was prepared (89 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-[4-[(7-benzyloxy-6-methoxyquinolin-4-yl)oxy]-3-fluorophenyl]amide N-(4-fluorophenyl)amide, which was prepared (48 %) from trifluoromethanesulfonic acid 7-benzyloxy-6-methoxyquinolin-4-yl ester and cyclopropane-1,1-dicarboxylic acid N-(3-fluoro-4-hydroxyphenyl)amide N-(4-fluorophenyl)amide, which was prepared (85 %) by deprotection of cyclopropane-1,1-dicarboxylic acid N-(4-benzyloxy-3-fluorophenyl)amide N-(4-fluorophenyl)amide, which was prepared (98 %) from (4-benzyloxy-3-fluorophenyl)amine and 1-(4-fluorophenylcarbamoyl)cyclopropanecarboxylic acid; addnl. details are given in the examples.

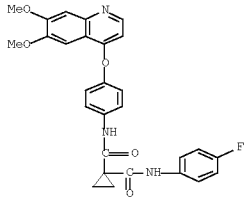
IT 849217-68-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinolines and quinazolines as inhibitors of c-Met and other tyrosine kinases and therapeutic uses against proliferative diseases)

RN 849217-68-1 CAPLUS

CN 1,1-Cyclopropanedicarboxamide, N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N-(4-fluorophenyl)- (CA INDEX NAME)



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