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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/818,463	10/27/2009	7608261	5050A	2028

26693 7590 10/07/2009
REGENERON PHARMACEUTICALS, INC
777 OLD SAW MILL RIVER ROAD
TARRYTOWN, NY 10591

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 47 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):

Eric Furfine, Concord, MA;
Daniel Dix, LaGrangeville, NY;
Kenneth S. Graham, Pleasant Valley, NY;
Kelly Frye, Pomona, NY;

IR103 (Rev. 10/09)

UNITED STATES PATENT AND TRADEMARK OFFICE

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NOTICE OF ALLOWANCE AND FEE(S) DUE

26693 7590 06/22/2009

REGENERON PHARMACEUTICALS, INC
777 OLD SAW MILL RIVER ROAD
TARRYTOWN, NY 10591

EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/22/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/818,463	06/14/2007	Eric Furfine	5050A	2028

TITLE OF INVENTION: VEGF ANTAGONIST FORMULATIONS SUITABLE FOR INTRAVITREAL ADMINISTRATION

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	09/22/2009

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 SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

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.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
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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)

26693 7590 06/22/2009

REGENERON PHARMACEUTICALS, INC
777 OLD SAW MILL RIVER ROAD
TARRYTOWN, NY 10591

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.
11/818,463	06/14/2007	Eric Furfine	5050A	2028

TITLE OF INVENTION: VEGF ANTAGONIST FORMULATIONS SUITABLE FOR INTRAVITREAL ADMINISTRATION

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	09/22/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
LOCKARD, JON MCCLELLAND	1647	514-002000

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 credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information 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.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/818,463	06/14/2007	Eric Furfine	5050A	2028

26693 7590 06/22/2009

REGENERON PHARMACEUTICALS, INC
777 OLD SAW MILL RIVER ROAD
TARRYTOWN, NY 10591

EXAMINER
LOCKARD, JON MCCLELLAND

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/22/2009

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 47 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 47 day(s).

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 Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

Notice of Allowability	Application No.	Applicant(s)	
	11/818,463	FURFINE ET AL.	
	Examiner	Art Unit	
	JON M. LOCKARD	1647	

-- 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 *the Amendment and Response filed 28 April 2009*.

2. ☒ The allowed claim(s) is/are *1-16 and 19 (renumbered as claims 1-17, respectively)*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   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.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ 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. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/J. M. L./ Examiner, Art Unit 1647	/Christine J Saoud/ Primary Examiner, Art Unit 1647

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11818463	FURFINE ET AL.
	Examiner	**Art Unit**
	JON M LOCKARD	1647

ORIGINAL		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
424	134.1	A	6	1	K	38 / 18 (2006.01.01)						
CROSS REFERENCE(S)		C	0	7	K	14 / 71 (2006.01.01)						

CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				
424	192.1				
514	2	12			
530	350				
536	23.4				

☒ 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	1		17												
2	2		18												
3	3	17	19												
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14	14														
15	15														
16	16														

/JON M LOCKARD/ Examiner.Art Unit 1647 (Assistant Examiner)	06/15/2009 (Date)	**Total Claims Allowed:** 17	
/Christine J Saoud/ Primary Examiner.Art Unit 1647 (Primary Examiner)	06/18/2009 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure NONE

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination
	11/818,463	FURFINE ET AL.

Document Code - DISQ	Internal Document – DO NOT MAIL

TERMINAL DISCLAIMER	☒ APPROVED	☐ DISAPPROVED
Date Filed : 4/28/09	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:
ANDRE ROBINSON

U.S. Patent and Trademark Office

Docket No.: 5050A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application of: FURFINE et al.	Confirmation No.: 2028
Application No.: 11/818,463	Art Unit: 1647
Filed: 14 June 2007	Examiner: LOCKARD, Jon M.
For: VEGF Antagonist Formulations Suitable for Intravitreal Administration	Customer No.: 26693

AMENDMENT IN RESPONSE TO NON-FINAL OFFICE ACTION

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

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Office Action dated 30 January 2009, please amend the above-identified U.S. patent application as follows:

Amendments to the Specification begin on page 3 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 4 of this paper.

Remarks begin on page 7 of this paper.

FEE CALCULATION

Any additional fee required has been calculated as follows:

	Claims Remaining After Amendment	Highest Number Previously Paid	Number Extra Claims Present	Rate	Additional Fee
Total	17	- 20* =	0	x 52.00	.00
Independent	3	- 3** =	0	x 220.00	.00
First presentation of Multiple Dependent Claim(s) (if applicable)				390.00	.00
				TOTAL	.00

*not less than 20 ** not less than 3

No additional fee is required.

In the event a fee is required or if any additional fee during the prosecution of this application is not paid, the Patent Office is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 18-0650.

CONTINGENT EXTENSION REQUEST

If this communication is filed after the shortened statutory time period had elapsed and no separate Petition is enclosed, the Commissioner for Patents and Trademarks is hereby petitioned, under 37 C.F.R. § 1.136(a), to extend the time for filing a response to the outstanding Office Action by the number of months which will avoid abandonment under 37 C.F.R. § 1.135. Please charge any fee due under 37 C.F.R. § 1.17 to Deposit Account No. 18-0650.

Amendments to the Specification

Please replace paragraph [0059] with the following corrected paragraph:

[0059] A liquid formulation containing 50 mg/ml VEGF Trap (SEQ ID NO:4), 10 mM phosphate, 50 mM NaCl, 3% polyethylene glycol 3350, 5% sucrose, and pH 6.25, was stored at 5 °C in 3 ~~nil~~ ml glass vials and samples tested at 3, 6, 9, 12, 18 and 24 months. Stability results are shown in Table 2. Turbidity, percent recovered protein and purity was determined as described above.

Please replace paragraph [0061] with the following corrected paragraph:

[0061] A liquid formulation containing 40 mg/ml VEGF trap (SEQ ID NO:4), 10 mM phosphate, 40 mM NaCl, 0.03% polysorbate 20, 5% sucrose, and pH 6.3, was stored at 5 °C in 1 ml prefilled luer glass syringe with 4023/50 ~~FluroTec~~ FLUROTEC™ coated (elastomer coated) plunger and samples tested at 0.5, 1, 2, 3, and 4 months. Stability results are shown in Table 4. Turbidity, percent recovered protein and purity was determined as described above.

Please replace paragraph [0063] with the following corrected paragraph:

[0063] A liquid formulation containing 40 mg/ml VEGF trap (SEQ ID NO:4), 10 mM phosphate, 135 mM NaCl, 0.03% polysorbate 20, and pH 6.3, was stored at 5 °C in 1 ml prefilled glass luer syringe with 4023/50 ~~FluorTec~~ FLUROTEC™ coated (elastomer coated) plunger and samples tested at 0.5, 1, 2, 3, 4, and 5 months. Stability results are shown in Table 6. Turbidity, percent recovered protein and purity was determined as described above.

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (currently amended) An ophthalmic formulation of a vascular endothelial growth factor (VEGF) antagonist, comprising

a) 1-100 mg/ml of a VEGF antagonist comprising the amino acid sequence of SEQ ID NO:4;

b) 0.01-5% of one or more organic co-solvent(s) which is one or more of polysorbate, polyethylene glycol (PEG), and propylene glycol;

c) 30-150 mM of a tonicity agent selected from sodium chloride or potassium chloride; and,

d) 5-40 mM of sodium phosphate buffer.

2. (currently amended) The ophthalmic formulation of claim 1, further comprising 1-7.5% of a stabilizing agent ~~is~~ selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, or mannitol, pH between about 5.8-7.0.

3. (original) The ophthalmic formulation of claim 2, comprising about 1-100 mg/ml of the VEGF antagonist, 10 mM sodium phosphate buffer, 40 mM NaCl, 0.03% polysorbate, and 5% sucrose, pH about 6.2-6.3.

4. (original) The ophthalmic formulation of claim 3, comprising about 10-80 mg/ml of the VEGF antagonist.

5. (original) The ophthalmic formulation of claim 4, comprising VEGF antagonist at a concentration selected from the group consisting of 10 mg/ml, 20 mg/ml, 40 mg/ml, and 80 mg/ml.

6. (original) The ophthalmic formulation of claim 1, comprising 10-80 mg/ml VEGF antagonist, 10 mM sodium phosphate, 0.03% polysorbate, and 135 mM sodium chloride, pH about 6.2-6.3.

7. (original) The ophthalmic formulation of claim 6, comprising VEGF antagonist at a concentration selected from the group consisting of 10 mg/ml, 20 mg/ml, 40 mg/ml, and 80 mg/ml.

8. (original) A lyophilizable formulation of a vascular endothelial growth factor (VEGF) antagonist, comprising

a) 5-50 mg/ml of the VEGF antagonist, comprising the amino acid sequence of SEQ ID NO:4;

b) 5-25 mM of sodium phosphate buffer, pH about 5.8-7.0;

c) 0.01-0.15% of an organic co-solvent, selected from the group consisting of polysorbate, polyethylene glycol (PEG), propylene glycol, and a combination thereof; and,

d) 1-10% of a stabilizing agent selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, and mannitol.

9. (original) The lyophilizable formulation of claim 8, comprising about 20 mg/ml of the VEGF antagonist, about 10 mM sodium phosphate buffer, about 0.03% polysorbate, about 0.1% PEG, and about 2.5% sucrose, pH about 6.2-6.3.

10. (original) The lyophilizable formulation of claim 8, comprising about 20 mg/ml of the VEGF antagonist, about 5 mM sodium phosphate buffer, about 0.015% polysorbate, about 2.5% sucrose, and further comprising sodium chloride at about 20 mM, pH about 6.2-6.3.

11. (original) The lyophilizable formulation of claim 8, comprising about 20 mg/ml of the VEGF antagonist, about 5 mM sodium phosphate buffer, about 0.015% polysorbate, and further comprising sodium chloride at about 67.5 mM, pH about 6.2-6.3.

12. (original) A lyophilizable formulation of a vascular endothelial growth factor (VEGF) antagonist, comprising

a) 5-50 mg/ml of the VEGF antagonist, comprising the amino acid sequence of SEQ ID NO:4;

b) 5-25 mM of a phosphate buffer, pH about 5.8-7.0;

c) 0.01-0.15% of an organic co-solvent, selected from the group consisting of polysorbate, polyethylene glycol (PEG), propylene glycol, and a combination thereof; and

d) 20-150 mM of a tonicity agent.

13. (original) The lyophilizable formulation of claim 12, wherein the tonicity agent is sodium chloride at a concentration selected from the group consisting of 20 mM and 67.5 mM.

14. (original) The lyophilizable formulation of claim 12, wherein the organic co-solvent is polysorbate at 0.015%.

15. (original) The lyophilizable formulation of claim 12, wherein the VEGF antagonist is at a concentration selected from the group consisting of 5 mg/ml, 10 mg/ml, 20 mg/ml, and 40 mg/ml.

16. (original) The lyophilizable formulation of claim 12, wherein the sodium phosphate buffer is at 5 mM.

17-18. (canceled)

19. (original) A pre-filled syringe suitable for intravitreal administration comprising the formulation of claim 1.

REMARKS

Claims 1-16 and 19 are pending.

Claims 1 and 2 are amended to correct minor errors as suggested by the Examiner.

The specification is amended at paragraph [0059] to correct a typographical error, and at paragraphs [0061] and [0063] to recite proper use of a trademark and add a generic description of the trademarked subject matter.

The amendments to the specification and the claims add no new matter, and the Examiner is respectfully requested to enter them.

Formal Matters

A. The Examiner objected to the specification for improper use of trademarks. The specification has been amended to recite proper use of trademarks, and to add a generic description of the trademarked subject matter. It is believed that the rejection may now be withdrawn.

B. The Examiner objected to claim 1 for reciting "1-100 mg/ml a VEGF" rather than "1-100 mg/ml of a VEGF" and objected to claim 2 for reciting "stabilizing agent is selected" rather than "stabilizing agent selected." Claims 1 and 2 have been amended as suggested by the Examiner. It is believed that the objections may now be withdrawn.

Double Patenting Rejections

The Examiner provisionally rejected claims 1, 2, 8, 12, 15, and 16 on the ground of nonstatutory obviousness-type double patenting over claims 15 and 16 of copending USSN 11/998,746; and claims 1-16 and 19 on the ground of nonstatutory obviousness-type double patenting over claims 15 and 16 of USSN 11/998,746 in view of Dix et al. WO 2006/104852. In response, Applicants herein submit a Terminal Disclaimer

disclaiming the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of USSN 11/998,746. Accordingly, it is believed that this rejection may now be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicant believes all the pending claims are now in condition for allowance, an early notification of which is earnestly requested.

Dated: 28 April 2009

Respectfully submitted,

By _____

Valeta Gregg, Ph.D., Reg. No. 35,127

Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591
Direct Tel.: (914) 593-1077

PTO/SB/25 (03-09)
Approved for use through 04/30/2009. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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TERMINAL DISCLAIMER TO OBVIATE A PROVISIONAL DOUBLE PATENTING REJECTION OVER A PENDING "REFERENCE" APPLICATION

Docket Number (Optional) 5050A

In re Application of: Eric FURFINE et al.

Application No.: 11/818,463

Filed: 14 June 2007

For: VEGF Antagonist Formulations Suitable for Intravitreal Administration

The owner*, Regeneron Pharmaceuticals, Inc., of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on pending **reference** Application Number 11/998,746, filed on 30 November 2007, as such term is defined in 35 U.S.C. 154 and 173, and as the term of any patent granted on said **reference** application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending **reference** application. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent granted on the **reference** application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term as defined in 35 U.S.C. 154 and 173 of any patent granted on said **reference** application, "as the term of any patent granted on said **reference** application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending **reference** application," in the event that: any such patent: granted on the pending **reference** application: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as shortened by any terminal disclaimer filed prior to its grant.

Check either box 1 or 2 below, if appropriate.

1. ☐ For submissions on behalf of a business/organization (e.g., corporation, partnership, university, government agency, etc.), the undersigned is empowered to act on behalf of the business/organization.

I hereby 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 issued thereon.

2. ☑ The undersigned is an attorney or agent of record. Reg. No. 35,127

Valeta Gregg — Signature

28 April 2009 — Date

Valeta Gregg — Typed or printed name

(914) 593-1077 — Telephone Number

☑ Terminal disclaimer fee under 37 CFR 1.20(d) is included.

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.

*Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner). Form PTO/SB/96 may be used for making this statement. See MPEP § 324.

This collection of information is required by 37 CFR 1.321. 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. 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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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/818,463	06/14/2007	Eric Furfine	5050A	2028

26693 7590 01/30/2009
REGENERON PHARMACEUTICALS, INC
777 OLD SAW MILL RIVER ROAD
TARRYTOWN, NY 10591

EXAMINER
LOCKARD, JON MCCLELLAND

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
01/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	11/818,463	FURFINE ET AL.	
	Examiner	Art Unit	
	JON M. LOCKARD	1647	

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

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

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)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/5/08, 5/29/08*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-16 and 19, in the reply filed on 17 October 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of Application, Amendments, and/or Claims

2. The Amendment filed on 17 October 2008 has been entered in full. Claims 17 and 18 have been cancelled. Therefore, claims 1-16 and 19 are pending and the subject of this Office Action.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on 05 May 2008 and 29 May 2008 have been considered by the Examiner.

Specification

4. The disclosure is objected to because of the following informalities:

5. The use of the trademarks has been noted throughout the Specification (See for example FLUROTEC™ (pg 11 and 12)). Trademarks should be capitalized wherever they appear and should be accompanied by the generic terminology. Applicant is encouraged to review and make appropriate corrections to the specification regarding the misuse of trademarks. Although the

use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. Appropriate correction is suggested.

Claim Objections

6. Claim 1 is objected to because of the following informalities: It is suggested that the phrase "1-100 mg/ml a VEGF" in part (a) of the claim be amended to recite "1-100 mg/ml <u>of</u> a VEGF". Appropriate correction is suggested.

7. Claim 2 is objected to because of the following informalities: It is suggested that the phrase "stabilizing agent is selected" be amended to recite "stabilizing agent selected". Appropriate correction is suggested.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

9. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may

be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

10. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1, 2, 8, 12, 15, and 16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15 and 16 of copending Application No. 11/998,746. Although the conflicting claims are not identical as they differ in scope, they are not patentably distinct from each other because the claims of the '746 Application are drawn to an ophthalmic composition comprising a VEGF antagonist in a pharmaceutically acceptable carrier, wherein the VEGF antagonist is VEGFR1R2-FcΔC1(a) polypeptide. It is noted that VEGFR1R2-FcΔC1(a) polypeptide recited in the claims of the '746 Application, which the Specification identifies as having the amino acid sequence set forth in SEQ ID NO:2 (See pg 1[0006]), shares 100% sequence identity with SEQ ID NO:4 of the instant Application. While the claims in '746 Application do not recite (a) a particular concentration of the VEGFR1R2-FcΔC1(a) polypeptide, (b) phosphate buffer, (c) a tonicity agent selected from sodium chloride or potassium chloride, (d) sucrose, (e) an organic co-solvent(s) such as polysorbate, PEG, or propylene glycol, or (f) having a particular pH, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to prepare the ophthalmic formulations recited in the instant claims. The motivation to do so is found in the specification of the '746 Application, which discloses formulations of the VEGFR1R2-FcΔC1(a)

polypeptide comprising (a) VEGFR1R2-FcΔC1(a) polypeptide at a concentration of 39.4, 50, 100, 103.6, or 200 mg/ml, (b) 5 mM phosphate buffer, (c) 50 or 100 mM sodium chloride, (d) 5% sucrose, (e) 0.0005 or 0.1% polysorbate, and (f) having a pH of 6 (See Example 1, pg 10-11; Example 4, pg 13; and Example 7, pg 14). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. It is noted however that a Notice of Allowance has been mailed (12 January 2009) in the '746 Application.

12. Claims 1-16 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15 and 16 of copending Application No. 11/998,746 in view of Dix et al. (WO 2006/104852; cited by Applicant).

13. The claims of the '746 Application are drawn to an ophthalmic composition comprising a VEGF antagonist in a pharmaceutically acceptable carrier, wherein the VEGF antagonist is VEGFR1R2-FcΔC1(a) polypeptide. It is noted that VEGFR1R2-FcΔC1(a) polypeptide recited in the claims of the '746 Application, which the Specification identifies as having the amino acid sequence set forth in SEQ ID NO:2 (See pg 1[0006]), shares 100% sequence identity with SEQ ID NO:4 of the instant Application. The claims in '746 Application do not recite do not recite (a) a particular concentration of the VEGFR1R2-FcΔC1(a) polypeptide, (b) phosphate buffer, (c) a tonicity agent selected from sodium chloride or potassium chloride, (d) a stabilizing agent selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, or mannitol, (e) an organic co-solvent(s) such as polysorbate, PEG, or propylene glycol, or (f) having a particular pH.

14. Dix et al. (WO 2006/104852; cited by Applicant) teach stable liquid and pre-lyophilized

(i.e., lyophilizable) pharmaceutical formulations comprising a VEGFR1R2 fusion protein, including the VEGFR1R2-FcΔC1(a) polypeptide. Dix et al. also teach said compositions comprising (a) VEGFR1R2-FcΔC1(a) polypeptide at varying concentrations, including 25, 10-50, 5-75, 12.5-75, and 50-100 mg/ml (See pg 1[0006] and pg 2[0007], [0009], and [0010]), (b) 5 mM and 1-10 mM phosphate buffer (See pg 1[0006]), (c) 50 mM, 100 mM, or 25-150 mM sodium chloride (See pg 1[0006] and pg 2[0007]), (d) 0.5-6%, 2.5%, 5-20%, and 5-30% sucrose (See pg 2[0006], [0007], [0009], and [0010], (e) 0.05-0.15% and 0.1-0.5% polysorbate, or 1-5% PEG, and (f) having a pH of 6-6.5 (See pg 2[0006]). Lastly, Dix et al. also disclose a pre-filled syringe comprising said pharmaceutical formulation (See pg 11[0047]).

15. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to have used the teachings of Dix et al. to obtain ophthalmic formulations suggested in the '746 Application. The person of ordinary skill in the art would have been motivated to do so since the '746 Application discloses that the claimed VEGFR1R2 fusion protein formulations are useful for treating eye disorders, and the formulations comprising the VEGFR1R2 fusion protein taught by the Dix et al. reference have increased stability. The expectation of success is high since the claimed VEGFR1R2 fusion protein in the '746 Application is identical to the VEGFR1R2 fusion proteins disclosed in the Dix et al. reference. Moreover, the exact values for the concentrations of the various components of the composition are part of routine optimization in the art. Furthermore, as for the specific amounts/concentrations used, it is noted that it is customary and routine to optimize dosages and ratios of the agents according to the type of dysfunction, and the severity and course of the disease. This is a <u>provisional</u> obviousness-type double patenting rejection because the

conflicting claims have not in fact been patented. It is noted however that a Notice of Allowance has been mailed (12 January 2009) in the '746 Application.

Summary

16. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao, Ph.D.**, can be reached on **(571) 272-0939**. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jon M. Lockard, Ph.D.
January 27, 2009

/Jon M Lockard/
Examiner, Art Unit 1647

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	11/818,463
Applicant	:	Furfine et al.
Filed	;	14 June 2007
TC/A.U.	:	1647
Examiner	:	Lockard, Jon McCleland
Docket No.	:	5050A
Customer No.	:	26693
Confirmation No.	:	2028

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

RESPONSE TO RESTRICTION DATED 30 SEPTEMBER 2008

Sir:

In response to the Restriction action dated 30 September 2008, please amend the above identified application as follows:

Amendments to the claims beginning at page 2; and

Remarks beginning at page 5.

Amendments to the Claims:

Please cancel claims 17-18 without prejudice or disclaimer.

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (original) An ophthalmic formulation of a vascular endothelial growth factor (VEGF) antagonist, comprising

a) 1-100 mg/ml a VEGF antagonist comprising the amino acid sequence of SEQ ID NO:4;

b) 0.01-5% of one or more organic co-solvent(s) which is one or more of polysorbate, polyethylene glycol (PEG), and propylene glycol;

c) 30-150 mM of a tonicity agent selected from sodium chloride or potassium chloride; and,

d) 5-40 mM of sodium phosphate buffer.

2. (original) The ophthalmic formulation of claim 1, further comprising 1-7.5% of a stabilizing agent is selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, or mannitol, pH between about 5.8-7.0.

3. (original) The ophthalmic formulation of claim 2, comprising about 1-100 mg/ml of the VEGF antagonist, 10 mM sodium phosphate buffer, 40 mM NaCl, 0.03% polysorbate, and 5% sucrose, pH about 6.2-6.3.

4. (original) The ophthalmic formulation of claim 3, comprising about 10-80 mg/ml of the VEGF antagonist.

5. (original) The ophthalmic formulation of claim 4, comprising VEGF antagonist at a concentration selected from the group consisting of 10 mg/ml, 20 mg/ml, 40 mg/ml, and 80 mg/ml.

6. (original) The ophthalmic formulation of claim 1, comprising 10-80 mg/ml VEGF antagonist, 10 mM sodium phosphate, 0.03% polysorbate, and 135 mM sodium chloride, pH about 6.2-6.3.

7. (original) The ophthalmic formulation of claim 6, comprising VEGF antagonist at a concentration selected from the group consisting of 10 mg/ml, 20 mg/ml, 40 mg/ml, and 80 mg/ml.

8. (original) A lyophilizable formulation of a vascular endothelial growth factor (VEGF) antagonist, comprising

a) 5-50 mg/ml of the VEGF antagonist, comprising the amino acid sequence of SEQ ID NO:4;

b) 5-25 mM of sodium phosphate buffer, pH about 5.8-7.0;

c) 0.01-0.15% of an organic co-solvent, selected from the group consisting of polysorbate, polyethylene glycol (PEG), propylene glycol, and a combination thereof; and,

d) 1-10% of a stabilizing agent selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, and mannitol.

9. (original) The lyophilizable formulation of claim 8, comprising about 20 mg/ml of the VEGF antagonist, about 10 mM sodium phosphate buffer, about 0.03% polysorbate, about 0.1% PEG, and about 2.5% sucrose, pH about 6.2-6.3.

10. (original) The lyophilizable formulation of claim 8, comprising about 20 mg/ml of the VEGF antagonist, about 5 mM sodium phosphate buffer, about 0.015% polysorbate, about 2.5% sucrose, and further comprising sodium chloride at about 20 mM, pH about 6.2-6.3.

11. (original) The lyophilizable formulation of claim 8, comprising about 20 mg/ml of the VEGF antagonist, about 5 mM sodium phosphate buffer, about 0.015% polysorbate, and further comprising sodium chloride at about 67.5 mM, pH about 6.2-6.3.

12. (original) A lyophilizable formulation of a vascular endothelial growth factor (VEGF) antagonist, comprising

a) 5-50 mg/ml of the VEGF antagonist, comprising the amino acid sequence of SEQ ID NO:4;

b) 5-25 mM of a phosphate buffer, pH about 5.8-7.0;

c) 0.01-0.15% of an organic co-solvent, selected from the group consisting of polysorbate, polyethylene glycol (PEG), propylene glycol, and a combination thereof; and

d) 20-150 mM of a tonicity agent.

13. (original) The lyophilizable formulation of claim 12, wherein the tonicity agent is sodium chloride at a concentration selected from the group consisting of 20 mM and 67.5 mM.

14. (original) The lyophilizable formulation of claim 12, wherein the organic co-solvent is polysorbate at 0.015%.

15. (original) The lyophilizable formulation of claim 12, wherein the VEGF antagonist is at a concentration selected from the group consisting of 5 mg/ml, 10 mg/ml, 20 mg/ml, and 40 mg/ml.

16. (original) The lyophilizable formulation of claim 12, wherein the sodium phosphate buffer is at 5 mM.

17-18. (canceled)

19. (original) A pre-filled syringe suitable for intravitreal administration comprising the formulation of claim 1.

Remarks

The Restriction action dated 30 September 2008 required the applicants to elect between Group I (claims 1-16 and 19) and Group II (claims 17-18). Applicants herein elect Group I. Accordingly, claims 17-18 are canceled as non-elected subject matter, without prejudice to renewal in a divisional application.

Conclusion

It is believed that this document is fully responsive to the Election/Restriction Requirement dated 30 September 2008. In light of the above amendments and remarks, it is believed that the claims are now in condition for allowance, and such action is respectfully urged.

Fees

Applicants contend that no fee is necessary in connection with the filing of this response. However, if any fee is deemed to be necessary, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 18-0650.

Respectfully submitted,

Valeta Gregg, Ph.D., Reg. No. 35,127
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, New York 10591
Tel.: (914) 593-1077

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/818,463	06/14/2007	Eric Furfine	5050A	2028

26693 7590 09/30/2008
REGENERON PHARMACEUTICALS, INC
777 OLD SAW MILL RIVER ROAD
TARRYTOWN, NY 10591

EXAMINER
LOCKARD, JON MCCLELLAND

ART UNIT	PAPER NUMBER
1647	

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09/30/2008	PAPER

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The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
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	Examiner	Art Unit	
	JON M. LOCKARD	1647	

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

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
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1)☒ Responsive to communication(s) filed on *14 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-19* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

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)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-16 and 19, drawn to formulations comprising a vascular endothelial growth factor (VEGF) antagonist, and a syringe comprising the same, classified in class 424, subclass 192.1, for example.

   II. Claims 17-18, drawn to a method for producing a lyophilized formulation of a VEGF antagonist, classified in class 424, subclass 489, for example.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the process as claimed can be used for making a materially different product, such as a structurally different fusion protein.

3. Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above <u>and</u> there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

   (a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

4. **Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined** even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

5. The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

6. If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

7. Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the

inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

9. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

10. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim

will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao, Ph.D.**, can be reached on **(571) 272-0939**. The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jon M. Lockard, Ph.D.
September 26, 2008

/Jon M Lockard/
Examiner, Art Unit 1647