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Application Number	
Filing Date	Herewith
First Named Inventor	AHMAD
Title	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
Art Unit	
Examiner Name	
Attorney Docket Number	20110.0024USU1

SIGNATURE of Applicant or Patent Practitioner

Signature	/amol h. kavathekar/	Date (Optional)	April 9, 2021
Name	Amol H. Kavathekar	Registration Number	63,975
Title (if Applicant is a juristic entity)			
Applicant Name (if Applicant is a juristic entity)			

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This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. 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 3 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.**

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I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date

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☑ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above: 52835

OR

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I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

Jina Pharmaceuticals, Inc.

☐ Inventor or Joint Inventor (title not required below)

☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☑ Assignee of Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature		Date (Optional)	
Name	Saifuddin Sheikh		
Title	Vice President		

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Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Filer:	Amol H. Kavathekar/Peggy Kerkhove
Attorney Docket Number:	20110.0024USU1

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
UTILITY APPLICATION FILING	1011	1	320	320
UTILITY SEARCH FEE	1111	1	700	700
UTILITY EXAMINATION FEE	1311	1	800	800
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**1820**

Electronic Acknowledgement Receipt	
EFS ID:	42413285
Application Number:	17226671
International Application Number:	
Confirmation Number:	1772
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Customer Number:	52835
Filer:	Amol H. Kavathekar/Peggy Kerkhove
Filer Authorized By:	Amol H. Kavathekar
Attorney Docket Number:	20110.0024USU1
Receipt Date:	09-APR-2021
Filing Date:	
Time Stamp:	15:29:44
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$1820
RAM confirmation Number	E202149F30354897
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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		Application_0024.pdf	117947 14d1c3d020deae20cd3e3cf7d8e154b373f153ce	yes	8
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Specification		1	6	
	Claims		7	7	
	Abstract		8	8	
Warnings:					
Information:					
2	Application Data Sheet	ADS_0024.pdf	1256205 8b1f05ac0a6ceec1a5d45fa9f832d71a2639cc26	no	9
Warnings:					
Information:					
3	Oath or Declaration filed	Declarations_0024.pdf	961528 937596af9a3e49dece0802c7a9692061140e0e78	no	10
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4	Power of Attorney	POA_0024.pdf	800172 ecf051803da9c7e6fcfc4d3ff857c3425fe3e04790	no	2
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5	Fee Worksheet (SB06)	fee-info.pdf	35005 9eecc6618ec9e94c7392a641d448fc8bc7ea1af7	no	2

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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

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ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

FIELD OF THE INVENTION

The present disclosure relates to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, wherein the said method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Further, the patient is not required to be administered rescue medication during the administration of the endoxifen citrate.

BACKGROUND OF THE INVENTION

Bipolar disorder is currently a major health problem. Bipolar disorder is a chronic, debilitating illness that affects up to 3 % of the US population. It causes significant morbidity and imposes a burden on the society. The causes of bipolar disorder are still unknown, and no agent has been specifically developed on the basis of an understanding of the pathophysiology of the illness or mechanism of action for effective treatments.

Several drugs have been approved for treatment of bipolar disorder, such as lithium, valproate or divalproex sodium, carbamazepine, and atypical antipsychotics for the treatment of acute bipolar mania. While these drugs have provided relief for many individuals with bipolar disorder, significant issues with tolerability, efficacy, and attempt suicide or have suicidal behaviour still remain. Further, there is also a need of rescue medications. Divalproex has a good tolerability but a high discontinuation rate. There is also a continuous need to observe the therapeutic dose monitoring in patients during the treatment. The clinicians, for example, may find themselves in situations in which better tolerated agents are less effective, and vice versa. Also, the adherence to the treatment is affected by adverse effects such as sedation, weight gain, thrombocytopenia, and thyroid disorders.

Available treatments help a substantial proportion of patients, but are not beneficial for an estimated 40-50 % of the population.

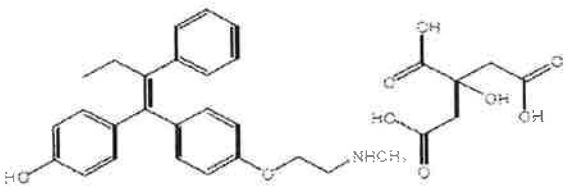
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SUMMARY OF THE INVENTION

Protein kinase C (PKC) appears to have a role in bipolar disorder. PKC is involved in controlling the function of proteins through the phosphorylation of hydroxyl groups of serine and threonine amino acid residues on these proteins, which are known to play a vital role in cell signalling pathways. It regulates multiple neuronal processes implicated in mood regulation. In current clinical practice, mood stabilizers and antidepressants have been shown to modulate the PKC pathway. Disrupted PKC activity has been found both in post-mortem brains and platelet from patients with mood disorders. Accumulating evidence suggests an imbalance of the PKC signalling system in mood disorders. Thus, PKC is considered as a novel molecular target for the development of innovative medicine for bipolar disorder.

Targeting the PKC signalling pathway for bipolar disorder can improve the patient compliance, when therapeutic dose monitoring is not required in patient, and such treatment can provide significant improvement in mania and depression.

Endoxifen is a non-steroidal selective estrogen receptor modulator (SERM) of the triphenylethylene group. It is an active metabolite of tamoxifen and has been found to be effective in patients that have failed previous hormonal therapies (tamoxifen, aromatase inhibitors, and fulvestrant). The prodrug tamoxifen is metabolized by the CYP2D6 enzyme to produce afimoxifene (4-hydroxytamoxifen) and endoxifen. The chemical name of endoxifen citrate is (Z) – 1 - (4-Hydroxyphenyl) - 1- {4 - [2 -(monomethylamino) ethoxy] phenyl} – 2 – pheny l -1-butene citrate. The empirical formula of endoxifen citrate is $C_{25}H_{27}NO_2$–$C_6H_8O_7$, and has following chemical structure as given below (formula I):



(I)

The exact mechanism by which endoxifen exerts its therapeutic effects have not been established in bipolar disorder. However, the efficacy of endoxifen could be mediated through

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PKC. The PKC represents a family of enzymes highly enriched in brain, where it plays a major role in regulating both pre- and post-synaptic aspects of neurotransmission. Excessive activation of PKC results in symptoms related to bipolar disorder. The PKC signalling pathway is clearly a target for the actions of two structurally dissimilar antimanic agents – lithium and valproate. Tamoxifen, a widely used breast cancer drug is also known to inhibit PKC and demonstrate antimanic properties in human. Endoxifen exhibited four-fold higher potency compared to tamoxifen in inhibiting the PKC activity and is not dependent on the isozyme cytochrome P450 2D6 (CYP2D6) for action on the target tissues. Endxifen is a PKC inhibitor and is effective in the treatment of bipolar disorder. Further, endoxifen has a broad therapeutic index as compared to divalproex sodium.

An object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient, wherein the patient has manic episodes with or without mixed features.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient, wherein the patient has depression or associated with depressive episodes.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I

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disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days, wherein the patient does not require rescue medication.

The objects described herein are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Further, the said method as per the present disclosure, wherein the patient does not require rescue medication.

DETAILED DESCRIPTION OF THE INVENTION

All terms as used herein in this application, unless otherwise stated, shall be understood in their ordinary meaning as known in the art. Other more specific definitions for certain terms as used in the present application are as set forth below and are intended to apply uniformly throughout the specification and claims unless an otherwise expressly set out definition provides a broader definition.

For the purposes of the present application, any ranges given include both the lower and the upper end points of the range. Ranges given should be considered approximate, unless specifically stated.

The term "EOT" refers to end of treatment.

The term "therapeutically effective concentration" refers to a concentration of endoxifen in plasma which is sufficient to decrease or prevent or cure the symptoms associated with a medical condition or infirmity or to normalize body functions in disease or disorders that result in impairment of specific bodily functions.

The term "rescue medication" refers to an additional medication necessary to treat breakthrough or recurring symptoms. For present disclosure, the rescue medications are selected from the group of lithium, valproate, lamotrigine, benzodiazepines, anticholinergics and like thereof.

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The term "enteric coating" refers to any pharmaceutically acceptable coating preventing the release of the active agent in the stomach and sufficiently disintegrating in the intestine tract (by contact with approximately neutral or alkaline intestine juices) to allow the resorption of the active agent through the walls of the intestinal tract. The enteric coating remains intact in the acidic environment of the stomach and then solubilize in the more alkaline environment of the small intestine. Generally speaking, enteric coating helps in preventing gastric mucosal irritation and can be used for acid labile drugs which gets denatured in acidic medium.

In one embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient, wherein the patient has manic episodes with or without mixed features.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient, wherein the patient has depression or associated with depressive episodes.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days.

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In another embodiment of the present application is to provide a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days, wherein the patient does not require rescue medication.

The embodiments described herein are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, wherein the method comprises an administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Further, the said method as per the present disclosure, wherein the patient does not require rescue medication.

The present application has been described by way of example only, and it is to be recognized that modifications thereto falling within the scope, and spirit of appended claims, and which would be obvious to a person skilled in the art based upon the disclosure herein, are also considered to be within the scope of this disclosure.

Clinical study data:

Clinical study of an enteric coated tablet comprising endoxifen citrate formulation was carried out by administering to the patient doses of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days according to the present application.

Design of the study:

The clinical study was a multicenter, randomized, double-blind, double-dummy, active controlled, parallel study to assess the efficacy and safety of endoxifen enteric coated tablet 8 mg and divalproex sodium extended release tablet 1000 mg in patients of bipolar I disorders.

Total 228 patients were enrolled in the study. All 228 patients were qualified for safety trial.

At the EOT, none of the patient required rescue medications, no rescue medications were administered to any of the patients, and none of the patient discontinue from the study.

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CLAIMS

1. A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

   administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days; wherein the patient is not administered rescue medication during the said treatment.

2. The method of claim 1, wherein the patient has manic episodes with mixed features.

3. The method of claim 1, wherein the patient has manic episodes without mixed features.

4. The method of claim 1, wherein the patient has depression.

5. The method of claim 1, wherein the patient associated with depressive episodes.

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ABSTRACT

A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder is provided. The said method includes administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Further, the patient is not required to be administered rescue medication during the administration of the endoxifen citrate.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

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.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Ateeq		AHMAD	

Residence Information (Select One) ● US Residency Non US Residency Active US Military Service

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Residence Information (Select One) ◉ US Residency Non US Residency Active US Military Service

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Residence Information (Select One) ◉ US Residency Non US Residency Active US Military Service

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

City	Wadsworth	State/Province	IL	Country of Residence	US

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Legal Name

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	Shoukath M		ALI	

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Country	US

Inventor 5 — Remove

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	Saifuddin		SHEIKH	

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City	Libertyville	State/Province	IL	Country of Residence	US

Mailing Address of Inventor:

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Address 2	
City	Libertyville
State/Province	IL
Postal Code	60048
Country	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. — Add

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For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Customer Number	52835		
Email Address		Add Email	Remove Email

Application Information:

Title of the Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		
Attorney Docket Number	20110.0024USU1	**Small Entity Status Claimed**	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	0	**Suggested Figure for Publication (if any)**	

Filing By Reference:

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For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

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). Either enter 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	52835		

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim 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.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status: [ ] Remove

Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Claims benefit of provisional	63/008162	2020-04-10

Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button. Add

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. 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. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove

Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1 — Remove

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

Clear

● Assignee	Legal Representative under 35 U.S.C. 117	Joint Inventor
Person to whom the inventor is obligated to assign.	Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name: Jina Pharmaceuticals, Inc.

Mailing Address Information For Applicant:

Address 1	28100 N Ashley Circle, Suite 103		
Address 2			
City	Libertyville	**State/Province**	IL
Country	US	Postal Code	60048
Phone Number		Fax Number	
Email Address			

Additional Applicant Data may be generated within this form by selecting the Add button. Add

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Assignee 1

Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

Remove

If the Assignee or Non-Applicant Assignee is an Organization check here. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1			
Address 2			
City		**State/Province**	
Country i		Postal Code	
Phone Number		Fax Number	
Email Address			

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. Add

Signature:

Remove

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/amol h. kavathekar/			Date (YYYY-MM-DD)	2021-04-09
First Name	Amol H.	Last Name	Kavathekar	Registration Number	63,975

Additional Signature may be generated within this form by selecting the Add button. Add

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

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.**

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 CooperationTreaty.

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.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

As the below named inventor, I hereby declare that:

This declaration is directed to:

- [✓] The attached application, or
- [ ] United States application or PCT international application number _____ filed on _____

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Shoukath M ALI Date (Optional): March 19, 2014

Signature: _____

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. 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 1 minute 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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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.
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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

As the below named inventor, I hereby declare that:

This declaration is directed to:

- [x] The attached application, or
- [ ] United States application or PCT international application number _____

filed on _____

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

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LEGAL NAME OF INVENTOR

Inventor: Abeeq AHMAD Date (Optional): _____

Signature: Abeeq Ahmad

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/A/A01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. 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 1 minute 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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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).
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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.
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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

As the below named inventor, I hereby declare that:

This declaration is directed to: ☑ The attached application, or ☐ United States application or PCT international application number _____ filed on _____

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available

LEGAL NAME OF INVENTOR
inventor: Imran AHMAD Date (Optional): _____
Signature: _____

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/AIA/01 form for each additional inventor

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. 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 1 minute 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

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.

PTO/AIA/01 (06-12)
Approved for use through 01/31/2014. 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.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

As the below named inventor, I hereby declare that:

This declaration is directed to:

- [✓] The attached application, or
- [ ] United States application or PCT international application number _____ filed on _____

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

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LEGAL NAME OF INVENTOR

Inventor: Moghisuddin AHMAD Date (Optional): _____

Signature: Moghisuddin Ahmad

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/A/07 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. 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 1 minute 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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PTO/AIA/01 (06-12)
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- [x] The attached application, or
- [ ] United States application or PCT international application number _____

filed on _____

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LEGAL NAME OF INVENTOR

Inventor: Saifuddin SHEIKH Date (Optional): _____

Signature: _____

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/A(A)01 form for each additional inventor.

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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	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
17/226,671	04/09/2021	1629	1820	20110.0024USU1	5	1

CONFIRMATION NO. 1772

FILING RECEIPT

52835
HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

Date Mailed: 04/19/2021

Receipt is acknowledged of this non-provisional utility 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 FIRST INVENTOR, 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 corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction 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 provided that the request is grantable.

Inventor(s)

Ateeq AHMAD, Wadsworth, IL;
Imran AHMAD, Libertyville, IL;
Moghisuddin AHMAD, Wadsworth, IL;
Shoukath M ALI, Vernon Hills, IL;
Saifuddin SHEIKH, Libertyville, IL;

Applicant(s)

Jina Pharmaceuticals, Inc., Libertyville, IL;

Power of Attorney: The patent practitioners associated with Customer Number 52835

Domestic Priority data as claimed by applicant

This appln claims benefit of 63/008,162 04/10/2020

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: Yes

Permission to Access Search Results: Yes

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00035

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 04/15/2021

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 17/226,671**

Projected Publication Date: 10/14/2021

Non-Publication Request: No

Early Publication Request: No

Title

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Preliminary Class

514

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

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).

SelectUSA

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

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technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00038

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 17/226,671

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	320
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	700
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	800
TOTAL CLAIMS (37 CFR 1.16(i))	5 minus 20 =	*			OR	x 100 =	0.00
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*				x 480 =	0.00
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).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	1820

APPLICATION AS AMENDED - PART II

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

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE(S)	ADDITIONAL FEE($)
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	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

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Doc description: Information Disclosure Statement (IDS) Filed

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Application Number	17226671
Filing Date	2021-04-09
First Named Inventor	AHMAD
Art Unit	1615
Examiner Name	
Attorney Docket Number	20110.0024USU1

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	1	9,333,190		2016-05-10	Ahmad, et al.	
	2	10,376,479		2019-08-13	Ahmad, et al.	

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	1	Ahmad, et al., "Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of Endoxifen", Clin Transl Sci (2016) 9, 252–259	
	2	Ali, et al., "Endoxifen is a new potent inhibitor of PKC: A potential therapeutic agent for bipolar disorder", Bioorganic & Medicinal Chemistry Letters 20 (2010) 2665–2667	

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	Art Unit	1615
	Examiner Name	
	Attorney Docket Number	20110.0024USU1

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).

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Name/Print	Masako Yoshida	Registration Number	70,057

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(74) Agent: **Dr Alpesh Pathak**; Global IP Head, Astron Division, Intas Pharmaceuticals Ltd., Premier House - 1, S G Highway, Ahmedabad 380054, Gujarat (IN).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, 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.

[Continued on next page]

(54) Title: ENDOXIFEN CITRATE POLYMORPH AND PROCESS FOR PREPARING THE SAME

(57) Abstract: The present invention provides a novel crystal line form of Endoxifen citrate and process for preparation thereof.

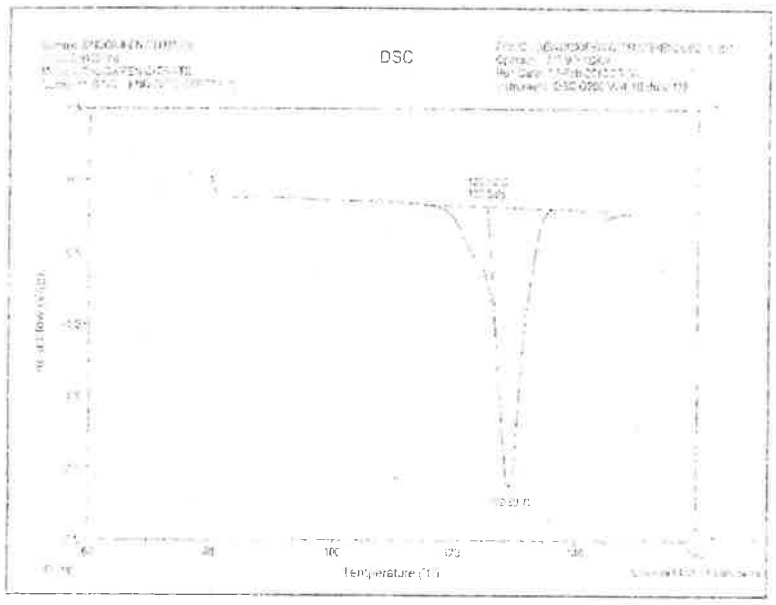


FIG. 2

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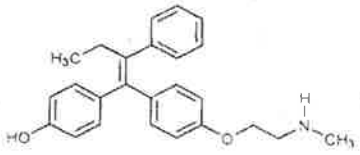
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FIELD OF THE INVENTION

The present invention relates to a novel crystalline polymorph of Endoxifen citrate and process for the preparation thereof.

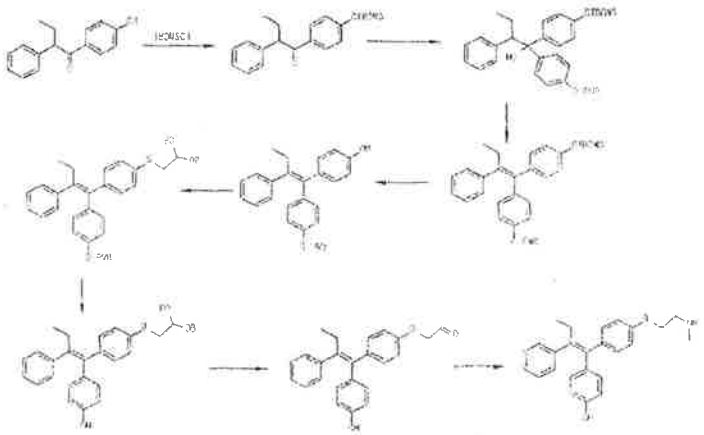
BACKGROUND OF THE INVENTION

Endoxifen, chemically named N-desmethyl-4-hydroxytamoxifen is an active metabolite of tamoxifen, a drug used in the treatment of breast cancer.



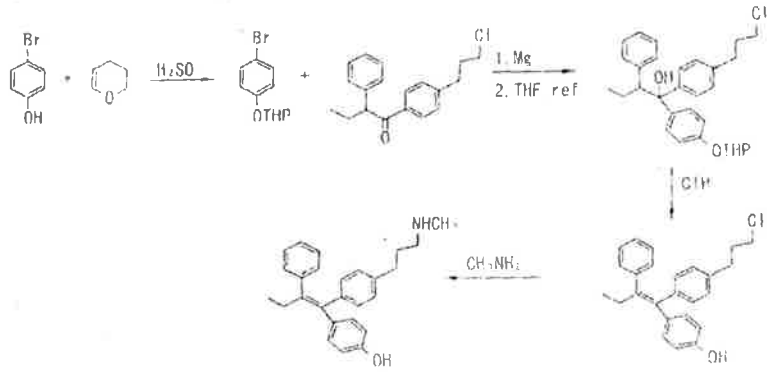
Methods of synthesizing Endoxifen which is the active metabolite of tamoxifen are disclosed in literature. For example, US 2009/0291124A1 discloses a method of preparing Endoxifen starting from 4-hydroxybromobenzene.

WO 2009/120999A2 discloses the following method of preparing Endoxifen:



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WO 2008/070463 discloses the following method of preparing Endoxifen.



Bioorganic & Medical Chemistry Letters (2010) disclosed a method of preparing Endoxifen including separating Z-form Endoxifen by RP-HPLC is disclosed.

WO 2012/050263A1 disclosed a process for the preparation of Endoxifen citrate by treating Endoxifen with anhydrous citric acid in the presence of water and isolating the solid obtained. This patent application neither disclosed the polymorph of Endoxifen citrate nor provides any characterization data of the compound obtained.

New crystalline polymorph of a drug substance may display different melting point, hygroscopicity, stability, solubility and/or dissolution rate, crystallinity, crystal habits, bioavailability and formulation handling characteristics, which are among the numerous properties that need to be considered in preparing medicament that can be effectively administered. Therefore, the regulatory agencies require a definitive control of polymorphic form of the active component in solid pharmaceutical dosage forms.

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The present inventors have also made their efforts to make an amorphous form of Endoxifen citrate. But during the preparation of an amorphous form of Endoxifen citrate certain practical difficulties were encountered, for instance the product is stucked to walls of test tube or during spray drying process product is stucked and causing problems in isolation. So, the inventors of the present invention explored an alternate form which is free from practical difficulties and industrially feasible.

Accordingly, there is an ongoing need to search new polymorphic forms of Endoxifen citrate that have better thermal stability and material flow character, lower water contents, and offer advantages for preparing reproducible pharmaceutical formulations. The new polymorphic form of Endoxifen citrate of the present invention helps fulfill this and other needs.

Therefore, the present invention provides not only novel polymorph of Endoxifen citrate but also provides the characterization data for analysis of this form.

OBJECTS OF THE INVENTION

The main object of the present invention is to provide a novel crystalline polymorphic form of Endoxifen citrate.

Another object of the present invention is to provide a novel crystalline polymorphic form of Endoxifen citrate which is characterized by an XRD pattern comprising 2 theta value at about 10.8 degree two-theta ± 0.2.

Another object of the present invention is to provide a novel crystalline polymorphic form of Endoxifen citrate which is characterized by an XRD pattern

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comprising 2 theta values at about 5.4, 10.8, 11.7, 13.6, 14.5, 18.3, 19.4 and 21.8 degree two-theta ± 0.2.

Another object of the present invention is to provide a crystalline form of Endoxifen citrate, which is characterized by X-ray powder diffraction pattern (XRPD) as depicted in figure 1.

Another object of the present invention is to provide a crystalline form of Endoxifen citrate, which is characterized by differential scanning calorimetry (DSC) endotherm at about 129.50°C ± 2.

Another object of the present invention is to provide a process for preparation of crystalline form of Endoxifen citrate.

SUMMARY OF THE INVENTION

The present invention provides a novel crystalline polymorphic form of Endoxifen citrate which is characterized by an XRD pattern comprising 2 theta value at about 10.8 degree two-theta ± 0.2.

The novel crystalline polymorph of Endoxifen citrate of the present invention, further characterized by an XRD pattern comprising 2 theta values at about 5.4, 11.7, 13.6, 14.5, 18.3, 19.4 and 21.8 degree two-theta ± 0.2.

Further the present invention discloses a method for preparing the said polymorph of Endoxifen citrate.

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BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 is X-ray Diffractogram (XRD) of crystalline form of Endoxifen citrate as per the present invention.

Fig. 2 is Differential Scanning Calorimetry (DSC) of crystalline form of Endoxifen citrate as per the present invention.

DETAILED DESCRIPTION

In an embodiment the present invention provides novel polymorphic form of Endoxifen citrate. In a preferred embodiment of the invention polymorphic form is crystalline form.

In another embodiment of the present invention novel crystalline polymorphic form of Endoxifen citrate which is characterized by an XRD pattern comprising 2 theta value at about 10.8 degree two-theta ± 0.2.

In another embodiment of the present invention novel crystalline polymorph of Endoxifen citrate, further characterized by an XRD pattern comprising 2 theta values at about 5.4, 11.7, 13.6, 14.5, 18.3, 19.4 and 21.8 degree two-theta ± 0.2.

In another embodiment the present invention discloses novel crystalline polymorph of Endoxifen citrate, which is characterized by an XRD pattern comprising 2 theta values at about 5.4, 10.8, 11.7, 13.6, 14.5, 18.3, 19.4 and 21.8 degree two-theta ± 0.2.

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The crystalline form of Endoxifen citrate can be characterized by PXRD pattern as set forth in figure 1.

The XRD main peaks with positions and relative intensities have been extracted from the diffractogram in Figure1 are given below.

Angle Degree two-theta (±0.2)	d value Angstrom	Intensity %
5.4	16.3	73.8
10.8	8.1	100
11.7	7.5	49.4
13.6	6.4	50.3
14.5	6.0	78.5
18.3	4.8	62.2
19.4	4.5	54.4
21.8	4.0	51.4

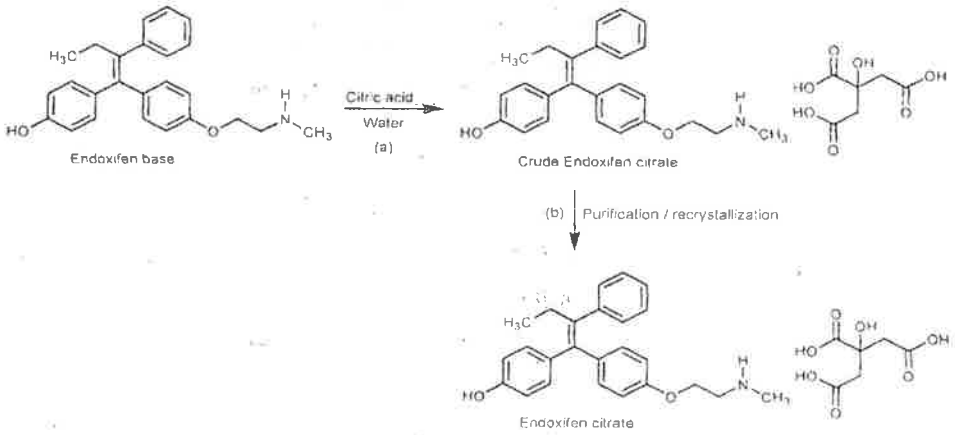
The crystalline form of Endoxifen citrate can also be characterized by an endotherm at about 129.50°C ± 2 in a DSC. The DSC thermogram of crystalline form of Endoxifen citrate is as set forth in figure 2.

The crystalline form of Endoxifen citrate can also be characterized by IR spectroscopy at about 3523, 3500, 3483, 3332, 3307, 3142, 3022, 2970, 2931, 2872, 2829, 2735, 2669, 2540, 2492, 2378, 2320, 2096, 2083, 2071, 2019, 1953, 1892, 1734, 1710, 1602, 1573, 1506, 1435, 1402, 1367, 1336, 1309, 1261, 1236,

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1174, 1130, 1105, 1076, 1055, 1028, 991, 923, 875, 840, 769, 731, 704, 644, 609, 588, 563, 518, 486 and 426 cm^{-1}.

Another embodiment of the present invention is to provide a process for the preparation of novel crystalline form of Endoxifen citrate by the reaction of Endoxifen base with citric acid to give Endoxifen citrate salt. Endoxifen Citrate obtained can be purified / recrystallized from a solvent or mixture thereof.



In the above reaction step (a), Endoxifen base used in the preparation of Endoxifen citrate can be E-isomer or Z-isomer or mixture thereof. Preferably, Endoxifen is mixture of E- and Z-isomers of Endoxifen.

Citric acid used in the above step (a) of the reaction may be either anhydrous or hydrous. Preferably citric acid used is anhydrous.

The above reaction step (a) can be carried out at room temperature or higher temperature. After that, the reaction mixture can be cooled to room temperature or

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lower temperature followed by filtration of reaction mass to obtain crude solid Endoxifen citrate, which may be further washed with water and methanol.

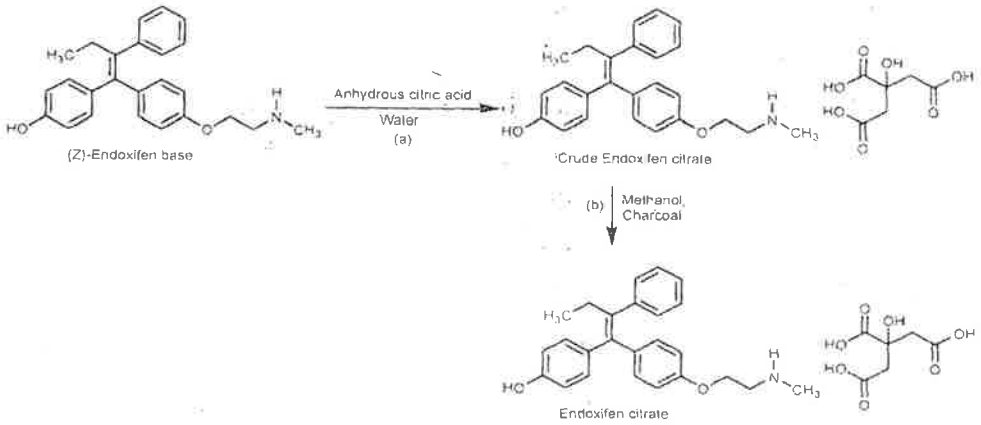
Purification / recrystallization of crude Endoxifen citrate step (b) can be carried out in presence of suitable solvent or mixture thereof, wherein solvent is selected from either organic or an inorganic solvent.

Organic solvent includes but not limited to alcoholic solvents, hydrocarbon solvents, ester solvents or ether solvents. Alcoholic solvent includes but not limited to methanol, ethanol, propanol, butanol, isobutanol, pentanol or hexanol. In a preferred embodiment of the present invention, alcoholic solvent is methanol.

The purification step (b) can be carried out at room temperature or higher temperature. Activated charcoal can be added for the above step (b) in order to remove any color impurities. The reaction mixture can be filtered and washed with methanol to give pure crystalline form of Endoxifen citrate.

In another embodiment of the invention novel crystalline polymorph of the present invention is prepared by reacting the solution of Endoxifen base ((Z)-4-(1-(4-(2-(methylamino)ethoxy)phenyl)-2-phenylbut-1-en-1-yl)phenol) with a solution of anhydrous citric acid to give Endoxifen citrate salt. The Endoxifen citrate obtained is purified with methanol and charcoal. The reaction can be summarized as below:

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The above reaction step (a) can be carried out at room temperature or higher temperature. After that, the reaction mixture can be cooled to room temperature or lower temperature followed by filtration of reaction mass. The obtained Endoxifen citrate solid can be washed with water and methanol to give crude Endoxifen citrate.

Purification / recrystallization of crude Endoxifen citrate step (b) can be carried out in presence of methanol and activated charcoal at room temperature or higher temperature. The reaction mixture can be filtered and washed with methanol to give pure crystalline form of Endoxifen citrate.

Endoxifen base used in the present invention can be prepared by any of the known prior art process, for example as disclosed in examples of the present invention.

Experimental part:

Identification of solids obtained by the present invention can be made by methods known in the art, such as X-Ray Diffraction, Differential Scanning Calorimetry

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(DSC) and Infrared Spectroscopy (IR). It should be understood that operator, instrument and other similar changes may result in some margin of error with respect to analytical characterization of the solid.

The XRD, DSC and IR methods used for the identification and characterization of crystalline form of Endoxifen citrate are described below:

a) XRPD method: Analytical characterization of the compound of present invention was carried out by using X-ray powder diffraction using D8 Advance of Bruker AXS make. The details of the same are given in Table No 1.

Table No 1

Instrument	D8 Advance
Make,	Bruker AXS
Detector	-Lynx-eye

b) DSC method: The DSC (Differential Scanning Calorimetry) analysis of the compound of present invention was recorded at a temperature range from 60°C to 160°C. The details of the same are given in Table No 2.

Table No 2

Instrument name	TA Q200
Scanning range	60°C-160°C

c) IR method: The IR (Infrared Spectroscopy) analysis of the compound of present invention was recorded by IR Affinity – 1 of Shimadzu (manufacturer).

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The following examples are intended to illustrate the present invention. It should be understood that the invention is not limited to those specific examples. Numerous changes and modifications may be made to the embodiments of the invention without departing from actual scope of the invention.

Example 1: Preparation of Endoxifen

(A) Preparation of 2-(4-bromophenoxy)tetrahydro-2H-pyran

p-bromo phenol (800 gm) and 3,4-dihydro-2H-pyran (1200 gm) were charged in a RBF. The reaction mixture thus obtained was stirred at room temperature followed by cooling. Sulphuric acid (5ml) were added to the reaction mixture and the temperature of the reaction mixture was raised to room temperature. After completion of the reaction, layers separated. Organic layer was distilled off, obtained residue was washed with isopropanol to give 900 gm of title compound.

(B) Preparation of 1-(4-(2-chloroethoxy)phenyl)-2-phenyl-1-[4-((tetrahydro-2H-pyran-2-yl)oxy)phenyl]butan-1-ol

Freshly prepared Mg turning (20 gm) and THF (175 ml) were charged in a RBF. Reaction mixture thus obtained was heated to 60-70°C. Iodine crystals and ethyl bromide (1ml) were charged into reaction mixture. 2-(4-bromophenoxy)tetrahydro-2H-pyran (200 gm) was added to the reaction mixture; followed by cooling to room temperature. A solution of 1-(4-(2-chloroethoxy)phenyl)-2-phenylbutan-1-one was added to the reaction mixture at room temperature. After completion of the reaction the reaction mixture was heated to 60-75°C and again cooled to room temperature. 300 ml of HCl solution was added to reaction mixture and raised temperature to room temperature. After

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separation of layers, organic layer was washed with water (400 ml), sodium bicarbonate solution and sodium chloride solution to obtain 300 gm of residue of title compound.

(C) Preparation of (E/Z)-4-(1-(4-(2-chloroethoxy)phenyl)-2-phenylbut-1-en-1-yl)phenol

Residue of 1-(4-(2-chloroethoxy)phenyl)-2-phenyl-1-[4-((tetrahydro-2H-pyran-2 yl)oxy)phenyl]butan-1-ol (300 gm) prepared according to above example B and methanol (1200 ml) were charged in a RBF. The obtained reaction mixture was cooled to room temperature, followed by addition of conc. HCl (300 ml). The reaction mixture was heated at 70-80°C and again cooled to room temperature. Water (300 ml) and methylene chloride (900 ml) were charged to reaction mixture. After separation of layers, the organic layer was distilled off to obtain 250 gm of of title compound.

(D) Preparation of Endoxifen base

(E/Z)-4-(1-(4-(2-chloroethoxy)phenyl)-2-phenylbut-1-en-1-yl)phenol (250 gm) prepared according to above example C and methanol (2 L) were charged in a RBF. Mono methyl amine solution (7.5 L) was added to the reaction mass at room temperature. After completion of the reaction the reaction mass was heated to 60-70°C followed by cooling to room temperature. Di isopropyl ether (4 L) was charged into reaction mass. After separation of layers, the organic layer was filtered off to give residue (200 gm). Ethyl acetate (400 ml) was charged into residue at room temperature. The reaction mass was filtered and the obtained solid was washed with ethyl acetate (200 ml) to give Endoxifen base (140 gm).

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Endoxifen base (140 gm) and ethyl acetate (150 ml) were charged in a RBF. The reaction mass was filtered and washed with ethyl acetate (150 ml) to give residue of Endoxifen base (80 gm).

Endoxifen base residue (80 gm) and isopropyl alcohol (600 ml) were charged in a RBF. n-heptane (1700 ml) was added to the reaction mass at room temperature. The reaction mass was filtered off to obtain 40 gm of Endoxifen base solid.

Example 2: Purification of Endoxifen base

Endoxifen base (40 gm) prepared from example 1 and chlorobenzene (250 ml) was charged in a RBF. Thus formed reaction mixture was heated to 60-70°C and then cooled to room temperature. The reaction mixture was filtered to obtain 25 gm of pure Endoxifen base.

Example 3: Preparation of Endoxifen citrate from Endoxifen

Citric acid (75 gm) and water (150 ml) were charged in a RBF. The obtained solution was heated at a temperature of 30-50°C, followed by addition of Endoxifen (25 gm). After completion of the reaction, the reaction mixture was cooled to room temperature. The reaction mixture was filtered to obtain 30 gm of Endoxifen citrate solid.

Example 4: Preparation of crystalline form of Endoxifen citrate

Endoxifen citrate (30 gm) prepared from example 3 and methanol (400 ml) were taken in a RBF. The reaction mixture was heated to 60-70°C followed by cooling

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to room temperature. The reaction mixture was filtered; solid thus obtained was dried to give 24 g of title compound.

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We claim:

1. A crystalline form of Endoxifen citrate.

2. The crystalline form of Endoxifen citrate as claimed in claim 1, which is characterized by characteristic peaks at about 5.4, 10.8, 11.7, 13.6, 14.5, 18.3, 19.4 and 21.8 degree two-theta ± 0.2.

3. The crystalline form of Endoxifen citrate as claimed in claim 1, which is characterized by X-ray powder diffraction pattern (XRPD) as depicted in figure 1.

4. A crystalline form of Endoxifen citrate, which is characterized by differential scanning calorimetry (DSC) endotherm at about 129.50°C ± 2.

5. The crystalline form of Endoxifen citrate as claimed in claim 4, which is characterized by differential scanning calorimetry (DSC) as depicted in figure 2.

6. A process for preparation of crystalline form of Endoxifen citrate comprising:
(a) reaction of Endoxifen with citric acid to give Endoxifen citrate; and
(b) purification of Endoxifen citrate with suitable solvent or mixture thereof.

7. The process as claimed in claim 6, wherein solvent is organic solvent or an inorganic solvent.

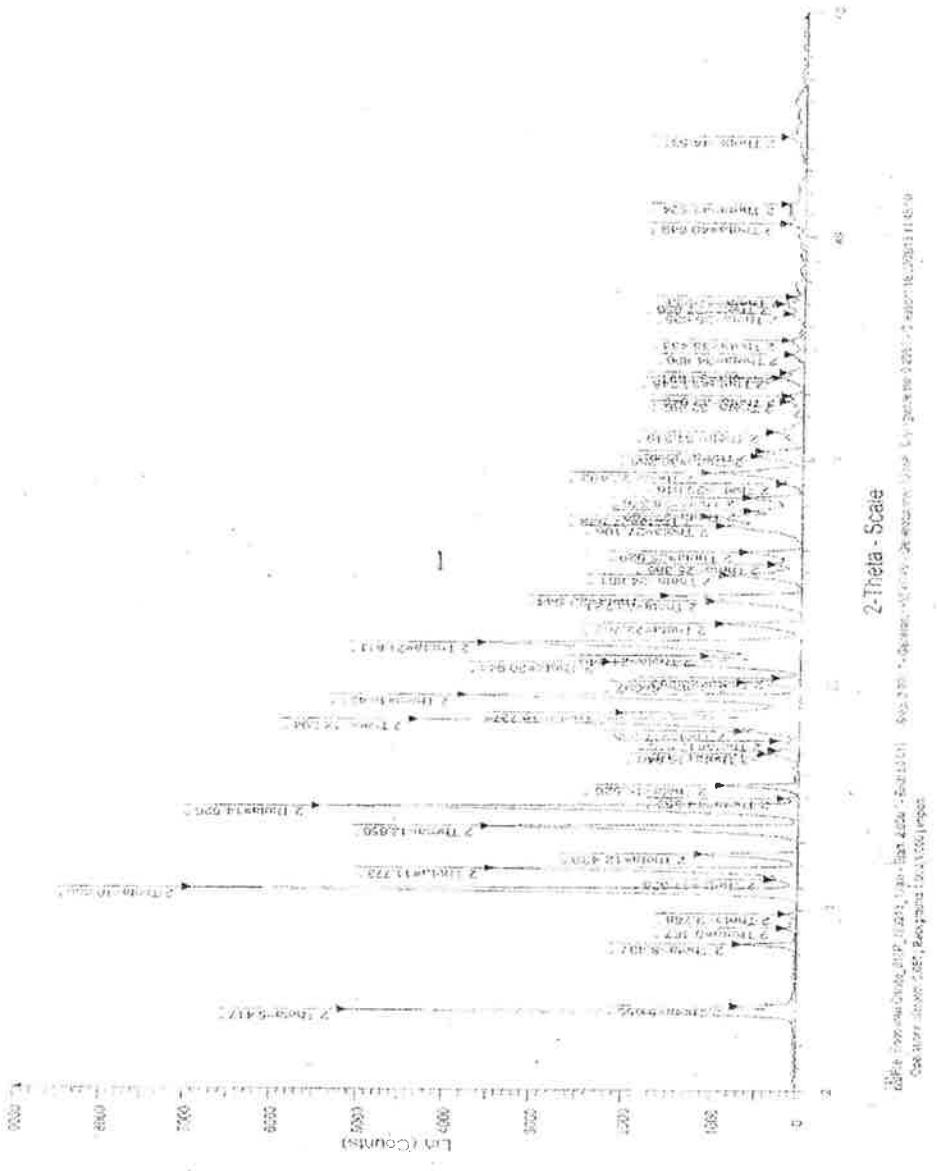
8. The process as claimed in claim 7, wherein organic solvent is an alcoholic solvent comprising methanol, ethanol, n-propanol, isopropanol, butanol, isobutanol and pentanol.

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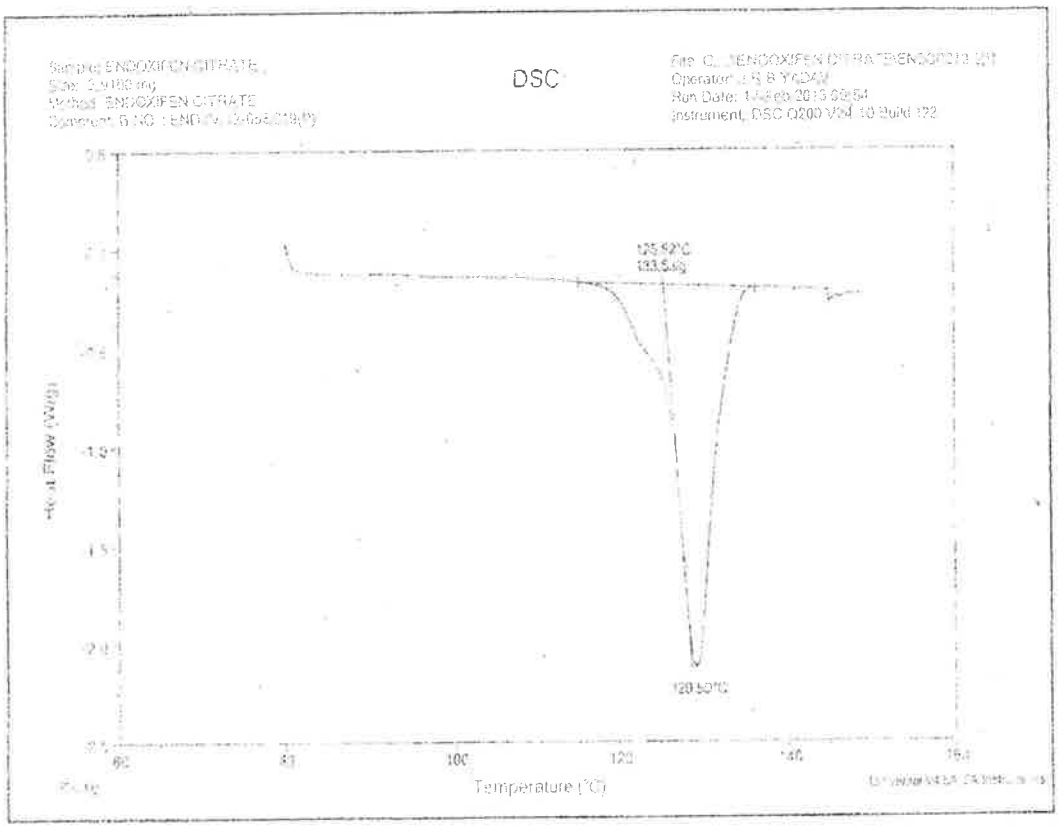
9. The process as claimed in claim 6, wherein charcoal is added in the purification of Endoxifen citrate.

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DSC
125.92°C
193.5J/g
120.50°C
Temperature (°C)

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

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.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Ateeq		AHMAD	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

City	Wadsworth	State/Province	IL	Country of Residence	US

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Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Imran		AHMAD	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

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Mailing Address of Inventor:

Address 1	5420 Belmont Court
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City	Libertyville	State/Province	
Postal Code	60048	Country	US

Inventor 3 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Moghisuddin		AHMAD	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

City	Wadsworth	State/Province	IL	Country of Residence	US

Mailing Address of Inventor:

Address 1	3050 N Forrest Hills Court		
Address 2			
City	Wadsworth	State/Province	IL
Postal Code	60083	Country	US

Remove

Inventor 4

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Shoukath M		ALI	

Residence Information (Select One) (•) US Residency ( ) Non US Residency ( ) Active US Military Service

City	Vernon Hills	State/Province	IL	Country of Residence	US

Mailing Address of Inventor:

Address 1	10 Southfield Drive		
Address 2			
City	Vernon Hills	State/Province	IL
Postal Code	60061	Country	US

Remove

Inventor 5

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Saifuddin		SHEIKH	

Residence Information (Select One) (•) US Residency ( ) Non US Residency ( ) Active US Military Service

City	Libertyville	State/Province	IL	Country of Residence	US

Mailing Address of Inventor:

Address 1	1995 S Egret Court		
Address 2			
City	Libertyville	State/Province	IL
Postal Code	60048	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.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Customer Number	52835		
Email Address		Add Email	Remove Email

Application Information:

Title of the Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		
Attorney Docket Number	20110.0024USU1	Small Entity Status Claimed	X
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	0	Suggested Figure for Publication (if any)	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

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). Either enter 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	52835		

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
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Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim 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.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status		Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Claims benefit of provisional	63/008162	2020-04-10

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 priority to a foreign application. 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. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove			
Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. **Priority Document Exchange (PDX)** - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. **Search Results from U.S. Application to EPO** - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

Clear

◉ Assignee	○ Legal Representative under 35 U.S.C. 117	○ Joint inventor
○ Person to whom the inventor is obligated to assign.	○ Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	Jina Pharmaceuticals, Inc.		
Mailing Address Information For Applicant:			
Address 1	28100 N Ashley Circle, Suite 103		
Address 2			
City	Libertyville	**State/Province**	IL
Country	US	Postal Code	60048
Phone Number		Fax Number	
Email Address			

Additional Applicant Data may be generated within this form by selecting the Add button.

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	20110.0024USU1
	Application Number	
Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

Assignee 1

Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

If the Assignee or Non-Applicant Assignee is an Organization check here. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1			
Address 2			
City		**State/Province**	
Country		Postal Code	
Phone Number		Fax Number	
Email Address			

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button.

Signature:

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Masako Yoshida/			Date (YYYY-MM-DD)	2021-07-13
First Name	Masako	Last Name	Yoshida	Registration Number	70,057

Additional Signature may be generated within this form by selecting the Add button.

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Title of Invention	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

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.**

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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 CooperationTreaty.

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.

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Electronic Acknowledgement Receipt

EFS ID:	43236974
Application Number:	17226671
International Application Number:	
Confirmation Number:	1772
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Customer Number:	52835
Filer:	Masako Yoshida/Peggy Kerkhove
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Attorney Docket Number:	20110.0024USU1
Receipt Date:	13-JUL-2021
Filing Date:	09-APR-2021
Time Stamp:	15:15:23
Application Type:	Utility under 35 USC 111(a)

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Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	US_Form_SB08_0024.pdf	1034622 100d2dc05...d3da1	no	4

Warnings:

Information:					
2	Foreign Reference	FR1_WO2014141292A2.pdf	589333 bf703e8a568c5aab6c53925c7052a2238ba8da70	no	20
Warnings:					
Information:					
3	Non Patent Literature	NPL1_Ahmad.pdf	418674 d8ed744db2410cb7d56080f964c670fce01c6250	no	8
Warnings:					
Information:					
4	Non Patent Literature	NPL2_Ali.pdf	227359 e9a6c621ac341a798d4a1ef3f6f5d86706d8c20e	no	3
Warnings:					
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5	Application Data Sheet	updated_ADS_0024.pdf	265745 44b8449271cc627f7c44bcb5b99ded836db6eac	no	9
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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

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Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	17226671
Filing Date	2021-04-09
First Named Inventor	AHMAD
Art Unit	1615
Examiner Name	
Attorney Docket Number	20110.0024USU1

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	1	20120201908		2012-08-09	Miller	
	2	20190231687		2019-08-01	Ahmad, et al.	

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	1	2009/152430	WO		2009-12-17			
	2	2008/048194	WO		2008-04-24			

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17226671
	Filing Date	2021-04-09
	First Named Inventor	AHMAD
	Art Unit	1615
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	1	International Search Report and Written Opinion issued in International Application No. PCT/IB2021/052972, July 15, 2021, 9 pages	

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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.GOV or 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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PGR2026-00015
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17226671
	Filing Date	2021-04-09
	First Named Inventor	AHMAD
	Art Unit	1615
	Examiner Name	
	Attorney Docket Number	20110.0024USU1

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

X 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

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X 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	/Masako Yoshida/	Date (YYYY-MM-DD)	2021-08-10
Name/Print	Masako Yoshida	Registration Number	70,057

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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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.

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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.

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PATENT TERM ADJUSTMENT STATEMENT UNDER 37 CFR 1.704(d)

Application Number	17226671
Filing Date	2021-04-09
First Named Inventor	AHMAD
Art Unit	1615
Examiner Name	
Practitioner Docket No.	20110.0024USU1

APPLICANT HEREBY STATES THE FOLLOWING (please review 37 CFR 1.704(d) before filing this form):

☒ Each item of information contained in the information disclosure statement was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in 37 CFR 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

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INSTRUCTIONS:

- **This form will not satisfy the requirement of 37 CFR 1.97(e).** The present statement is filed under 37 CFR 1.704(d) and will not substitute for compliance with any of the requirements of 37 CFR 1.97 and 1.98. For an information disclosure statement to comply with 37 CFR 1.97(c) or (d), the information disclosure statement must be accompanied by a statement under 37 CFR 1.97(e) notwithstanding any statement filed under 37 CFR 1.704(d).
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Signature	/Masako Yoshida/	Date	August 10, 2021
Typed or Printed Name	Masako Yoshida	Practitioner Registration Number	30,300

Note: *Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required in accordance with 37 CFR 1.33 and 11.18. Please see 37 CFR 1.4(d) for the form of the signature. If necessary, submit multiple forms for more than one signature, see below*.*

☐ *Total of _____ forms are submitted.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

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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.

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(71) Applicant *(for all designated States except US)*: **REPLIGEN CORPORATION** [US/US]; 41 Seyon Street, Building 1, Suite 100, Waltham, MA 02453 (US).

(72) Inventor; and
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(74) Agent: **FASSE, J., Peter**; Fish & Richardson P.C., P.O. Box 1022, Minneapolis, MN 55440-1022 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: 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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— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) **Title**: METHODS OF TREATMENT OF BIPOLAR DISORDER

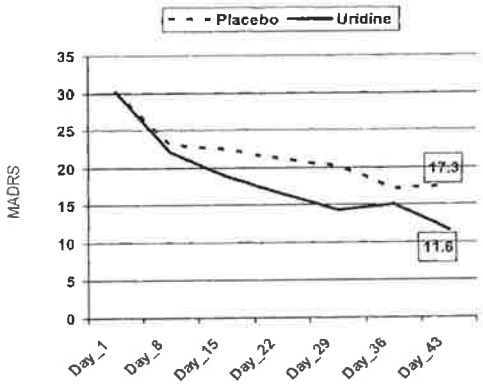


FIG. 8

(57) **Abstract**: A method of treating an individual diagnosed with bipolar disorder, comprises determining the number of manic episodes and/or depressive episodes experienced by an individual exhibiting one or more symptoms of bipolar disorder (e.g., bipolar disorder I); and if the number of manic episodes and/or the number of depressive episodes is each 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 10 or greater, or 15 or greater), administering to the individual an effective amount of a uridine composition.

WO 2009/152430 A2

METHODS OF TREATMENT OF BIPOLAR DISORDER

CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority to U.S. Application Serial No. 61/061,061, filed on June 12, 2008, the entire contents of which are incorporated by reference herein.

TECHNICAL FIELD

This invention relates to the treatment of bipolar disorder.

BACKGROUND

Bipolar disorder, also known as manic-depressive illness, is a brain disorder characterized by periods of excitability (mania) alternating with periods of depression. About 5.7 million American adults or about 2.6 percent of the population age 18 and older in any given year, have bipolar disorder.

SUMMARY

The invention is based, in part, on the discovery that individuals diagnosed with one or more symptoms of bipolar disorder who have a history of two or more episodes of mania (e.g., three or more, four or more, five or more, six or more, ten or more, or 15 or more) and/or two or more episodes of depression (e.g., three or more, four or more, five or more, six or more, ten or more, or 15 or more) derive a greater benefit from treatment with one or more pyrimidines, such as uridine, than individuals with fewer episodes of mania and/or depression.

Thus, the invention features methods of treating an individual diagnosed with bipolar disorder, that include: determining the number of manic episodes and/or depressive episodes experienced by an individual exhibiting one or more symptoms of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder); and if the number of manic episodes (e.g., manic episodes and/or hypomanic episodes) or the number of depressive episodes (e.g., major depressive episodes) is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater), administering to the individual an effective amount of a uridine composition. In some embodiments, if the number of manic episodes is fewer

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than 2 (e.g., fewer than 3, 4, 5, 6, 7, 8, 9, 10, 12, or 15), a uridine composition is not administered to the individual.

In a further aspect, the invention features methods of treating an individual diagnosed with bipolar disorder that include: determining the number of manic episodes experienced by an individual exhibiting one or more symptoms of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder); determining the number of depressive episodes (e.g., major depressive episodes) experienced by the individual; and if the number of manic episodes (e.g., manic episodes and/or hypomanic episodes) is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater) and the number of depressive episodes (e.g., major depressive episodes) is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater), administering to the individual an effective amount of a uridine composition. In some embodiments, the individual is administered an effective amount of a uridine composition if the number of manic episodes is 2 or greater and the number of depressive episodes is 5 or greater. In some embodiments, if the number of manic episodes is fewer than 2 (e.g., fewer than 3, 4, 5, 6, 7, 8, 9, 10, 12, or 15) and/or the number of depressive episodes is fewer than 2 (e.g., fewer than 3, 4, 5, 6, 7, 8, 9, 10, or 15), a uridine composition is not administered to the individual.

In other aspects, the invention features use of a uridine composition in the preparation of a medicament for the treatment of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) with a history of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of mania (e.g., mania and/or hypomania) or depression (e.g., major depression); use of a uridine composition for the treatment of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) with a history of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of mania (e.g., mania and/or hypomania) or depression (e.g., major depression); use of a uridine composition in the preparation of a medicament for the treatment of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) with a history of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more,

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10 or more, 12 or more, or 15 or more) episodes of mania (e.g., mania and/or hypomania) and two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of depression (e.g., major depression); use of a uridine composition for the treatment of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) with a history of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of mania (e.g., mania and/or hypomania) and two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of depression (e.g., major depression); use of a uridine composition in the preparation of a medicament for the treatment of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) with a history of two or more episodes of mania (e.g., mania and/or hypomania) and five or more episodes of depression (e.g., major depression); and use of a uridine composition for the treatment of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) with a history of two or more episodes of mania (e.g., mania and/or hypomania) and five or more episodes of depression (e.g., major depression).

In another aspect, the invention features methods of selecting an individual for treatment of bipolar disorder that include: evaluating whether an individual exhibits one or more symptoms of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder); determining the number of manic episodes (e.g., manic episodes and/or hypomanic episodes) and depressive episodes (e.g., major depressive episodes) experienced by the individual; and selecting the individual for treatment with a uridine composition if the number of manic episodes or depressive episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater). In some embodiments, methods include selecting the individual for treatment with a uridine composition only if the number of manic episodes or depressive episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater).

In another aspect, the invention features methods of selecting an individual for treatment of bipolar disorder that include: evaluating whether an individual exhibits one

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or more symptoms of bipolar disorder (e.g., bipolar I disorder or bipolar II disorder); determining the number of manic episodes (e.g., manic episodes and/or hypomanic episodes) experienced by the individual; determining the number of depressive episodes (e.g., major depressive episodes) experienced by the individual; and selecting the individual for treatment with a uridine composition if the number of manic episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater) and the number of depressive episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater). In some embodiments, the methods include selecting the individual for treatment with a uridine composition only if the number of manic episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater) and the number of depressive episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater). In some embodiments, the methods include selecting the individual for treatment with a uridine composition if (e.g., only if) the number of manic episodes is 2 or greater and the number of depressive episodes is 5 or greater.

In some embodiments of the above methods and uses, an effective amount of the uridine composition provides about 1 to 50 mg of a uridine composition/kg of body weight/day, e.g., about 3 to 10 mg, about 3 to 20 mg, about 5 to 15 mg, or about 7 to 10 mg of a uridine composition/kg of body weight/day.

In some embodiments of the above methods and uses, the individual is diagnosed under DSM-IV guidelines as having bipolar disorder and/or an effective amount of the uridine composition comprises between 250 and 2000 mg of uridine composition/day.

In some embodiments of the above methods and uses, the uridine composition is administered in two or three doses/day.

In some embodiments of the above methods and uses, the uridine composition is uridine, triacetyl uridine, uridine monophosphate, uridine diphosphate, or uridine triphosphate.

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In some embodiments of the above methods and uses, the uridine composition is prepared in a form for oral administration.

In another aspect, the invention features kits that include a medicament that includes a uridine composition (e.g., uridine, triacetyl uridine, uridine monophosphate, uridine diphosphate, or uridine triphosphate) and instructions to administer an effective amount of the composition to an individual with bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) if the individual has a history of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of mania (e.g., mania and/or hypomania) and/or two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of depression (e.g., major depression).

The invention also features methods of evaluating a candidate treatment for bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) that include: obtaining a population of individuals that exhibit one or more symptoms of bipolar disorder; determining the total number of manic episodes (e.g., manic episodes and/or hypomanic episodes) and or depressive episodes (e.g., major depressive episodes) experienced by each individual; selecting a subpopulation of the population of individuals for whom the total number of manic episodes or depressive episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater); and administering a candidate treatment for bipolar disorder to the subpopulation. In some embodiments, the methods further include determining the effect of the candidate treatment to treat, reduce, or alleviate one or more symptoms of bipolar disorder in the individuals of the subpopulation. In some embodiments, the methods further include administering a placebo to some individuals of the subpopulation and assaying whether the candidate treatment is effective to treat, reduce, or alleviate one or more symptoms of bipolar disorder to a greater extent than the placebo does.

The invention also features methods of evaluating a candidate treatment for bipolar disorder (e.g., bipolar I disorder or bipolar II disorder) that include: obtaining a population of individuals that exhibit one or more symptoms of bipolar disorder; determining the total number of manic episodes (e.g., manic episodes and/or hypomanic

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episodes) experienced by each individual; determining the total number of depressive episodes (e.g., major depressive episodes) experienced by each individual; selecting a subpopulation of the population of individuals for whom the total number of manic episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater) and the total number of depressive episodes is 2 or greater (e.g., 3 or greater, 4 or greater, 5 or greater, 6 or greater, 7 or greater, 8 or greater, 9 or greater, 10 or greater, 12 or greater, or 15 or greater); and administering a candidate treatment for bipolar disorder to the subpopulation. In some embodiments, a subpopulation of individuals is selected for whom the total number of manic episodes is 2 or greater and the total number of depressive episodes is 5 or greater. In some embodiments, the methods further include determining the effect of the candidate treatment to treat, reduce, or alleviate one or more symptoms of bipolar disorder in the individuals of the subpopulation. In some embodiments, the methods further include administering a placebo to some individuals of the subpopulation and assaying whether the candidate treatment is effective to treat, reduce, or alleviate one or more symptoms of bipolar disorder to a greater extent than the placebo does.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

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DESCRIPTION OF DRAWINGS

FIG. 1 is a graph showing the weekly change from baseline (S) of the average Montgomery Åsberg Depression Rating Scale (MADRS) scores for the placebo and uridine treated groups. The graph depicts scores for each time point in the treatment phase of the study, S depicts start date (baseline) and the numbers refer to the weeks on study (e.g., 6 is week 6 the final study assessment). The scores are shown as mean change of the MADRS from baseline (study day 1). Boxes represent the difference in the response; hatched boxes depict treatment effect that favors uridine, solid boxes depict treatment effect that favors placebo.

FIG. 2 is a graph depicting weekly values for the average Clinical Global Impression of Severity of Bipolar Disorder (CGI-C-BP) (Overall) for placebo and uridine groups for each evaluation. The boxes represent the magnitude of the difference between uridine and placebo.

FIG. 3 is a graph depicting the weekly values for the change from baseline of the average MADRS scores for subjects with a history of ≥ 15 episodes of depression.

FIG. 4 is a graph depicting the weekly values for the change from baseline of the average MADRS scores for subjects with a history of < 15 episodes of depression.

FIG. 5 is a graph depicting the weekly values for the change from baseline of the average MADRS scores for subjects with a history of ≥ 10 episodes of depression (Day 43, $p = 0.18$; $\Delta = 5.8$).

FIG. 6 is a graph depicting the weekly values for the change from baseline of the average MADRS scores for subjects with a history of < 10 episodes of depression (Day 43, $\Delta = -1.7$).

FIG. 7 is a graph depicting the weekly values for the change from baseline of the average MADRS scores for subjects with a history of ≥ 15 episodes of mania or hypomania.

FIG. 8 is a graph depicting the weekly values for the change from baseline of the average MADRS scores for subjects with a history of ≥ 2 episodes of mania or hypomania (Day 43, $p = 0.11$; $\Delta = 5.7$).

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FIG. 9 is a graph depicting the weekly values for the change from baseline of the average MADRS scores for subjects with a history of < 2 episodes of mania or hypomania (Day 43, $\Delta = -8.2$).

DETAILED DESCRIPTION

The new methods and uses described herein are based on the surprising discovery that individuals diagnosed with bipolar disorder who have a history of two or more episodes of mania and/or two or more episodes of depression derive a greater benefit from treatment by the administration of one or more pyrimidines, such as uridine, prodrugs of uridine, and undine analogs, than individuals diagnosed with bipolar disorder who have a history of fewer episodes of mania and/or depression. Such individuals can be selected for treatment by the administration of an effective amount of a pyrimidine composition such as a uridine composition, for example, by oral or systemic intravenous administration. The new uses and methods are based on the results of a human clinical trial to determine the effectiveness of uridine for treatment of patients with bipolar disorder.

Bipolar Disorder

Bipolar disorder is a chronic illness associated with substantial morbidity and mortality, ranking worldwide behind only unipolar depression and alcohol abuse among psychiatric illnesses for related disabilities and overall economic burden of illness. The lifetime financial burden of bipolar disorder in the United States is about $625,000 per patient (Begley et al., 2001, Pharmacoeconomics, 19:483-495). Lithium and anticonvulsants such as divalproex have substantially improved the prognosis of bipolar disorder (Bowden, 2000, J. Clin. Psychiatry, 61(Suppl 9):35-40). However, many individuals are unable to tolerate treatment-related side-effects, and have incomplete clinical responses, with relapse and recurrence common clinical problems (Hirschfeld et al., 2007, Psychopharmacol. Bull., 40:7-14).

The symptoms of bipolar disorder can be severe, and can result in emotional problems, poor job or school performance, and even suicide. The name "bipolar" comes from the patients' mood swings, which can alternate between the "poles" of mania

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(highs) and depression (lows). These mood swings can be quite dramatic, from overly "high" and/or irritable to sad and hopeless, and then back again, often with periods of normal mood in between, and severe changes in energy and behavior go along with these changes in mood. Bipolar disorder typically develops in late adolescence or early adulthood. However, some people have their first symptoms during childhood or late in life. This disorder is not always viewed as an illness, and people may suffer for years before proper diagnosis.

Bipolar disorder has been separated into two categories, Type I and Type II, and can be diagnosed following the guidelines in the Diagnostic and Statistical Manual of Mental Disorders (DSM) Fourth Edition, 1994 (American Psychiatric Association, 1400 K Street NW, Suite 1101, Washington, DC 20005-2403 USA). The fourth edition of these guidelines, DSM- IV, identifies the diagnostic features of Bipolar I Disorder as follows.

Bipolar I Disorder (DSM-IV, p. 350)

This disorder is a clinical course that is characterized by the occurrence of one or more Manic Episodes or Mixed Episodes. Often individuals have also had one or more Major Depressive Episodes. Episodes of Substance-Induced Mood Disorder (due to the direct effects of a medication, or other somatic treatments for depression, a drug of abuse, or toxin exposure) or of Mood Disorder Due to a General Medical Condition do not count toward a diagnosis of Bipolar I Disorder. In addition, the episodes are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

The diagnostic features of Bipolar II Disorder are as follows.

Bipolar II Disorder (DSM-IV, p. 359)

This disorder is a clinical course that is characterized by the occurrence of one or more Major Depressive Episodes accompanied by at least one Hypomanic Episode. Hypomanic Episodes should not be confused with the several days of euthymia that may follow remission of a Major Depressive Episode. Episodes of Substance- Induced Mood Disorder (due to the direct effects of a medication, or other somatic treatments for depression, a drug of abuse, or toxin exposure) or of Mood Disorder Due to a General

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Medical Condition do not count toward a diagnosis of Bipolar I Disorder. In addition, the episodes are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

The following diagnostic criteria, also from the DSM-IV apply.

Criteria for Major Depressive Episode (DSM-IV, p. 327)

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. Symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations should not be included.

- Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). Note: In children and adolescents, can be irritable mood.

- Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)

- Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.

- Insomnia or hypersomnia nearly every day. - Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

- Fatigue or loss of energy nearly every day. - Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).

- Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).

- Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms do not meet criteria for a Mixed Episode.

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C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

Criteria for Manic Episode (DSM-IV, p. 332)

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary).

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

- Inflated self-esteem or grandiosity.
- Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).
- More talkative than usual or pressure to keep talking.
- Flight of ideas or subjective experience that thoughts are racing.
- Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli).
- Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.
- Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The symptoms do not meet criteria for a Mixed Episode.

D. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

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E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatments) or a general medical condition (e.g., hyperthyroidism).

Manic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of Bipolar I Disorder.

Criteria for Mixed Episode (DSM-IV, p. 335)

A. The criteria are met both for a Manic Episode and for a Major Depressive Episode (except for duration) nearly every day during at least a 1-week period.

B. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

C. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

Criteria for Hypomanic Episode (DSM-IV, p. 338)

A. A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual nondepressed mood.

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

- Inflated self-esteem or grandiosity.
- Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).
- More talkative than usual or pressure to keep talking.
- Flight of ideas or subjective experience that thoughts are racing.
- Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli).
- Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.

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- Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features.

F. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

Hypomanic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of Bipolar II Disorder.

The diagnosis of symptoms of bipolar disorders (e.g., mania, hypomania, and depression (e.g., major depression)) in an individual or one or more of a population of individuals can be determined by a person skilled in the art, e.g., a psychiatrist, psychologist, or clinician. Diagnostic rating scales can be used to aid in diagnosis of bipolar disorders and specific symptoms, e.g., MADRS (Montgomery Åsberg Depression Rating Scale); CGI-BP-S (Clinical Global Impression of Severity of Bipolar Disorder); Hamilton Anxiety Scale (HAM-A); YMRS (Young Mania Rating Scale); and CGI-BP-C (Clinical Global Impression of Change in Bipolar Disorder).

MADRS is a clinical assessment of depression that has been used in many clinical studies of therapeutic intervention. The scale is a 10 item inventory of the core symptoms and cognitive features in which symptoms are rated on a 0-6 scale (Montgomery, 1979, Br. J. Psychiatry, 134:382-389). The scale is used to measure symptom severity for a specified interval. Total scores correlate highly with the Hamilton rating scale (HAM-D) and with training show a high inter-rater reliability (Williams, 2008, Br. J. Psychiatry, 192: 52-58).

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The CGI-BP scale is a modification of the clinical global impression for use in bipolar disorder as a global assessment of patient severity and change of status (Spearing et al., 1997, Psychiatry Res., 73:159-171). The CGI-BP-S rates the severity of the illness on a 7 point scale. The CGI-BP-C rates the change in the severity of disease compared to baseline. This also uses a 7 point scale, anchored by a score of 4 which correlates to no change since the initiation of treatment. Lower scores correspond to improvement, higher to worsening.

The YMRS is an 11 item scale designed to measure core manic symptoms (Young et al., Br. J. Psychiatry, 133:429-435). A cumulative score of 15 or greater on the YMRS was considered evidence of a treatment emergent affective switch. The HAM-A scale is a measure of global anxiety, including cognitive and somatic symptoms.

Uridine Compositions

A uridine composition is either purified uridine, a compound or product that contains uridine, a compound that increases the level of uridine in the patient, or a compound or molecule that mimics the biological function of uridine. Such a compound can be a uridine precursor or prodrug, which is processed, e.g., metabolized, degraded, or cleaved, in the body to form uridine. Such a compound can also be a uridine derivative, which includes uridine, and other molecules or compounds bound (e.g., covalently or non-covalently) to uridine, but that do not impair uridine's biological activity in patients with increased purine levels. Such compounds can also be uridine mimetics, such as other nucleotides or small molecules that have a sufficiently similar three-dimensional shape or electron configuration that the compound has at least 50 percent of the biological activity of uridine. Such compounds can also be drugs or other compounds that induce the body to produce uridine, or drugs or compounds that inhibit degradation or otherwise prolong the half-life of uridine in the body.

Uridine precursors or prodrugs include orotic acid, mono-, di- or tri-esters of uridine, including mono-, di-, and triacetyl uridine, and mono, di- or tri-phosphates of uridine including uridine monophosphate (UMP) uridine diphosphate (UDP) and uridine triphosphate (UTP). Uridine mimetics include cytidine and mono-, di-, or tri-phosphates of cytidine including cytidine monophosphate, as well as mono-, di-, or tri-esters of

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cytidine including triacetyl cytidine. Deoxy- versions of these and other ribonucleosides may also be useful.

Uridine compositions also include encapsulated uridine, e.g., liposome- or polymer-encapsulated uridine. Uridine compositions also include uridine linked (e.g., covalently or non- covalently) to various antibodies, ligands, or other targeting and enveloping or shielding agents (e.g., albumin or dextrose), to allow the uridine to reach the target site (e.g., the central nervous system, muscle cells, or the peripheral nervous system) prior to being removed from the blood stream, e.g., by the kidneys and liver, and prior to being degraded.

Uridine salts or food products containing uridine that transform into uridine upon administration to a host such as human can also be used.

Useful uridine-containing compounds include, without limitation, any compound comprising uridine, UTP, UDP, or UMP.

Oral uridine-based compounds have been investigated in patients with hereditary orotic aciduria (Webster, D.R., "Hereditary Orotic Aciduria and Other Disorders of Pyrimidine Metabolism," in *The Metabolic and Molecular Bases of Inherited Disease* (Vol II), C.R. Scriver et al., Eds. 1995, McGraw-Hill), adenyl succinate lyase deficiency (Salerno et al., 2000, Adv. Exp. Med. Biol., 486:75-78), autism and pervasive developmental delay (Page et al., 1997, Proc. Natl. Acad. Sci. USA, 94:11601-06; Page and Coleman, 1998, Adv. Exp. Med. Biol., 431:793-796; Page and Coleman, 2000, Biochim. Biophys. Acta, 1500:291-296; Page. and Moseley, 2002, Prog. Neuropsychopharm. Biol. Psychiat., 26:397-400), diabetic neuropathy (Gallai et al., 1992, Acta Neurol. Scand., 86:3-7), patients undergoing chemotherapy with fluorouracil (5-FU) (van Groeningen et al., 1991, J. Natl. Cancer Inst., 83:437-441), and retroviral therapy in patients with HIV (Banasch et al., 2006, AIDS, 20:1554-56). The largest experience has been in hereditary orotic aciduria where some patients have been treated for over twenty years at doses as high as 300 mg/kg/d. The side effects noted with high dose oral uridine were diarrhea and abdominal cramps, typically at doses greater than 240 mg/kg, which raised plasma uridine levels to 60-80 μM.

Intravenous (IV) uridine has been used in the context of cancer chemotherapy at doses that have resulted in sustained elevations in plasma uridine, sometimes exceeding

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2,000 μM (van Groeningen et al., 1986, Cancer Treat. Rep., 70:745-750; Leyva et al., 1984, Cancer Res., 44:5928-33). The main side effects seen with IV uridine were infusion site phlebitis and transient shivering and fever.

Triacetyluridine (TAU) is converted to uridine in the gut mucosa, therefore it is essentially a pro-drug of uridine. Studies with TAU have been performed in children with mitochondrial disease, patients undergoing chemotherapy with 5-fluorouracil (5-FU), and in patients with monopolar depression. In the studies of children with mitochondrial disease, doses of TAU at 2 g/m^2, three times daily were used for up to two years. Significant symptomatic improvement was noted, particularly in the frequency of seizures and in the accompanying renal tubular acidosis, and no adverse events were reported (Naviaux et al., "Clinical Experience with Uridine and triacetyluridine (PN401) Therapy of Mitochondrial Disease," in *Mitochondrial Dysfunction in Human Pathology*. 1998. Melboune, Australia; Naviaux et al., "Correction of Renal Tubular Acidosis (RTA) in Mitochonrdrial Disease Patients Treated with Triacetyluridine (PN401)," in *Society for Inherited Metabolic Disorders Annual Meeting*. 1999. Atlanta, Georgia; Naviaux, R.K., "Pyrimidine Therapy of Mitochondrial Disease," in *NIH minisymposium*. 2000). In the chemotherapy studies, patients received 6 g of TAU four times a day with no adverse effects (Kelsen et al., 1997, J. Clin. Oncol., 15:1511-17; Hidalgo et al., 2000, J. Clin. Oncol., 18:167-177).

General Methods of Therapy

The new methods involve the administration of an effective amount of a pyrimidine composition, such as a uridine composition, or a candidate treatment for bipolar disorder to an individual diagnosed with one or more symptoms of bipolar disorder and a history of two or more episodes of mania and/or two or more episodes of depression. The uridine composition or candidate treatment can be formulated into a therapeutic composition and administered using a variety of known routes of administration, and in various dosage forms.

To formulate pharmaceutical grade therapeutic compositions, the uridine composition can be purified by standard methods, e.g., filtration, to remove contaminants, if present. The final compositions can be lyophilized and resuspended in

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sterile, deionized water before further compounding. The therapeutic compositions can be formulated as solutions, suspensions, suppositories, tablets, granules, powders, capsules, ointments, or creams. In the preparation of these compositions, at least one pharmaceutical excipient can be included. Examples of pharmaceutical excipients include solvents (e.g., water or physiological saline), solubilizing agents (e.g., polysorbates, or Cremophor EL7), agents for achieving isotonicity, preservatives, antioxidizing agents, lactose, crystalline cellulose, mannitol, maltose, calcium hydrogen phosphate, light silicic acid anhydride, calcium carbonate, binders (e.g., starch, polyvinylpyrrolidone, hydroxypropyl cellulose, ethyl cellulose, carboxy methyl cellulose, or gum arabic), lubricants (e.g., magnesium stearate, talc, or hardened oils), or stabilizers (e.g., lactose, mannitol, maltose, polysorbates, macrogols, or polyoxyethylene hardened castor oils). If desired, glycerin, dimethylacetamide, lactate, surfactant, or basic substances such as sodium hydroxide, ethylenediamine, ethanolamine, sodium bicarbonate, arginine, meglumine, or trisaminomethane can be added. Common disintegrants that can be included in the composition include croscarmellose sodium, crospovidone, gellan gum, and sodium starch glycolate.

When the pyrimidine composition, e.g., a uridine composition, is ingested, the excipient or carrier can be water, a flavored beverage such as a fruit juice, broth, carbonated beverage, milk, or milk shake.

Biodegradable polymers such as poly-D,L-lactide-co-glycolide or polyglycolide can be used as a bulk matrix if slow release of the composition is desired (see, e.g., U.S. Patent Nos. 5,417,986, 4,675,381, and 4,450,150). Pharmaceutical preparations such as solutions, tablets, granules or capsules can be formed with these components. If the composition is to be administered orally, flavorings and/or colors can be added.

The new compositions can be administered via any appropriate route, e.g., intravenously, intraarterially, topically, transdermally, by injection, intraperitoneally, intrapleurally, orally, subcutaneously, intramuscularly, sublingually, nasally, by inhalation, intraepidermally, or rectally, using standard techniques.

Dosages administered in practicing the new methods will depend on factors including the specific uridine composition used and its concentration in the composition, the mode and frequency of administration, the age, weight, sex, and general health of the

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subject, and the severity of the manic and/or depressive symptoms. In general, the new compositions can be administered in amounts ranging between 1.0 mg and 200 mg of uridine per kilogram of body weight per day, e.g. , 2, 3, 5, 10, 20, 50, or 100 mg/kg/day.

A typical dosage is between 3 and 100 mg/kg/day, e.g., which can be 0.25 to 7 grams (e.g., 0.25, 0.5, or 1 grams) per patient per day. Oral tablets of triacetyl uridine can be used. The daily dosage is administered on an ongoing basis until symptoms subside.

An exemplary oral administration form of uridine contains 500 mg of active substance and percent composition weight/weight: Uridine, 66.7%; Croscarmellose, 3.0%; Microcrystalline Cellulose, 10.0%; Maltodextrin, 8.0%; Lactose, 10.9%; Magnesium Stearate, 1.25%; and Silicon Dioxide, 0.2%.

Dosages can be administered with meals or once, twice, or more times per day to achieve the best relief of symptoms. The dosage should be adjusted to provide a reduction in symptoms. Once the proper dosage is determined, it can be easily maintained over time as required. Typically, 5 to 15 μM is the normal plasma concentration of uridine with a volume distribution around 0.634 liters/kg. Following administration of a uridine composition, e.g., triacetyl uridine, blood plasma levels of about 50 to 300 μM are in the typical therapeutic range.

Administration is repeated as necessary, as determined by one skilled in the art. By varying the amount of the composition or dosage, the administration protocol can be optimized based on the present disclosure to elicit a maximal improvement in symptoms of bipolar disorder. Physicians, pharmacologists, and other skilled artisans are able to determine the most therapeutically effective treatment regimen, which will vary from patient to patient. The potency of a specific composition and its duration of action can require administration on an infrequent basis, including administration in an implant made from a polymer that allows slow release of the uridine.

Skilled artisans are also aware that the treatment regimen must be commensurate with issues of safety and possible toxic effect produced by the uridine or other components in the compositions. Thus, before administering the above compositions to humans, toxicity testing can be conducted in animals, e.g., as described in Examples below. In an example of toxicity testing, the uridine compositions can be administered to mice via an oral or parenteral route with varying dosages of uridine in the composition,

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and the mice observed for signs of toxicity using standard techniques. Of course, if the uridine composition is pure uridine, long-term experience has shown that uridine has no known toxic effects at dosages of up to 1000 mg/kg/day. Higher dosages may cause mild diarrhea in some patients. See, e.g., Leyva et al., Cancer Res., 4:5928- 5933 (1984)(high dose uridine used to rescue patients from 5-fluorouracil toxicity) and Webster et al., Chapter 55, pages 1799-1837, in "The Metabolic and Molecular Bases of Inherited Disease," 7th Ed., Scriver et al. (eds.)(McGraw-Hill, Inc., New York, NY, 1995)(treatment of orotic aciduria with uridine, see, e.g., page 1815).

Combination with Other Therapeutics

The pyrimidine, e.g., uridine, compositions described herein can be administered as a monotherapy, as combinations of two or more different pyrimidines, e.g., uridine compositions (or uridine and cytidine compositions), or in combination with other compounds for the treatment of bipolar disorders. For example, the pyrimidine compositions can be administered in conjunction with lower doses of current treatments for bipolar disorder, including stimulants and antidepressants. For example, divalproex sodium (DEPAKOTE®) has been used to treat bipolar disorder. In particular examples, the pyrimidine compositions may be administered in combination with an antidepressant, anticonvulsant, antianxiety, antimanic, antipyschotic, antiobsessional, sedative, stimulant, or anti-hypertensive medication. Examples of these medications include, serotonin reuptake inhibitors, monoamine oxidase inhibitors, tricyclic antidepressants, dopamine agonists (e.g., bromocriptine, pergolide), bupropion, venlafaxine, nefazodone, benzodiazepine, trazodone, lithium (Li), risperidone, topiramate, lamotrigine, gabapentin, nimodipine, divalproex, quetiapine, divalproex, lamotrigine, carbamazepine, clozapine, olanzapine, topiramate, thyroid hormone (e.g., T3 or T4), Omega-3 fatty acids, calcium channel blockers (other than nimodipine), tiagabine, cholinesterase inhibitors, tamoxifen, and phenytoin.

Kits

A uridine composition, e.g., uridine, triacetyl uridine, uridine monophosphate, uridine diphosphate, or uridine triphosphate, can be provided in a kit. The kit can include

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(a) the composition, e.g., a dosage form that includes the uridine composition, and (b) informational material, such as a label. The informational material can be descriptive, instructional, marketing, or other material that relates to the methods described herein and/or the use of the uridine composition for the methods described herein.

In one embodiment, the informational material can include instructions to administer the uridine composition in a suitable manner to perform the methods described herein, e.g., in a suitable dose, dosage form, or mode of administration (e.g., a dose, dosage form, or mode of administration described herein). In another embodiment, the informational material can include instructions to administer the uridine composition to a suitable subject, e.g., an individual with bipolar disorder with a history of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of mania (e.g., mania and/or hypomania); an individual with bipolar disorder with a history of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of depression (e.g., major depression); or an individual with bipolar disorder with a history of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of mania (e.g., mania and/or hypomania) and/or two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of depression (e.g., major depression). In some embodiments, the informational material can include instructions not to administer the composition to a patient with fewer than 2 (e.g., fewer than 3, 4, 5, 6, 7, 8, 9, 10, 12, or 15) episodes of mania and/or fewer than 2 (e.g., fewer than 3, 4, 5, 6, 7, 8, 9, 10, 12, or 15) episodes of depression.

The informational material of the kits is not limited in its form. In many cases, the informational material, e.g., instructions, is provided in printed matter, e.g., a printed text, drawing, and/or photograph, e.g., a label or printed sheet. However, the informational material can also be provided in other formats, such as Braille, computer readable material, video recording, or audio recording. In another embodiment, the informational material of the kit is contact information, e.g., a physical address, electronic mail address, web address, or telephone number, where a user of the kit can obtain substantive information about the uridine composition and/or its use in the

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methods described herein. Of course, the informational material can also be provided in any combination of formats.

In addition to the uridine composition, the composition of the kit can include other ingredients, such as a solvent or buffer, a stabilizer, a preservative, a fragrance or other cosmetic ingredient, and/or a second agent for treating a condition or disorder described herein. Alternatively, the other ingredients can be included in the kit, but in different compositions or containers than the uridine composition. In such embodiments, the kit can include instructions for admixing the uridine composition and the other ingredients, or for using the agent together with the other ingredients.

The uridine composition can be provided in any form, e.g., liquid, dried or lyophilized form. It is preferred that the agent be substantially pure and/or sterile. When the uridine composition is provided in a liquid solution, the liquid solution is typically an aqueous solution, e.g., a sterile aqueous solution. When the uridine composition is provided as a dried form, reconstitution generally is by the addition of a suitable solvent. The solvent, e.g., sterile water or buffer, can optionally be provided in the kit.

The kit can include one or more containers for the uridine composition. In some embodiments, the kit contains separate containers, dividers, or compartments for the composition and informational material. For example, the composition can be contained in a bottle, vial, or syringe, and the informational material can be contained in a plastic sleeve or packet. In other embodiments, the separate elements of the kit are contained within a single, undivided container. For example, the composition is contained in a bottle, vial or syringe that has attached thereto the informational material in the form of a label. In some embodiments, the kit includes a plurality (e.g., a pack) of individual containers, each containing one or more unit dosage forms (e.g., a dosage form described herein) of the agent. For example, the kit includes a plurality of syringes, ampules, foil packets, or blister packs, each containing a single unit dose of the agent. The containers of the kits can be air tight and/or waterproof.

The kit optionally includes a device suitable for administration of the composition, e.g., a syringe, inhalant, pipette, forceps, measured spoon, dropper (e.g., eye dropper), swab (e.g., a cotton swab or wooden swab), or any such delivery device.

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Methods of Evaluation

Methods of evaluating a candidate treatment for bipolar disorder will typically include selecting a population of individuals for study, administering the candidate treatment to at least a portion of the individuals, and monitoring the response to the treatment of the portion administered the treatment. In some embodiments, the methods will also include administering a control treatment (e.g., a placebo) to at least a portion of the individuals, e.g., the portion not administered the candidate treatment.

Individuals can be selected such a study based on several negative and positive factors. For example, individuals can be selected who have been diagnosed with bipolar disorder and have a history of either or both of two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of mania (e.g., mania and/or hypomania) and/or two or more (e.g., 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, 10 or more, 12 or more, or 15 or more) episodes of depression (e.g., major depression). In some embodiments, individuals with fewer than 2 (e.g., fewer than 3, 4, 5, 6, 7, 8, 9, 10, 12, or 15) episodes of mania and/or fewer than 2 (e.g., fewer than 3, 4, 5, 6, 7, 8, 9, 10, 12, or 15) episodes of depression are excluded from the study. Individuals can also be selected to be included in the study or excluded from the study based on, e.g., age, current symptoms, history of drug or substance dependence, known history of sensitivity to the treatment.

The response to the treatment can be monitored by standard methods of diagnosis and evaluation of bipolar disorder, e.g., MADRS (Montgomery Åsberg Depression Rating Scale); CGI-BP-S (Clinical Global Impression of Severity of Bipolar Disorder); Hamilton Anxiety Scale (HAM-A); YMRS (Young Mania Rating Scale); and CGI-BP-C (Clinical Global Impression of Change in Bipolar Disorder). Typically, the response of the individuals administered the candidate treatment is compared to the response of the individuals administered the control treatment to determine if there was an effect of the treatment, e.g., a statistically significant effect. The response can be monitored over a set period of time, e.g., two weeks, three weeks, four weeks, six weeks, eight weeks, ten weeks, twelve weeks, four months, five months, six months, or one year.

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EXAMPLE

A six-week, double blind, placebo-controlled, dose-escalation study was performed to assess the safety and efficacy of uridine in bipolar I depression. Eight-four (84) patients of both sexes were enrolled at twelve sites, randomized on a 1:1 basis to receive either placebo or uridine. To decrease the probability of a false negative result, uridine or placebo were given as monotherapy, and no concurrent bipolar medications, including mood stabilizers, atypical antipsychotics, antidepressants, anticonvulsants or other psychotropic medications were allowed during the study. Patients taking such medications were tapered gradually during the 28 days prior to initiation of the trial. Patients were evaluated each week over the 6-week trial period, with an extensive intervention plan for any patient having exacerbation of bipolar or depressive symptoms. After the trial period, patients were eligible to initiate therapy for bipolar disease and a follow-up visit occurred at week ten.

Patients were selected that had a DSM-IV-TR diagnosis of Bipolar I Disorder, Most Recent Episode Depressed, as confirmed on the MINI; 18 to 65 years of age, inclusive; currently depressed, as measured by MADRS > 20 at Screening and Day 1, with duration of current depressive episode of at least four weeks by Day 1. Informed consent was provided by all patients. Patients were excluded who had a manic/hypomanic/mixed episode as determined by the MINI evaluation at Screening and/or a Young Mania Rating Scale (YMRS) score of > 12 at Screening and/or Day 1; dementia or any current Axis I diagnosis other than bipolar I requiring pharmacological treatments; a history of alcohol or substance dependence within six months of Day 1, or a history of alcohol or substance abuse within three months of Day 1; urine drug screen positive for amphetamines, cocaine metabolites, opiates and/or phencyclidine (PCP); an Axis II diagnosis that was likely to interfere with protocol compliance, initiation of or increase in psychotherapy within 4 weeks of Screening; psychotropic medication (excluding fluoxetine) within 24 hours of initiation of study drug on Day 1; fluoxetine within 2 weeks of initiation of study drug on Day 1; serious suicidal or homicidal risk as determined by the investigator and/or a score of > 5 on the suicide item #10 of the MADRS at Screening and/or Day 1; history of sensitivity to any of the ingredients in the study drug; clinically significant abnormality in any screening laboratory results;

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clinically significant organic disease, including cardiovascular, endocrine, hepatic, pulmonary, neurologic, or renal disease, or any other medical condition, serious intercurrent illness, or extenuating circumstances that, in the opinion of the investigator, would interfere with the performance or interpretability of, or put the patient at risk from, the study procedures; women who were pregnant, breastfeeding, or refused to use adequate birth control; current seizure disorder; participation in an investigational drug study within twenty-eight days of Day 1; current psychotic episode; clozaril use and/or electroconvulsive therapy within six months of Day 1; failure of three or more adequate trials of standard therapies for depression during the current episode; or current episode of depression longer than one year.

Patients could be withdrawn from the study for any of the following reasons: a score of 5 or greater on item #10 of the MADRS; a 30% increase on Total MADRS Score from Day 1; psychotic episode based on DSM-IV-TR criteria; a score of > 15 on any administration of the YMRS and/or a patient's meeting DSM-IV-TR criteria for a manic, mixed or hypomanic episode; use of any psychotropic medications other than benzodiazepines (equivalent to a total daily dose of 2 mg lorazepam) and sedatives/hypnotics (equivalent to a total daily dose of 10 mg zolpidem); use of 1) benzodiazepines for more than 14 days or 2) sedatives/hypnotics for more than 14 days during the treatment phase of the study; initiation of or increase in psychotherapy during the treatment phase; occurrence of a clinically unacceptable adverse event; violation of the study protocol; patient declines further study participation; in the investigator's judgment, it was in the patient's best interest (i.e. investigator becomes aware of suicidal ideation/plan).

Subjects in the uridine treatment group were given either 2 g per day (low dose) or 4 g per day (high dose) of uridine. Subjects in the placebo group were given tablets of identical size and appearance with identical dosing instructions.

A dose of 1 g orally twice daily (2 g/day) was chosen to initiate treatment, with an increase to 2 g orally twice daily (4 g/day) in the absence of clinical improvement. On Day 1, all patients received a single dose of either placebo or uridine (2 g). This loading dose was done in order to compare pharmacokinetics of uridine at study start and end. Beginning on Day 2, patients received either placebo and uridine at a dose of 2 g/day

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administered as 1 g orally twice daily (2 tablets twice daily) for one week. At the Day 8 visit, the dose was increased to 4 g/day administered as 2 g orally twice daily (4 tablets twice daily) if there had been no serious untoward drug-related adverse events, and if the subject had less than a 25% improvement on the MADRS from baseline (Day 1). Patients that remained on 2 g/day were increased to 4 g/day at a subsequent visit if the improvement from baseline on the MADRS was less than 25%. Likewise, subjects having adverse events at the high dose were decreased to the low dose at the discretion of the investigator. On Day 43, all patients received a single dose of either placebo or uridine administered as 2 g orally twice daily (4 tablets twice daily), regardless of dose regimen. This was the patients' last dose of study drug.

The MINI is a brief psychiatric inventory that was administered to the subject at Screening in order to confirm the clinical diagnosis of bipolar I disorder, most recent episode depressed.

MADRS was administered at Screening and at every subsequent visit. This metric was the measure of depression severity during the trial. It was also a formalized measure of suicide risk (item #10). A response of 4 to item 10 required a signed risk assessment plan to be implemented and a response of 5 was to result in study discontinuation and a therapeutic intervention.

YMRS was administered at Screening and at every subsequent visit. This metric was the measure of mania severity during the study. A total score of $\geq$ 15 at any administration of the YMRS was to result in study termination and therapeutic intervention.

In order to reduce both inter-rater and intra-rater variability of clinical outcome measures, and to ensure the clinical quality control of the raters, the study used an interactive patient interview to confirm that the current symptomatology was being captured accurately. The computer interview was voluntary and the data was not used in any efficacy analysis. If there were discordances in the patient's reported symptoms and the clinical outcome measures recorded for that visit, the raters were queried and the scores were justified. This clinical quality control was performed by a centralized auditor, Concordant Rater Systems.

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Clinical investigators were chosen with significant experience using the neuropsychiatric metrics employed by this study. To minimize the inter- and intra-rater variability, raters were re-trained on evaluation methods at the outset of the trial. During the course of the trial, rater evaluations were corroborated by remote site monitoring performed by Concordant Rating Systems (Lexington, MA). At each scheduled visit, patients were asked about their bipolar depression symptoms, using a personal computer interview. This data was employed as a rater quality control tool, to ensure that symptoms were being captured during the assessment. The rating assessment was intended to maintain the standardization of multi-center evaluation techniques throughout the course of the study.

83 patients were included in the trials to determine efficacy of uridine to treat bipolar disorder. The primary efficacy outcome was the mean MADRS assessment of the uridine group compared to placebo using a mixed effects repeat measures model. The difference of the mean MADRS scores for the uridine group in comparison to placebo was statistically significant, for both total scores ($p = 0.011$) and percent change from baseline ($p = 0.014$). Table 1 shows the mean MADRS score and percent change from baseline for uridine and placebo at each study evaluation. The baseline MADRS assessment was similar for the two groups, which was expected because it was a randomization criterion. This study was not adequately powered to detect differences between groups at single time points. Despite this, there are trends towards treatment difference at week 3 ($p = 0.10$) and week 4 ($p = 0.06$).

The week 6 end of study assessments demonstrated a strong change from baseline for the RG2417-treated group, with a mean change of 17.6 points (58.1%). The final assessment 4 weeks after study drug administration was completed showed no rebound in the MADRS assessments for either group. The MERM change in mean MADRS score of the RG2417 compared to placebo was used to calculate an effect size of 0.43 for difference with baseline adjusted as a covariate. This effect size is indicative of a treatment benefit.

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Table 1. Average MADRS scores for treatment groups at each weekly assessment

Time	n[1]	Placebo	Δ (%)[2]	n[1]	RG2417	Δ (%)[2]	P[3]
Baseline[4]	44	30.68	0	39	30.28	0	0.75
Wk 1	41	22.20	-27.6	37	22.46	-25.8	0.89
Wk 2	37	21.38	-30.3	36	18.81	-37.9	0.23
Wk 3	33	19.76	-35.6	29	15.90	-52.5	0.10
Wk 4	30	18.40	-40.0	30	13.93	-54.0	0.06
Wk 5	27	15.96	-48.0	29	14.97	-50.6	0.69
Wk 6	25	16.13	-47.4	29	12.69	-58.1	0.26
Wk 10[5]	21	19.05	-37.9	23	15.91	-47.5	0.41
MERM[6] p (score difference) = 0.011; p (% change from baseline) = 0.014							

1. The number of patients evaluated at each time point
2. The change from baseline evaluation (Study Day 1), stated as a percentage of the baseline score
3. Pairwise comparisons of the scores for each treatment group for that time point.
4. The baseline evaluation was at Study Day 1
5. The treatment phase of the study concluded at week 6. A follow-up visit at week 10 a month after treatment has concluded.
6. Mixed effects repeat measure from day 1 to day 43

The change from baseline (study day 1) in the mean MADRS assessment for RG2417 and placebo is illustrated in Figure 1. A clear treatment difference was observed over the course of the study, with treatment benefit designated by the hatched boxes at each time point. The true difference in the mean, i.e., the difference in response corrected for baseline [$(\text{baseline}_{\text{Uridine}} - \text{week } 6_{\text{Uridine}})-(\text{baseline}_{\text{Placebo}} - \text{week } 6_{\text{Placebo}})$] MADRS scores favored uridine from week 2, with an average difference of 3.2 points from week 3 to week 6. There was a deviation in the treatment difference at a single time point, week 5, in which there was a mild decrement in the treatment response and a substantial increase in the placebo response. Indeed, the study was characterized by an improvement in the placebo scores for weeks 4, 5, and 6. In prior published successful efficacy studies in bipolar depression, MADRS placebo responses of 10-12 points are typical (Tohen et al., 2003, Arch. Gen. Psychiatry, 60:1079-88; Sysko et al., 2007, J. Clin. Psychiatry, 68:1213-17).

The CGI-BP is a clinical impression scale that has been adapted for bipolar disorder and is comprised of an overall score, a depression score and a mania score. The

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CGI in this study used the severity of disease (CGI-BP-S) at study day 1 as the anchor point and the change from baseline (CGI-BP-C) in subsequent evaluations. Each assessment was intended to measure the change from the study start. The severity of disease (baseline) was similar between groups (Uridine = 4.48; Placebo = 4.68, n.s.), which are similar in magnitude to published efficacy trials in bipolar I depression (Brown et al., 2006, J. Clin. Psychiatry, 67:1025-33; Calabrese et al., 1999, J. Clin. Psychiatry, 60:79-88; Thase et al., 2006, J. Clin. Psychiatry, 26:600-609; Tohen et al., 2003, Arch. Gen. Psychiatry, 60:1079-88; Goldberg et al., 2007, Am. J. Psychiatry, 164:1348-55; Nierenberg et al., 2006, Am. J. Psychiatry, 163:210-216). The mean CGI-BP-C (overall) and CGI-BP-C (depression) for RG2417 in comparison to placebo is shown in Table 2, below. The primary outcome for CGI is the difference between RG2417 and placebo using MERM analysis of the treatment period. There was a significant difference to the change in CGI associated with RG2417 treatment ($p = 0.044$).

Similar to the MADRS evaluations, the greatest difference in treatment occurred at weeks 3 and 4, with some erosion in the separation of the two groups at weeks 5 and 6, predominantly due to increase in placebo response. Comparison between groups of the overall CGI-BP-C showed no single time point with a significant difference between treatment and placebo, however there was a trend towards significance at week 3 ($p = 0.07$). Analysis of the CGI-BP-C depression scale showed a more robust difference between uridine and placebo, achieving significance at week 3 ($p = 0.03$) and week 4 ($p = 0.05$).

Table 2. Average clinical global impression of change for bipolar disorder (CGI-C-BP)

	CGI-C-BP (Overall)[1]			CGI-C-BP (Depression)[2]		
Time	Placebo	RG2417	p	Placebo	RG2417	P
Wk 1	3.20	3.19	0.98	3.10	3.05	0.86
Wk 2	3.05	2.92	0.58	3.03	2.72	0.23
Wk 3	2.97	2.45	0.07	2.94	2.31	0.03
Wk 4	2.70	2.33	0.21	2.67	2.10	0.05
Wk 5	2.44	2.31	0.64	2.41	2.14	0.34

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Wk 6	2.43	2.21	0.52	2.43	2.03	0.27
p-value[3]	0.044			0.029		

[1]CGI-C-BP is scored as the change from baseline (Study Day 1) on a 7-point scale: 1- very much improved, 2- much improved, 3- minimally improved, 4- no change, 5- minimally worse, 6- much worse, 7- very much worse.
[2]CGI-C-BP for depression is the specific evaluation of the effect of treatment on the clinical symptoms of depression.
[3]Mixed effects repeat measure from study day 1 to day 43.

The mean CGI-BP-C over the study period for uridine and placebo is shown also in Figure 2. The magnitude of the difference between groups is shown by the boxes at each time point. The magnitude of response appeared to be attained by week 4 for the uridine treatment and remained stable over the remainder of the study. The weeks 5 and 6 CGI-C assessments again revealed an increase in the placebo response, which reduced the overall difference in treatment effect at the later time points. A difficulty in the methodology of the CGI-C-BP was that the anchor point is at study start and so sequential assessments are incrementally more removed from the rating benchmark.

The mean change in the YMRS assessment of uridine treated subjects in comparison to placebo was also observed. The baseline evaluation at study day 1 showed a significant difference ($p = 0.01$) with the uridine group having a higher initial mean score. Although the difference at baseline makes comparative interpretation difficult, it is apparent that uridine treatment did not exacerbate the mean YMRS, as there were no visits on treatment in which the mean values exceeded the baseline value, in contrast to placebo in which 2 of the 6 mean weekly YMRS scores were mildly increased. Analysis using MERM while on treatment showed a significant decrease in the YMRS from baseline for uridine-treated subjects in comparison to placebo ($p = 0.025$).

The effect on anxiety in uridine-treated bipolar I depression subjects in comparison to placebo was evaluated using the mean HAM-A scores for each group. There was no single time point for which the mean HAM-A score was significantly different between groups. Likewise, there was no difference between groups over the treatment period using MERM analysis.

The response of bipolar I subjects with a history of 15 or more episodes of depression were analyzed by comparison of the mean MADRS score to placebo during the trial. This criterion was intended to analyze the response in individuals with a history

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of a more severe disease course. The overall response to treatment and the difference from placebo was greater for subjects with a greater history of depression (Fig. 3). The true difference in mean between groups is 6.35 at week 6, compared to 3.04 for the total score. The major component of this difference is in the placebo arm, in which the scores are less robust compared to the total group. For example, at study end (week 6) the placebo response in this subset was 36% (change from baseline), in comparison to 47% for the total efficacy cohort. The treatment response at study end was 58% for both the subset and the total group. The effect size ranges from 0.53 to 1.09 for weeks 3 to 6 in this subset. Clinical assessments were significant different between groups at week 4 and trend towards significance at week 3 and 5.

Subjects with a history of illness with fewer depressive episodes were also analyzed for efficacy response. This subset consisted of the remaining 49 subjects with <15 historic episodes of depression, of which the majority (34) had just 1-5 total episodes. This subset had no appreciable difference in mean MADRS scores between treatment and placebo groups (Fig. 4). The placebo response was extremely large, accounting for a 62% change from baseline at study end. The uridine group had a 58% improvement from baseline which was similar to the change in the overall scores.

Similar results were seen at a threshold of five or ten episodes of depression (Figs. 5-6. Patients with more than five episodes of depression over their entire life ($n = 50$) demonstrated greater improvements in their symptoms of depression compared to patients with 5 or fewer episodes of depression over their entire life. From weeks 2-6 of treatment, the patients with more than 5 episodes of depression over their entire life who received uridine had an average improvement on MADRS of 5.5 points over placebo ($p < 0.001$), compared to all patients in the study receiving RG2417 who had an average improvement on MADRS of 3.0 points over placebo ($p = 0.01$).

The response of bipolar I subjects with a history of 15 or more episodes of mania and/or hypomania were analyzed by comparison of the mean MADRS score to placebo during the trial. This criterion was intended to analyze the response in individuals with a more severe disease course. There was a large overlap with subjects in the depression severity subset, i.e., severe subjects tended to have many episodes of both depression and mania/hypomania. The overall response to treatment and the difference from placebo

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was greater for the subset of subjects with a greater history of mania and hypomania. The true difference in mean between groups was 9.46 at week 6, compared to 3.04 for the total score (Fig. 7). This difference was due to both a larger treatment response and a smaller placebo response than the total group.

Similar results were obtained when the response of bipolar I subjects with a history of 2 or more or 5 or more episodes of mania were analyzed by comparison of the mean MADRS score to placebo during the trial. The overall response to treatment and the difference from placebo was also greater for these subsets of subjects. The true difference in mean between subjects with a history of 2 or more episodes of mania as compared to placebo was 5.7 at week 6, compared to 3.04 for the total score (Fig. 8). No positive response was observed in patients with a history of fewer than 2 episodes of mania (Fig. 9). The true difference in mean between subjects with a history of 5 or more episodes of mania as compared to placebo was 5.88 at week 6, compared to 3.04 for the total score (Table 3).

Table 3. Improvement in MADRS score for patients with 5 or more manic episodes

Day	≥5 Episodes	<5 Episodes
	Improvement (Uridine vs Placebo)	
1	0.37	-0.64
8	1.63	-3.57
15	4.41	-1.39
22	6.33	-1.20
29	7.07	-1.76
36	3.20	-4.62
43	5.88	-6.56

OTHER EMBODIMENTS

A number of embodiments of the invention have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the invention. Accordingly, other embodiments are within the scope of the following claims.

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WHAT IS CLAIMED IS:

1. A method of treating an individual diagnosed with bipolar disorder, the method comprising:

determining the number of manic episodes experienced by an individual exhibiting one or more symptoms of bipolar disorder; and

if the number of manic episodes is 2 or greater, administering to the individual an effective amount of a uridine composition.

2. The method of claim 1, wherein if the number of manic episodes is fewer than 2, a uridine composition is not administered to the individual.

3. The method of claim 1 or 2, wherein an effective amount of the uridine composition provides about 1 to 50 mg of a uridine composition/kg of body weight/day.

4. The method of claim 1 or 2, wherein an effective amount of the uridine composition provides about 3 to 10 mg of a uridine composition/kg of body weight/day.

5. The method of claim 1 or 2, wherein the individual is diagnosed under DSM-IV guidelines as having bipolar disorder and wherein an effective amount of the uridine composition comprises between 250 and 2000 mg of uridine composition/day.

6. The method of claim 1 or 2, wherein the composition is administered in two or three doses/day.

7. The method of claim 1 or 2, wherein the composition is uridine, triacetyl uridine, uridine monophosphate, uridine diphosphate, or uridine triphosphate.

8. A method of claim 1 or 2, wherein an effective amount of the uridine composition is administered orally.

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9. A method of selecting an individual for treatment of bipolar disorder, the method comprising:

evaluating whether an individual exhibits one or more symptoms of bipolar disorder;

determining the number of manic episodes experienced by the individual; and

selecting the individual for treatment with a uridine composition if the number of manic episodes is 2 or greater.

10. The method of claim 9, wherein the method comprises selecting the individual for treatment with a uridine composition only if the number of manic episodes is 2 or greater.

11. Use of a uridine composition in the preparation of a medicament for the treatment of bipolar disorder with a history of two or more episodes of mania.

12. Use of a uridine composition for the treatment of bipolar disorder with a history of two or more episodes of mania.

13. A method of treating an individual diagnosed with bipolar disorder, the method comprising:

determining the number of manic episodes experienced by an individual exhibiting one or more symptoms of bipolar disorder;

determining the number of depressive episodes experienced by the individual; and

if the number of manic episodes is 2 or greater and the number of depressive episodes is 5 or greater, administering to the individual an effective amount of a uridine composition.

14. The method of claim 13, wherein if either the number of manic episodes is fewer than 2 or the number of depressive episodes is fewer than 5, a uridine composition is not administered to the individual.

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15. A method of selecting an individual for treatment of bipolar disorder, the method comprising:

evaluating whether an individual exhibits one or more symptoms of bipolar disorder;

determining the number of manic episodes experienced by the individual;

determining the number of depressive episodes experienced by the individual; and

selecting the individual for treatment with a uridine composition if the number of manic episodes is 2 or greater and the number of depressive episodes is 5 or greater.

16. Use of a uridine composition in the preparation of a medicament for the treatment of bipolar disorder with a history of two or more episodes of mania and five or more episodes of depression.

17. Use of a uridine composition for the treatment of bipolar disorder with a history of two or more episodes of mania and five or more episodes of depression.

18. A method of evaluating a candidate treatment for bipolar disorder, the method comprising:

obtaining a population of individuals that exhibit one or more symptoms of bipolar disorder;

determining the total number of manic episodes experienced by each individual;

selecting a subpopulation of the population of individuals for whom the total number of manic episodes is 2 or greater; and

administering a candidate treatment for bipolar disorder to the subpopulation.

19. A method of evaluating a candidate treatment for bipolar disorder, the method comprising:

obtaining a population of individuals that exhibit one or more symptoms of bipolar disorder;

determining the total number of depressive episodes experienced by each individual;

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selecting a subpopulation of the population of individuals for whom the total number of depressive episodes is 5 or greater; and

administering a candidate treatment for bipolar disorder to the subpopulation.

20. A method of evaluating a candidate treatment for bipolar disorder, the method comprising:

obtaining a population of individuals that exhibit one or more symptoms of bipolar disorder;

determining the total number of manic episodes experienced by each individual;

determining the total number of depressive episodes experienced by each individual;

selecting a subpopulation of the population of individuals for whom the total number of manic episodes is 2 or greater and the total number of depressive episodes is 5 or greater; and

administering a candidate treatment for bipolar disorder to the subpopulation.

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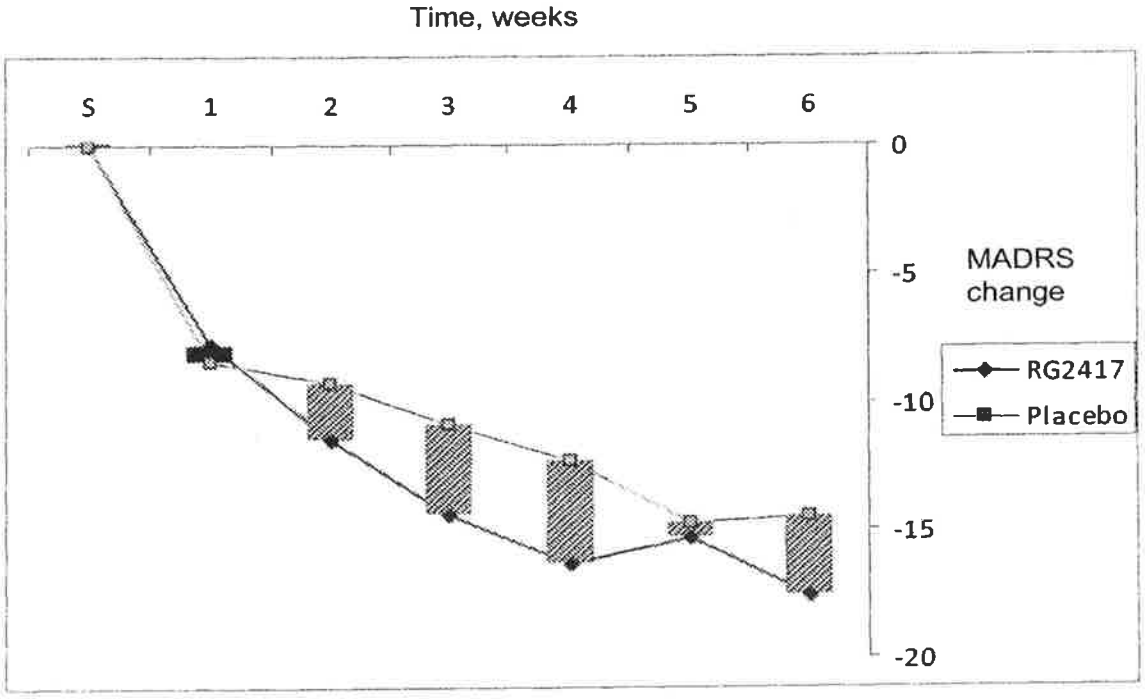


FIG. 1

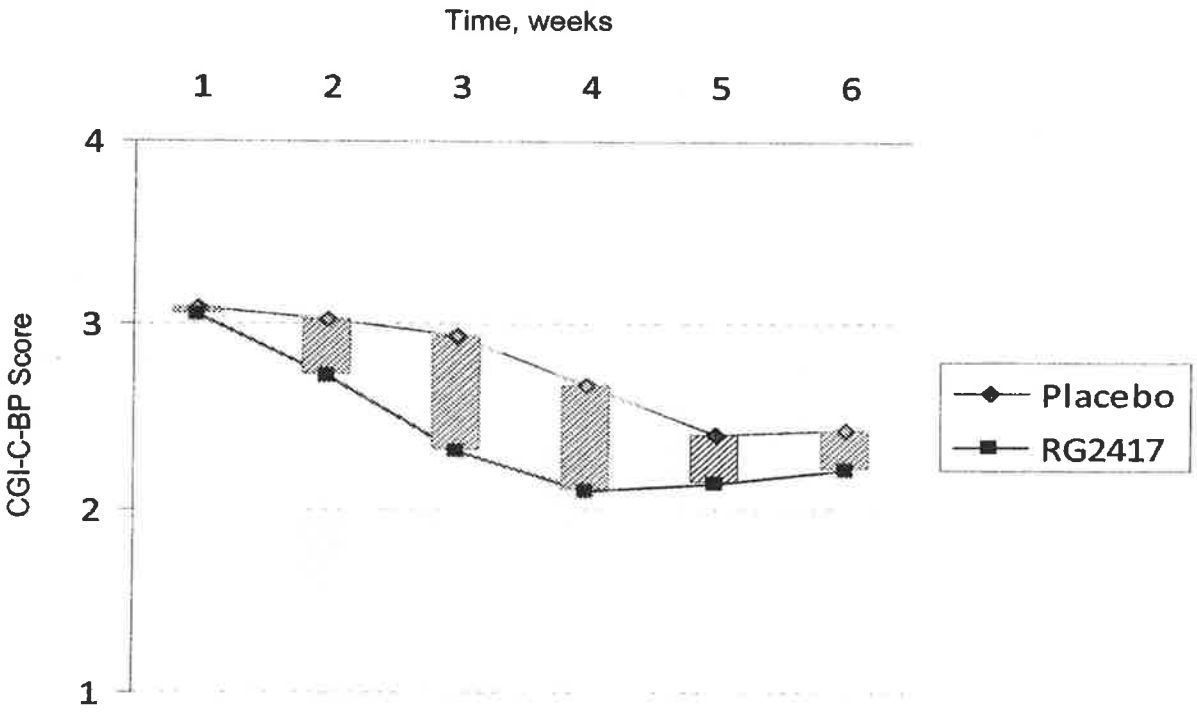


FIG. 2

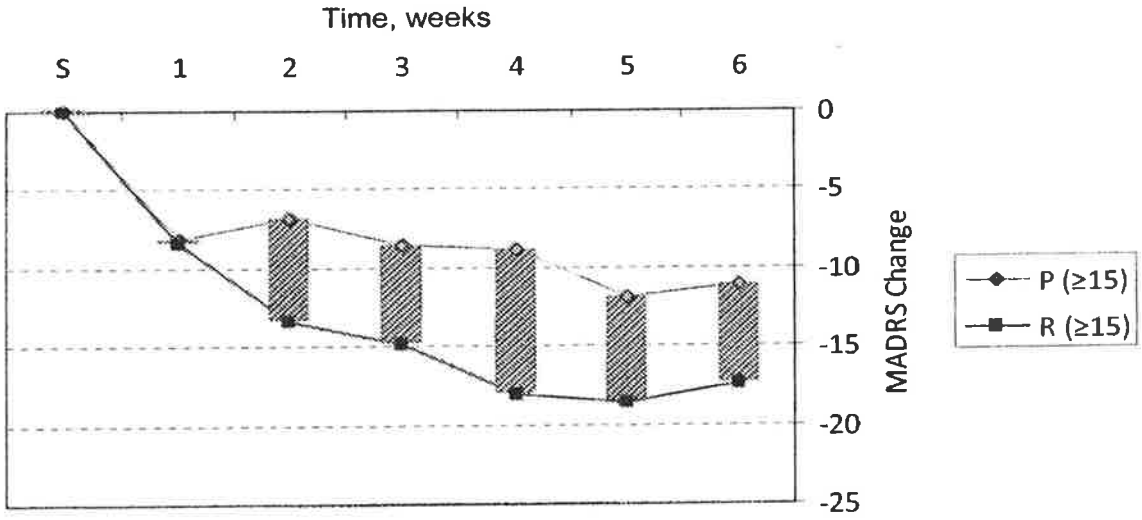


FIG. 3

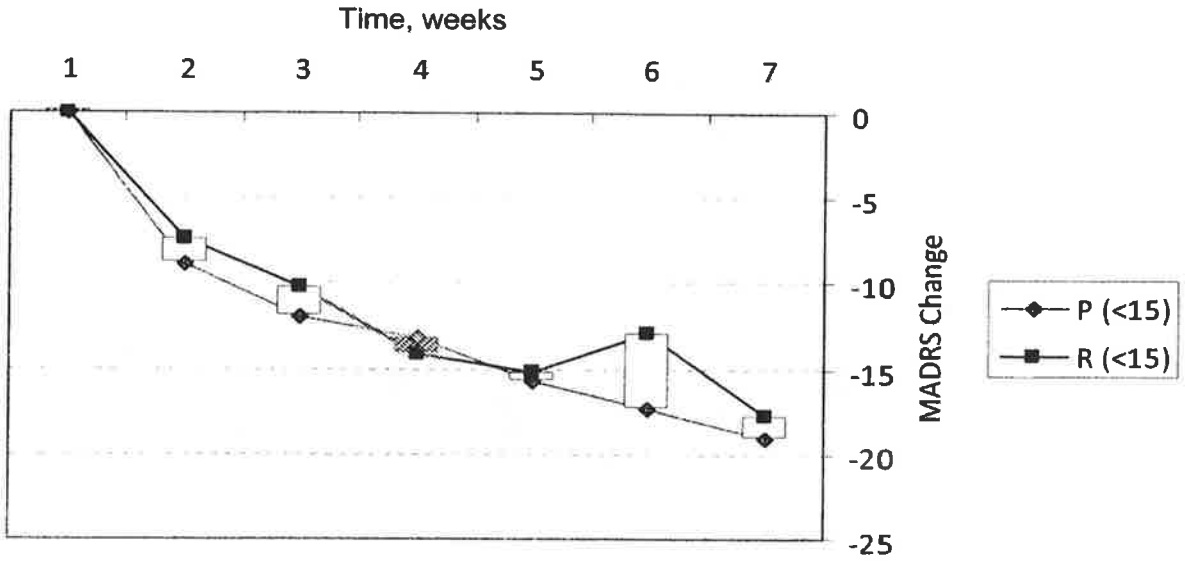


FIG. 4

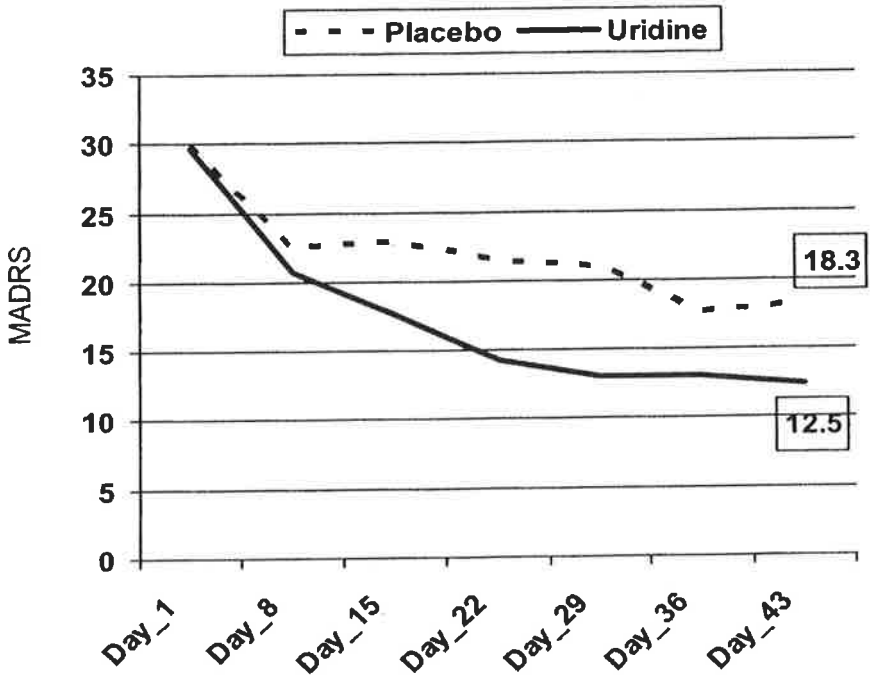

Placebo
Uridine
MADRS
35
30
25
20
15
10
5
0
18.3
12.5
Day_1
Day_8
Day_15
Day_22
Day_29
Day_36
Day_43

FIG. 5

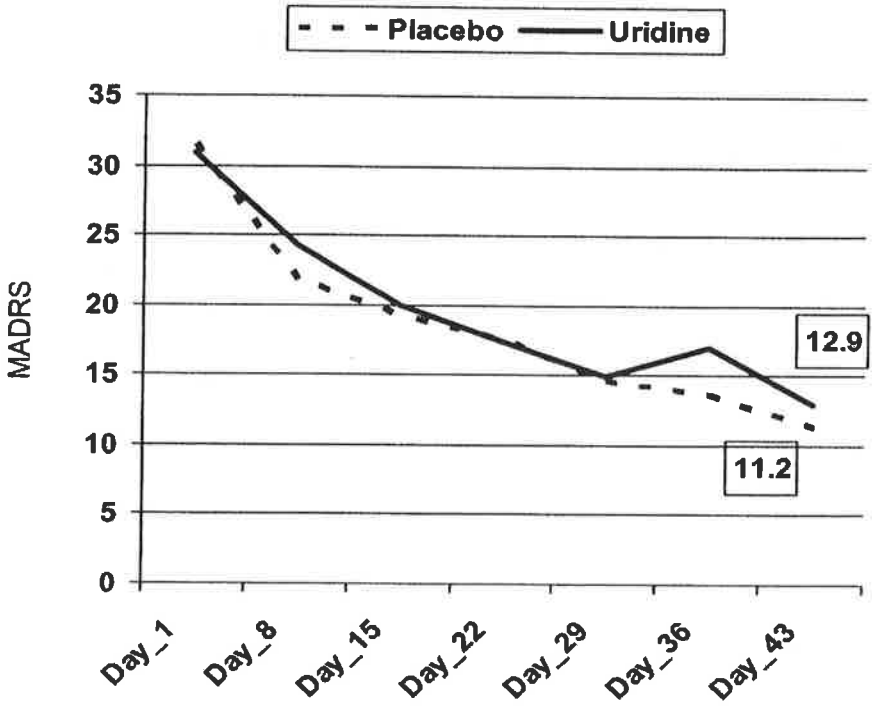

Placebo
Uridine
MADRS
35
30
25
20
15
10
5
0
12.9
11.2
Day_1
Day_8
Day_15
Day_22
Day_29
Day_36
Day_43

FIG. 6

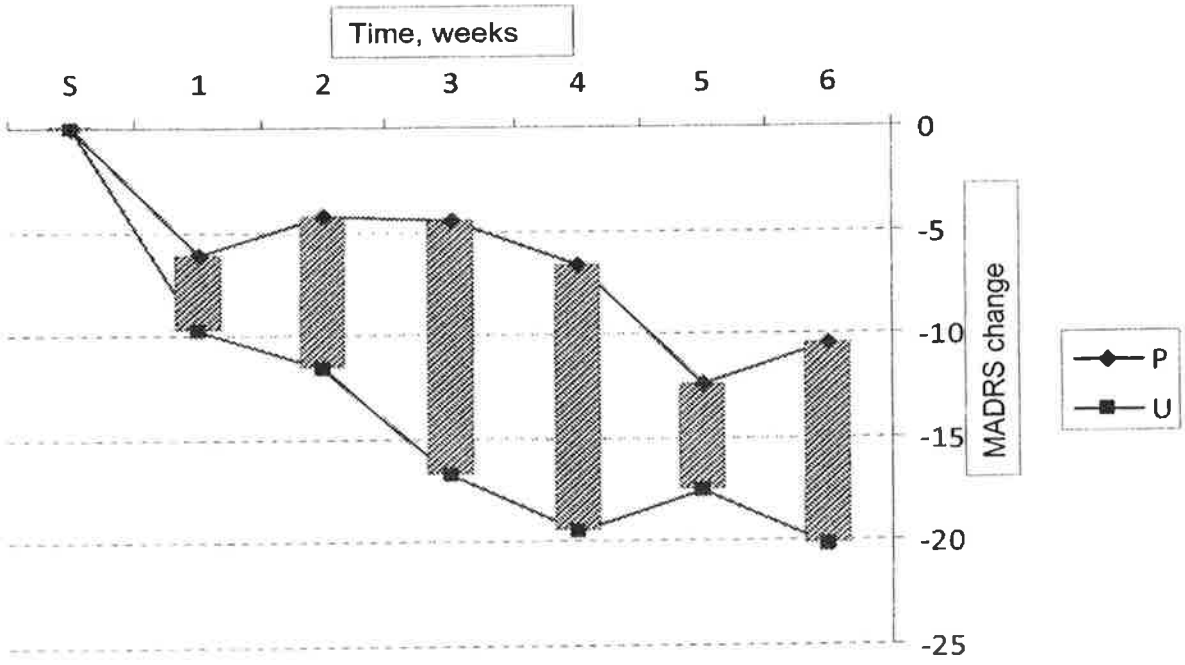


FIG. 7

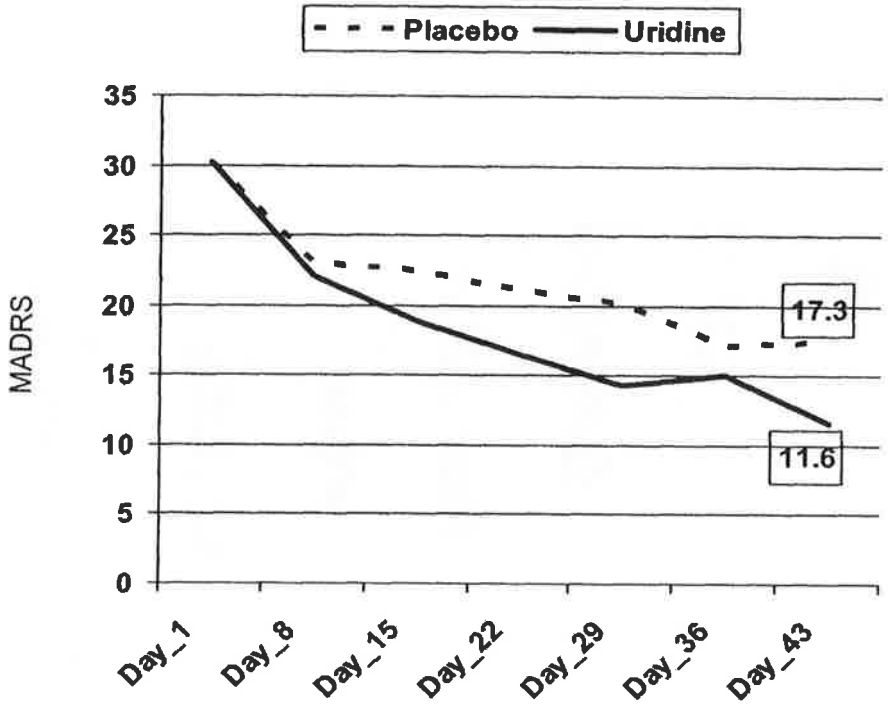

Placebo
Uridine
MADRS
35
30
25
20
15
10
5
0
17.3
11.6
Day_1
Day_8
Day_15
Day_22
Day_29
Day_36
Day_43

FIG. 8

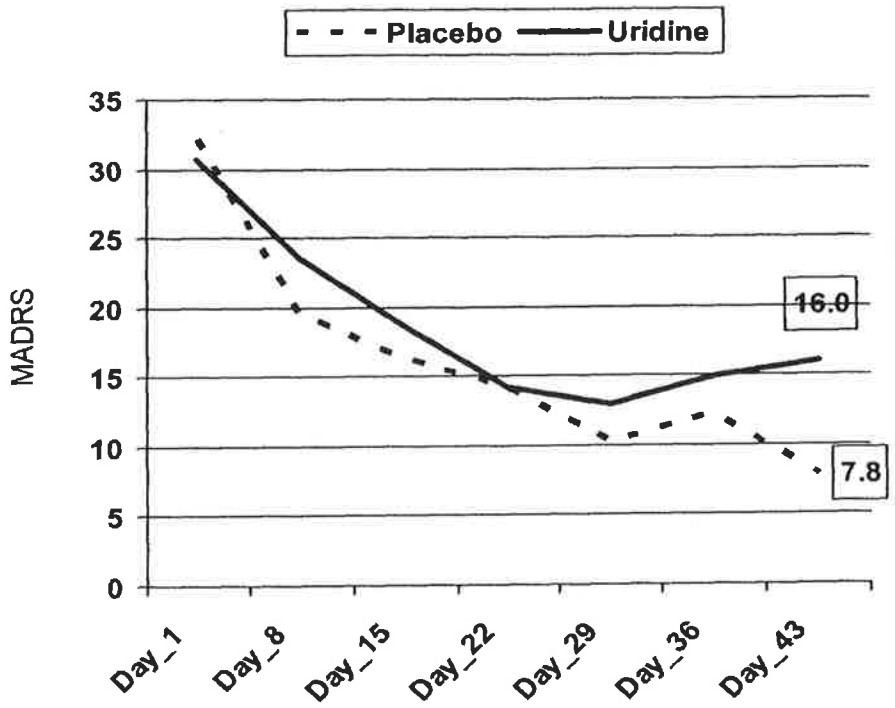

Placebo
Uridine
MADRS
35
30
25
20
15
10
5
0
16.0
7.8
Day_1
Day_8
Day_15
Day_22
Day_29
Day_36
Day_43

FIG. 9

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(54) Title: USE OF THE PROTEIN KINASE C INHIBITOR TAMOXIFEN FOR THE TREATMENT OF BIPOLAR DISORDER

(57) Abstract: Bipolar subjects with manic/mixed episode were randomly assigned to receive either tamoxifen (80mg/day) or identical placebo tablets in 1:1 ratio for three weeks. At the end of three weeks of trial tamoxifen treatment has been shown to have strong anti-manic properties. Protein kinase C inhibition seems to be one of the direct targets of lithium and valproate, The existing effective treatments in bipolar disorder/mania. These findings may lead to delineation of the underlying pathophysiology of bipolar disorder and development of novel therapeutics.

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USE OF THE PROTEIN KINASE C INHIBITOR TAMOXIFEN FOR THE TREATMENT OF BIPOLAR DISORDER

FIELD OF INVENTION:

In this study, Tamoxifen citrate has been compared to placebo for treatment of acute mania. Tamoxifen (Gador® OR Nolvadex®) is widely used for prophylaxis and treatment of breast cancer, and it's mechanism of action has similarities to the mechanism of action of Lithium and Valproate, which are the standard treatments for bipolar disorder/mania. For this reason it has been thought that Tamoxifen may also have an antimanic effect in bipolar patients. In this trial we aimed to investigate the antimanic effects of Tamoxifen in a large sample, which includes 50 bipolar patients. According to the findings of this study, there will be a significant progress in the understanding and treatment of bipolar illness.

Among the other treatment alternatives we have lithium and valproate as the most commonly used standard treatments for bipolar disorder. These drugs are known as the mood stabilizers, and they have the greatest success rates in treatment of bipolar illness among the existing treatment strategies. However, a significant amount of bipolar patients either fail to respond the standard treatments with lithium and/or valproate or respond only partially. For this reason, new and better treatment strategies for bipolar disorder need to be developed by the researchers. This study is designed to serve for that purpose and will have a significant contribution on the progress of science for bipolar disorder.

Background of the Invention:

Bipolar disorder (BD) is a chronic mental illness that affects 1-2% of the adult population[1,2] and is associated with a substantial risk of suicide among those affected[1,3].

Although, the efficacy of lithium and more recently valproate as mood stabilizing agents have generated a large body of clinical and experimental findings in BD, it has become increasingly appreciated that a substantial minority of patients fail to respond, or respond only partially, to these agents.[4,5] Thus, a critical task

becomes the development of newer therapeutic agents that will have a quicker, more potent, and more specific mode(s) of action with fewer side effects.[4]

While precise mechanisms underlying this disorder that affects millions is yet to be delineated, it has become increasingly clear that elucidation of the signaling pathways affected in BD will greatly facilitate not only the development of novel, improved therapeutics but our understanding of the pathophysiology underlying this intriguing disorder. [4]

It is known that signaling pathways are in a pivotal position in the brain, and they affect the functional balance between multiple neurotransmitter systems. Thus, it is likely that dysregulation of cellular signaling networks in the brain underlies the oscillations observed in mood disorders (such as the disruption of sleep and motor, cognitive and psychological function), and the so-called mood stabilizers work by compensating for this dysregulation in critical regions of the brain. [6] In keeping with this, recent findings from in vivo proton magnetic resonance spectroscopy studies suggest that while inhibition of inositol monophosphatase (IMPase) may represent an initiating lithium effect, reducing myo-inositol levels per se is not associated with therapeutic response.[7,8] Accordingly, it is likely that some of the initial actions of lithium may occur with a relative reduction of myo-inositol; this reduction of myo-inositol initiates a cascade of secondary changes in the protein kinase C (PKC) signaling pathway and gene expression in the brain, effects that are ultimately responsible for lithium's mood stabilizing efficacy.[7,8] Indeed, evidence accumulating from various laboratories has clearly demonstrated that lithium, at therapeutically relevant concentrations, exerts major effects on the PKC signaling cascade.[4, 9-11] PKC exists as a family of closely related subspecies, has a heterogeneous distribution in brain (with particularly high levels in presynaptic nerve terminals), and plays a major role in the regulation of neuronal excitability, neurotransmitter release, long-term alterations in gene expression and plasticity. Recently, it has been shown that chronic lithium produces izozyme-selective decreases in PKC α, and PKC ε. Moreover, it has been found that the structurally highly dissimilar, second mood stabilizer agent- valproate produces effects on the PKC signaling pathway that are strikingly similar to those of lithium's.[4,11,12] Additionally, it has been

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demonstrated that chronic lithium and also valproate dramatically reduce myristtoylated alanine-rich C kinase substrate (MARCKS), which is the most prominent substrate for PKC in brain, and implicated in regulating long-term neuroplastic events.[12,13]

There exist other direct and indirect evidence supporting a role for PKC in pathophysiology and treatment of bipolar disorder. Friedman and associates (1993), investigated PKC activity and translocation in response to serotonin in platelets obtained from bipolar disorder subjects before and during lithium treatment.[14] They found that the ratios of membrane-bound to cyctosolic PKC activities were elevated in platelets obtained from the manic subjects, compared with patients with schozophrenia and healthy controls. In addition, serotonin stimulated platelet PKC translocation was found to be enhanced in manic subjects. Moreover, lithium treatment for up to 2 weeks resulted in reduction in cytosolic and membrane-associated PKC activities and in an attenuated PKC translocation in response to serotonin. Recently, same laboratory found elevated levels of some PKC izosymes in brains obtained at postmortem from bipolar disorder patients compared to controls.[15,16]

Regulation of the levels of PKC α and ε in areas of rat brain by typical and atypical antipsychotics; increments in PKC activity by amphetamine; and blockade of the biochemical and behavioral responses to amphetamine and cocaine by PKC inhibitors are the other findings implicating PKC signaling system in the pathophysiology of BD.[4,6]

Based upon the above documented evidence suggesting involvement of protein kinase C signaling pathway in BD, Bebchuk JM et al (2000), have postulated that the attenuation of protein kinase C activity might play a major role in the antimanic effects of lithium and valproate and undertook a pilot feasibility study to test the hypothesis that a direct PKC inhibitor would possess antimanic efficacy.[17] In a single blind pilot (only 7 patients; single blind and underpowered) study of a protein kinase C inhibitor-tamoxifen in treatment of acute mania, they reported significant (in some case rapid and striking) improvement of manic symptoms in 5-14 days. The tamoxifen was well tolerated; only one patient has reported any adverse effects attributable to the medication, namely mild flushing

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on dose titration.[17]

Tamoxifen citrate is the only relatively selective PKC inhibitor available for human use. It is a synthetic nonsteroidal antiestrogen, has been widely used in the treatment of breast cancer.[18] Many of its effects are clearly due to estrogen receptor antagonism[18] but it is also a potent protein kinase C inhibitor[19-21] that crosses the blood-brain barrier[19]. Other than Bebchuk and colleague's study, there have been no previous published studies designed to specifically investigate the potential mood altering effects of tamoxifen, although mild to moderate depression has been described in patients receiving long term tamoxifen for breast cancer.[22]

Placebo-controlled, double-blind, randomized clinical trials have been recognized as the standard by which to establish a drug's safety, efficacy, and dose-relationships in most major psychiatric illnesses.[23] The justifications for using placebo control groups in such trials are the fluctuating natural course of most psychiatric illnesses, the wide variability in placebo response across patient groups, and the influence of psychosocial factors on treatment response.[24,25] There have been four potential alternatives to use of placebo control group proposed in studies of acute mania.[26,27] These are add-on studies, variable dose designs, establishing a priori threshold effect size with active comparison control, and comparisons with historical controls. However, as recently reviewed by Keck and colleagues (2000), mania is in fact associated with substantial placebo response and placebo-controlled studies are a viable and necessary standard by which to develop new antimanic agents.[23] The authors conclude that randomized, double blind, placebo controlled, parallel group trial in acute bipolar mania remains the "GOLD STANDARD" to determine whether a drug has antimanic properties.[23] After the Helsinki Declaration, in recent years, experts in the field have clearly stated the exceptionality of the psychiatric field in terms of placebo use by emphasizing the necessity of placebo control especially in the clinical trials of mania and depression in an evidence based manner.

Moreover, providing that a drug is efficacious in acute bipolar mania has classically been the first step in determining whether a drug is a mood stabilizer. The optimum duration of acute mania trials is unclear. However, in all the positive

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studies to date drug separation from placebo have occurred by day 7 to 21. Thus, there seems little justification for extending a placebo-controlled study in patients with acute mania beyond 21 days.[23] In this study we proposed a 3 week randomized double blind trial of tamoxifen-citrate or identical appearing placebo treatment in acute mania or mixed states in adults with Bipolar I Disorder. By providing data derived from the physiological response of the system (PKC signaling cascade) in affected individuals and addressing the critical dynamic interaction with a pharmacologic agent that may potentially modify the clinical expression of the pathophysiology; this tamoxifen-citrate trial in acute mania will be a promising step in bipolar research.

Recently, our group has detected several factors for which bipolar women seemed to have higher vulnerability than bipolar men. These are;

1. Lifetime history of psychosis was found to be more common in bipolar women[41]
2. Bipolar women who were exposed to antidepressant drugs before their first manic/hypomanic episode had higher rates of rapid cycling than the ones who were not, whereas there was no such association in bipolar men[42]
3. We found a significant association between rapid cycling and early age of onset in bipolar females but not in males. Rapid cycling was more common in women than men[43]

Given the antiestrogen effect of tamoxifen in the light of the above findings it will be interesting to look for any possible effect of gender in treatment response, since bipolar women may benefit from the antiestrogen effect in addition to the PKC inhibition.

SUMMARY OF THE INVENTION

Method:

Subjects are 50 adults diagnosed with bipolar affective disorder by using DSM-IV criteria, most recent episode manic or mixed, with or without psychotic features. All the diagnosis is based on the Structured Clinical Interview for the DSM-IV, administered by a trained investigator (PI).

A minimum total score of at least 20 on the Young-Mania Rating Scale (Y-MRS)[28] are required at the screening visit and on the day of randomization

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(baseline).

After the protocol explained to the bipolar patient to be included in the trial and their at least one first degree relative, patient and the relative are asked to give written informed consent for participation in the protocol.

Subject screening includes medical and psychiatric history, physical examination, and laboratory screen including LFT's, TSH, HCG, BUN, Cr, and serum toxicology. Blood samples are collected from the patients included in the study for the measurements of the PKC activity and PKC translocation in response to serotonin under the influence of tamoxifen at baseline and after the first week of treatment. To evaluate the brain chemistry of the patients, magnetic resonance imaging/spectroscopy are applied to the study patients under the influence of midazolam/fentanil sedation both in the manic state at baseline and study end point as well as after eutyhmia has been achieved. All psychotropic medication therapy (except benzodiazepines) are tapered during the screening period and discontinued at least 1 day before randomization.

Subjects successfully screened who meet inclusion and exclusion criteria are randomly assigned to receive the protein kinase C inhibitor, tamoxifen or identical placebo tablets in a 1:1 ratio and a double blind fashion for 3 weeks. Computer-generated codes are used to create randomized blocks of clinical trial material kits before study startup (randomization blocks are prepared by the ARGEFAR, a contract research organization). Each kit contains all clinical trial material to be used by a patient throughout the 3-week study. The starting dose of tamoxifen is 20 mg bid. After the first day of therapy, daily dose is adjusted upward, by 10 mg increments per day up to 80 mg/d in divided doses. Similar daily dose adjustments are applied for the placebo group. Concomitant use of lorazepam is allowed during double blind therapy as clinically indicated. Lorazepam use is avoided after the initial 12 days after randomization, whenever possible. Subjects are monitored weekly during the 3 week double blind trial. Young Mania Rating Scale (YMRS), Clinical Global Impressions-Biopolar Version of Severity of Ilness (CGI-BP) [29] mania score, Hamilton Depression Rating Scale (HAM-D)[30] and Positive and Negative Syndrome Scale (PANSS)[31], and side effect questionnaire (SEs) are administered by semi-structured interviews at each week.

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Inclusion Criteria:

1. Diagnosis of bipolar affective disorder I, most recent episode, manic or mixed based on the structural clinical interview for DSM-IV
2. Ages 18-65
3. Young Mania Rating Score > 20 at screening and baseline
4. Providing informed consent

Exclusion Criteria:

1. Currently pregnant, planning to become pregnant, or breast feeding
2. History of any coagulopathies, deep vein thrombosis, pulmonary embolus[32-29]
3. A history of hypersensitivity to tamoxifen
4. Drug screen positive for any drug of abuse at screening, active substance abuse in the past 2 weeks or substance dependence in the past 2 months (except nicotine and caffeine)
5. Diagnosis of schizophrenia, dementia, delirium, seizure disorder, obsessive compulsive disorder, or major cardiac, hepatic or renal disease that is unstable or that requires constant medical care
6. Administration of any investigational drug in the last 30 days
7. Clinically significant suicidal or homicidal ideation

Outcome Measures:

Assessment tools include Y-MRS, HAM-D, CGI-BP, and PANSS. Responders are defined as those subjects who demonstrate a 50 % or greater improvement over baseline in the Y-MRS score in the 3 week trial. The principle investigator, who is trained in the rating instruments and blind to treatment, performed all study assessments on a weekly basis by using all available clinical information. The primary efficacy variable is defined as the reduction from baseline of the Y-MRS total score after 3 weeks of therapy. Response is defined as at least 50 % improvement from baseline to the endpoint in the Y-MRS total score.

Following hypotheses are proposed to be tested;

1. There will be greater reduction in ratings of manic or mixed mood symptoms with tamoxifen citrate compared to placebo.
2. A greater proportion of subjects will respond to tamoxifen citrate when compared to placebo.

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Statistical methods used:

For the five studies demonstrating lithium superior to placebo in treatment of acute mania pooled response rates indicated that 87 out of 124 patients (70 %) experienced at least partial improvement with lithium.[40] Pooled response rates to valproate from the three double blind, parallel-design trials indicated that 54 % of patients displayed a significant reduction in manic symptoms. Keck et al (2000) reviewed all the acute mania studies to date and reported the mean effect size for drug-treated patients as 0.9-1.1.[23] In the preliminary trial made by Bebchuk et al (2000) response rate to tamoxifen was 71% as defined by at least 50 % reduction in Y-MRS score.[17]

Keck et al in the above mentioned work reported the mean percentage of placebo responders in all studies as 23% with an effect size of 0.4. Analysis of variables potentially associated with placebo response found that presence of patients with rapid cycling course in relatively longer duration trials (via confounding effect of spontaneous remissions), and large multi-center trials (via larger variation in inter rater reliability across many study sites) are the factors contributing to high placebo response in acute mania.[23]

Since this trial involves a single site with a relatively short study period, we were expecting a lower response rate in the placebo arm. Given that all the study assessments were performed by only one investigator (PI who is trained in the rating instruments), washout period was just 24 hours, and majority of patients were severely psychotic, placebo response rate was expected to be even lower. Based on the above documented response rates in the trials of acute mania we have predicted a 55-70% positive response rate in the tamoxifen arm, defined as at least 50 % reduction in Y-MRS score.

Power analysis has revealed that with 25 patients on placebo and 25 patients on tamoxifen there will be an 80% chance of detecting a significant difference at a two sided .05 significance level if the response rate in placebo group is 0.15 and the response rate of tamoxifen is 0.55.

Total scores from rating scales are derived from the individual items; if any single item is missing, the total score is treated as missing. All statistical evaluations are

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made by using SPSS 13.0. Mean baseline scores for each group are compared using the independent samples Student's t test. Lorazepam use in each group is compared on a weekly basis using the independent samples Student's t test. Response rates as defined by ≥ 50% improvement in the Y-MRS scores are compared by using the Chi-Square test. Statistical significance in the change scores of the Y-MRS, HAM-D, CGI-BP, and PANSS within and in between the groups are assessed by using the paired and unpaired samples Student's t test as appropriate. Drug effects are analyzed using repeated measures analysis of variance (ANOVA). Since in this study, most patients could complete the trial, analysis on an 'intent to treat basis' is not required.

Patient population enrolled & baseline characteristics table:

Age:

	Drug	N	Mean	Std. Deviation	Std. Error Mean	Sig. (2-Tailed)
Age	Placebo	21	36,90	12,720	2,776	0,529
	Tamoxifen	29	34,55	13,127	2,438	

Gender:

		Drug		Total
		Placebo	Tamoxifen	
Gender	Female	12	15	27
	Male	9	14	23
Total		21	29	50

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Education:

		Drug	
		Placebo	Tamoxifen
Education	None	0	1
	Primary School	3	1
	Secondary School	1	2
	High School	9	13
	University 2 years	3	1
	University 4 years	4	11
	Degreeafter university	1	0
Total		21	29

Marriage:

		Drug		Total
		Placebo	Tamoxifen	
Marriage	Married	6	13	19
	Single	10	13	23
	Divorced	4	2	6
	Widowed	1	1	2
Total		21	29	50

Current Episode:

		Drug		Total
		Placebo	Tamoxifen	
CurrentEp	Manic Ep	5	11	16
	PsychoticManic Ep	15	17	32
	Mixed Ep	1	1	2
Total		21	29	50

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Baseline Disease Severity for the Study Groups:

	Drug	N	Mean	Std. Deviation
YMRSbaseline	Tamoxifen	29	38,38	5,095
	Placebo	21	34,90	6,441
HAM17baseline	Tamoxifen	29	6,66	4,522
	Placebo	21	5,19	3,341
HAM23baseline	Tamoxifen	29	6,69	4,560
	Placebo	21	5,24	3,330
PANSSbaseline	Tamoxifen	29	67,79	13,415
	Placebo	21	64,38	15,526
Positbaseline	Tamoxifen	29	25,48	6,911
	Placebo	21	23,86	7,303
Negatbaseline	Tamoxifen	29	7,14	,743
	Placebo	21	7,33	1,528
Genelbaseline	Tamoxifen	29	35,17	7,354
	Placebo	21	32,62	7,256
CgiManiabaseline	Tamoxifen	29	5,97	,906
	Placebo	21	5,62	1,071
CgiDepbaseline	Tamoxifen	29	1,41	,907
	Placebo	21	1,19	,680
CgiGenbaseline	Tamoxifen	29	5,66	,721
	Placebo	21	5,48	,928
Age	Tamoxifen	29	34,55	13,127
	Placebo	21	36,90	12,720

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Results:

Efficacy:

Among the 67 patients randomized, 50 (74.6%) completed the three weeks of the trial and adhered to protocol. In the tamoxifen group 14 out of 29 (48%) patients achieved a positive response, defined as ≥ %50 improvement in Young Mania Rating Scale-YMRS, compared to only 1 out of 21 (5%) patients in the placebo group (χ2df,1=9.01, p=0.003). The tamoxifen group had a mean 18.07 (standard deviation, SD=11.21) decrease (t=8.681, df= 28, p< 0.001), whereas the placebo group had a mean 5.19 (SD=9.38) increase (t= -2.535, df= 20, p= 0.02) in YMRS at three weeks compared to baseline. ANOVA repeated measures indicated significance for change in YMRS and Clinical Global Impressions-CGI mania with respect to time between tamoxifen and placebo groups (F=13.584, p= 0.001; F=6.427, p= 0.015, respectively).

Response Rate according to the YMRS (≥ 50 improvement over baseline in the YMRS score):

	Drug		Total
	Placebo	Tamoxifen	
ResponseRateYMRS	20	15	35
	1	14	15
Total	21	29	50

Lorazepam use for the study groups:

	Drug	N	Mean	Std.Deviation	Sig. (2-tailed)
Lorazepam 1stweek	Tamoxifen	29	6,069	4,3337	0,270
	Placebo	21	7,595	5,3189	
Lorazepam 2ndweek	Tamoxifen	29	3,414	2,4314	0,046
	Placebo	21	5,976	5,2021	
Lorazepam 3dweek	Tamoxifen	29	,569	1,2154	0,005
	Placebo	21	5,310	6,8983	

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Table 1: Baseline and endpoint (end of 3 weeks) Young Mania Rating Scale (YMRS), Positive and Negative Syndrome Scale (PANSS), Positive Syndrome Scale, Clinical Global Impressions (CGI)-Mania, and Hamilton Depression Rating Scale (HAMD) scores of manic patients in tamoxifen and placebo arms. Δ= Change in score.

Assessment tool	***Tamoxifen N=29 Scores (Baseline) vs Scores (3 week)***	***Placebo N=21 Scores (Baseline) vs Scores (3 week)***	***Statistical Method Used***	***Statistical Test Value***	***P value***
YMRS	38.38 ± 5.1 vs 20.31 ± 11.2	34.90 ± 6.4 vs 40.1 ± 10.4	Paired t test for Tamoxifen group	t=8.681, df=28	p< 0.001
			Paired t test for Placebo group	t=-2.535, df=20	p= 0.02
ΔYMRS	18.07 ± 11.2	- 5.19 ± 9.38	Independent samples t test	t=7.74, df= 48	p< 0.001
YMRS (at baseline, week 1, 2, and 3; only baseline & week 3 is given here)	38.38 ± 5.1 vs 20.31 ± 11.2	34.90 ± 6.4 vs 40.1 ± 10.4	ANOVA Repeated Measures	F= 13.584	p= 0.001
PANSS (at baseline, week 1, 2, and 3; only baseline & week 3 is given here)	67.79 ± 13.4 vs 47.83 ± 13.5	64.38 ± 15.5 vs 76.86 ± 21.2	ANOVA Repeated Measures	F= 9.628	p= 0.003
Positive Symptom Scale (at baseline, week 1, 2, and 3; only baseline & week 3 is given here)	25.48 ± 6.9 vs 15.14 ± 7.0	23.86 ± 7.3 vs 29.48 ± 11.1	ANOVA Repeated Measures	F= 9.642	p= 0.003

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CGI-Mania(at baseline, week 1, 2, and 3; only base-line & week 3 is given here)	5.97 ± 0.9 vs 3.72 ± 1.7	5.62 ± 1.1 vs 5.95 ± 1.4	ANOVA Repeated Measures	F= 6.427	p= 0.015
HAMD-17(at baseline, week 1, 2, and 3; only base-line & week 3 is given here)	6.66 ± 4.5 vs 5.17 ± 5.4	5.19 ± 3.3 vs 5.33 ± 2.4	ANOVA Repeated Measures	F= 0.051	p= 0.822

What new insights this finding brings to the science:

Existing evidence suggests that two structurally dissimilar antimanic agents, lithium and valproate, attenuate Protein Kinase C-PKC function in a therapeutically relevant time frame, whereas promanic psychostimulants activate PKC. Although best known for its antiestrogenic properties, tamoxifen is also a potent PKC inhibitor at high concentrations. This is the first double-blind placebo-controlled study showing antimanic properties of tamoxifen in bipolar patients. This promising finding by leading to elucidation of the direct targets of lithium and valproate offers the potential not only for development of new target specific antimanic agents but also to delineate the underlying pathophysiology of bipolar disorder.

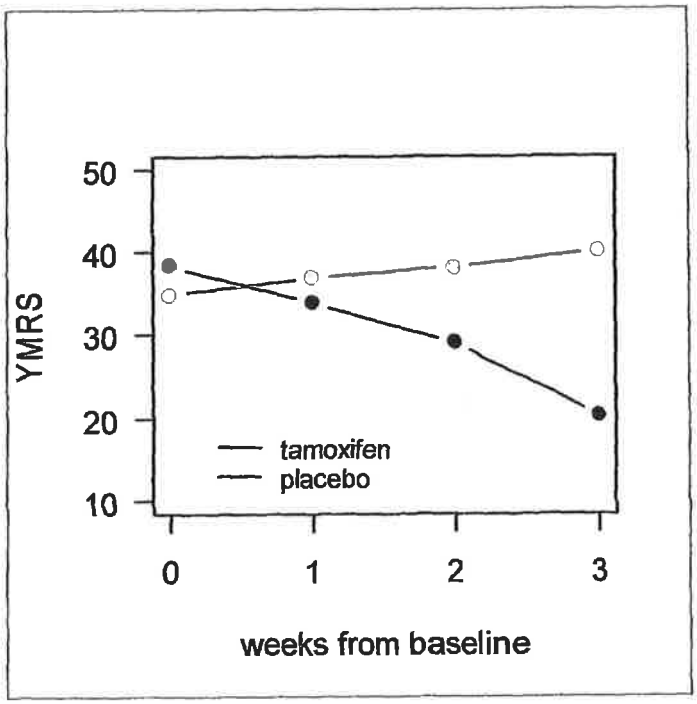
In most instances, an effective agent has first been discovered clinically as in the case with lithium and valproate, and this consequently initiated research into its potential mechanisms of action. Now, this relation became bidirectional, as the PKC inhibitor: tamoxifen, have been tested in acute mania based on the proposed mechanism of action of the existing mood stabilizer drugs. Many pre-clinical studies have priory suggested that PKC signaling is a target of mood stabilizing drugs, however, it has been difficult to establish the clinical relevance of these findings. Now, the present data demonstrating clinical efficacy of a PKC inhibitor-tamoxifen in treatment of bipolar disorder/mania proves that PKC signaling is a target of mood stabilizing drugs and this pathway can be used for development of targeted treatment strategies for bipolar disorder. Eventually,

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targeted treatment strategies for patients with bipolar disorder will be possible.

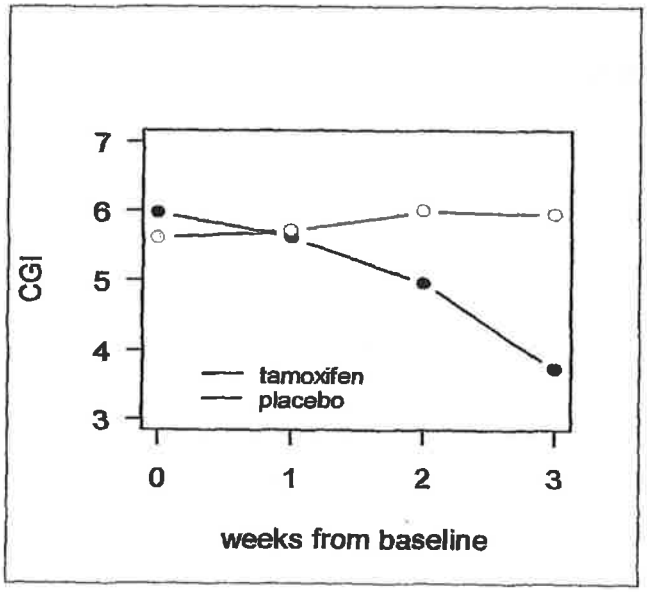
DRAWINGS/FIGURES:

Figure 1.



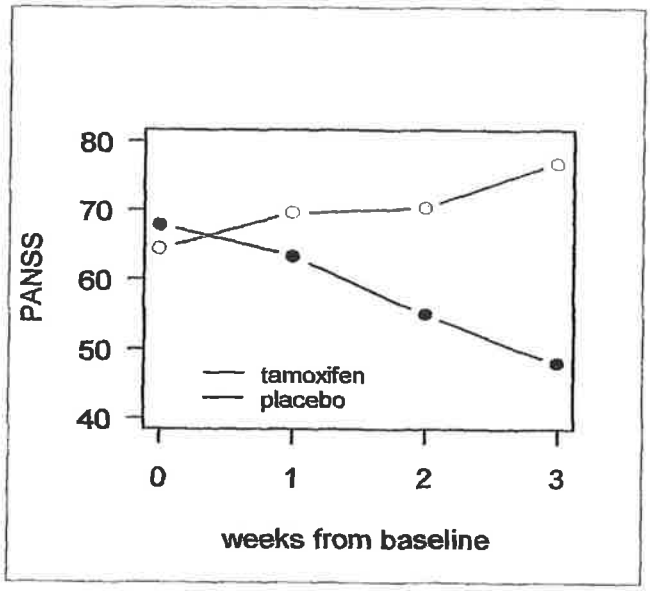
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Figure 2.



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Figure 3.



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Brief Description of the Drawings:

Figure 1. Change in YMRS scores in tamoxifen & placebo groups:
The primary efficacy variable is defined as the reduction from baseline of the Young Mania Rating Scale (YMRS) total score after 3 weeks of therapy. This figure shows that there is greater reduction the YMRS total score measuring manic or mixed mood symptoms in the tamoxifen citrate group as compared to the placebo group.

Figure 2. Change in CGI Mania scores in tamoxifen & placebo groups:
This figure shows that there is greater reduction in the Clinical Global Impressions-Bipolar Version of Severity of Illness (CGI-BP) mania score in the tamoxifen citrate group as compared to the placebo group.

Figure 3. Change in PANSS scores in tamoxifen & placebo groups:
This figure shows that there is greater reduction in the Positive and Negative Syndrome Scale (PANSS) score in the tamoxifen citrate group as compared to the placebo group.

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REFERENCES:

1. Goodwin FK, Jamison KR: Manic-Depressive Illness. New York, Oxford University Press, 1990

2. Weissman MM, Leaf PJ, Tishler GL, Blazer DG, Karno M, Bruce ML, Florio LP: Affective disorders in five United States communities. Psychol Med 1988; 18:141-153

3. Coppen A, Standish-Barry H, Bailey J, Houston G, Silcocks P, Hermon C: Long-term lithium and mortality. 1990; 335:1347

4. Manji HK, Lenox RH: The nature of bipolar disorder. J Clin Psychiatry 2000; 61(suppl 13):42-47

5. Tohen M, Grundy S: Management of acute mania. J Clin Psychiatry 1999; 60(suppl 5):31-34

6. Manji HK, Lenox RH: Signaling: cellular insights into pathophysiology of bipolar disorder. Biol Psychiatry 2000; 48:518-530

7. Moore GJ, Bebchuk JM, Parrish JK, Faulk MW, Arfken CL, Strahl-Bevacqua J, Manji HK: Temporal dissociation between lithium induced changes in frontal lobe myo-inositol and clinical response in manic-depressive illness. Am J Psychiatry 1999; 156:1902-1908

8. Yildiz A, Demopulos CM, Moore CM, Renshaw PF, Sachs GS: Effect of lithium on phosphoinositide metabolism in human brain: a proton-decoupled 31 P MRS Study. Biological Psychiatry 2001; 50:51-55

9. Jope RS: Anti-bipolar therapy: mechanism of action of lithium. Mol psychiatry 1999; 4:117-128

10. Jope RS: A bimodal model of the mechanism of action of lithium. Mol psychiatry 1999; 4:21-25

11. Manji HK, Lenox RH: Protein kinase C signaling in the brain: molecular transduction of mood stabilization in the treatment of bipolar disorder. Biol Psychiatry 1999; 46:1328-1351

12. Lenox RH, McNamara RK, Papke RL, Manji HK: Neurobiology of lithium: an update. J Clin Psychiatry 1998; 59(suppl 6):37-42

13. Lenox RH, McNamara RK, Watterson JM, Watson DG: Myrstoylated alanine-

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00144

rich C kinase substrate (MARCKS): a molecular target for the therapeutic action of mood stabilizers in the barin. J Clin Psychiatry 1996; 57(suppl 13):23-31

14. Friedman E, Wang HY, Levinson D, Connell TA, Singh H: Altered platelet protein kinase C activity in bipolar affective disorder, manic episode. Biol Psychiatry 1993; 33:520-525

15. Wang HY, Friedman E: Enhanced protein kinase C activity and translocation in bipolar affective disorder brains. Biol Psychiatry 1996; 40:568-575

16. Hahn CG, Friedman E: Abnormalities in protein kinase C signaling and the pathophysiology of bipolar disease. Bipolar Disorders 1999; 1:81-86

17. Bebchuk JM, Arfken CL, Dolan-Manji S, Murphy J, Hasanat K, Manji HK: A preliminary investigation of a protein kinase C inhibitor in the treatment of acute mania. Arch Gen Psychiatry 2000; 57:95-97

18. Jordon VC: A current view of tamoxifen for the treatment of breast cancer. Br J Pharmacol 1994; 110:507-517

19. Couldwell WT, Weiss MH, DeGiorgio CM, Weiner LP, Hinton DR, Ehresmann GR, Conti PS, Apuzzo ML. Clinical and radiographic response in a minority of patients with recurrent malignant gliomas treated with high-dose tamoxifen. Neurosurgery 1993; 32:485-489

20. Horgan K, Cooke E, hallet MB, Mansel RE: Inhibition of protein kinase C mediated signal transduction by tamoxifen: importance for antitumor activity. Biochem Pharmacol 1986; 35:4463-4465

21. O'Brian CA, Housey GM, Weinstein IB: Specific and direct binding of protein kinase C to an immobilized tamoxifen analogue. Cancer Res 1988; 48:3626-3629

22. Cathcart CK, jones Se, Pumroy CS, Peters GN, Knox SM, Cheek JH: Clinical recognition and management of depression in node negative breast cancer patients treated with tamoxifen. Breast Cancer Res Treatment 1993; 27:277-281

23. Keck PE Jr, Welge JA, McElroy SL, Arnold LM, Strakowski SM: Placebo effect in randomized, controlled studies of acute bipolar mania and depression. Biol Psychiatry 2000; 47:748-755

24. Stanley B: An integration of ethical and clinical considerations in the use of placebos. Psychopharmacol Bull 1988; 24:18-20

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00145

25. Quitkin FM: Placebos, drug effects, and study design: a clinician's guide. Am J Psychiatry 1999; 156:829-836

26. Leber P: The future controlled trials. Is there an alternative to randomized controlled trial. Psychopharmacol Bull 1991; 27:3-8

27. Leber P: Challenges to the ethicality of clinical research. Psychopharmacol Bull 1996; 32: 11-13

28. Young RC, Biggs JT, Ziegler VE, Meyer DA: A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry 1978; 133:429-435

29. Spearing MK, Post PM, Leverich GS, Brandt D, Nolen W: Modification of the clinical global impressions (CGI) scale for use in bipolar illness (BP): the CGI-BP: Psychiatry Res 1997; 73:150-171

30. Hamilton M: A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56-62

31. Kay S, Opler L, Fiszbein A: A positive and negative syndrome scale (PANSS) manual. North Tonawanda, NY: Multi-Health Systems 1986

32. Repetto L, Venturine A, Comandini D, Parodi S, Granetto C, Porcile G, Audisio RA, Rosso R: A loading dose of tamoxifen followed by a standard dose in frail older women with breast cancer is feasible and effective. J Am Geriatr Soc 2000; 48:346-348

33. Lerner HJ, Band PR, Israel L, Leung BS: Phase II study of tamoxifen: report of 74 patients with stage IV breast cancer. Cancer Treat Rep 1976; 60:1431-1435

34. Manni A, Trujillo J, Marshall JS, Pearson OH: Antiestrogen-induced remissions in stage IV breast cancer. Cancer Treat Rep 1976; 60:1445-1450

35. Love RR, Surawicz TS, Williams EC: Antithrombin III level, fibrinogen level, and platelet count changes with adjuvant tamoxifen therapy. Arch Intern med 1992: 152:317-320

36. Auger MJ, Mackie MJ: Effects of tamoxifen on blood coagulation. Cancer 1988; 61:1316-1319

37. Ogawa Y, Murata Y, Nishioka A, Inomata T, Yoshida S: Tamoxifen-induced fatty liver in patients with breast cancer. Lancet 1998; 351:725

38. Gorin MB, Day R, Costantino JP, Fisher B, Redmond CK, Wickerham L,

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Gomolin JE, Margolese RG, Mathen MK, Bowman DM, Kaufman DI, Dimitroy NV, Singerman LJ, Bornstein R, Wolmark N, Kaufmann D: Long-term tamoxifen citrate use and potential ocular toxicity. Am J Opthalmol 1998; 125:493-501

39. Larsen W, Fellowes G, Rickman LS: Life threatening hypercalcemia and tamoxifen. Am J Med 1990; 88:440-442

40. Keck PE Jr, Mendlwicz J, Calabrese JR, Fawcett J, Suppes T, Vestergaard PA, Carbonell C: A review of randomized, controlled clinical trails in acute mania. J Aff Disorders 2000; 59:S31-S37

41. Yildiz A, Sachs GS: Age onset of psychotic bipolar illness in men and women. J Affective Disorders 2003; 74:197-201

42. Yildiz A, Sachs GS: Do antidepressants induce rapid cycling; a gender specific association. J Clinical Psychiatry 2003; 64:814-818

43. Yildiz A, Sachs GS: Characteristics of rapid cycling bipolar-I patients in a bipolar specialty clinic. J Affective Disorders 2004; 79:247-251

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CLAIMS:

1. Any kind of existing pharmacological agent OR its derivatives OR New compounds to be developed for treatment of Bipolar Disorder wherein said compounds work through the Protein Kinase C signaling pathway.

2. Any kind of existing pharmacological agent OR its derivatives OR New compounds to be developed for treatment of Bipolar Disorder wherein said compounds have anti-estrogenic properties.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/TR2007/000063

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/138 A61K31/00 A61P25/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BEBCHUK J M ET AL: "A preliminary investigation of a protein kinase C inhibitor in the treatment of acute mania." ARCHIVES OF GENERAL PSYCHIATRY JAN 2000, vol. 57, no. 1, January 2000 (2000-01), pages 95-97, XP008084309 ISSN: 0003-990X cited in the application the whole document -/--	1,2

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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Date of the actual completion of the international search	Date of mailing of the international search report
8 October 2007	18/10/2007

Name and mailing address of the ISA/	Authorized officer
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KULKARNI JAYASHRI ET AL: "A pilot study of hormone modulation as a new treatment for mania in women with bipolar affective disorder" PSYCHONEUROENDOCRINOLOGY, vol. 31, no. 4, May 2006 (2006-05), pages 543-547, XP005334313 ISSN: 0306-4530 abstract page 544, column 1, paragraph 1 - column 2, paragraph 1 figure 1 page 545, column 2, paragraphs 1,2 page 545, column 2, paragraph 4 - page 546, column 2, paragraph 1	1,2
X	MANJI HUSSEINI K ET AL: "Modulation of CNS signal transduction pathways and gene expression by mood-stabilizing agents: Therapeutic implications" JOURNAL OF CLINICAL PSYCHIATRY, vol. 60, no. SUPPL. 2, 1999, pages 27-39, XP008084310 ISSN: 0160-6689 abstract page 32, column 2, paragraph 1	1,2
X	MANJI HUSSEINI K ET AL: "Protein kinase C signaling in the brain: Molecular transduction of mood stabilization in the treatment of manic-depressive illness" BIOLOGICAL PSYCHIATRY, vol. 46, no. 10, 15 November 1999 (1999-11-15), pages 1328-1351, XP002453972 ISSN: 0006-3223 cited in the application abstract page 1388, column 1, paragraph 2 - column 2, paragraph 2 page 1342, column 2, paragraph 2	1,2
X	WO 2005/030143 A (UNIV YALE [US]; ARNSTEN AMY F T [US]; BIRNBAUM SHARI G [US]) 7 April 2005 (2005-04-07) page 1, paragraphs 1,2 page 3, paragraphs 3,5 claims 1,4,10	1,2

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	YILDIZ-YESILOGLU AYSEGUL: "Targeted treatment strategies in mania: Anti-manic effects of a PKC inhibitor-tamoxifen" BIOLOGICAL PSYCHIATRY, vol. 61, no. 8, Suppl. S, April 2007 (2007-04), page 23S, XP008084313 & 62ND ANNUAL SCIENTIFIC MEETING OF THE SOCIETY-OF-BIOLOGICAL-PSYCHIAT RY; SAN DIEGO, CA, USA; MAY 17 -20, 2007 ISSN: 0006-3223 the whole document	1,2
P,X	ZARATE CARLOS A JR ET AL: "Efficacy of a protein kinase C inhibitor (tamoxifen) in the treatment of acute mania: a pilot study." BIPOLAR DISORDERS SEP 2007, vol. 9, no. 6, September 2007 (2007-09), pages 561-570, XP002453973 ISSN: 1398-5647 abstract page 563, column 1, paragraph 2 - column 2, paragraph 3 page 564, column 1, paragraph 3 - column 2, paragraph 2 page 568, column 1, paragraph 3 - column 2, paragraph 2 page 569, column 1, paragraph 3	1,2

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/TR2007/000063

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005030143 A	07-04-2005	AU 2004275852 A1	07-04-2005
		BR PI0414816 A	14-11-2006
		CA 2540151 A1	07-04-2005
		CN 1859846 A	08-11-2006
		EP 1662875 A2	07-06-2006
		JP 2007506784 T	22-03-2007
		MX PA06003423 A	27-06-2006
		US 2005070565 A1	31-03-2005

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
KAVATHEKAR, Amol H.

Hamre, Schumann, Mueller & Larson, P.C. 45 South Seventh Street, Suite 2700 Minneapolis, Minnesota 55402 USA

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 20110-0024WOU1	Date of mailing *(day/month/year)* 15 July 2021 (15.07.2021) **FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. **PCT/IB2021/052972**	International filing date *(day/month/year)* **09 April 2021 (09.04.2021)**

Applicant
JINA PHARMACEUTICALS, INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

How? Directly to the International Bureau of WIPO preferably through ePCT or on paper to, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 338 82 70

For more detailed instructions, see *PCT Applicant's Guide*, International Phase, paragraphs 9.004 , 9-011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

Within **22 months** from the priority date, the applicant may request that a supplementary international search be carried out by a different International Searching Authority, that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

Name and mailing address of the ISA/KR International Application Division Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon, 35208, Republic of Korea	Authorized officer COMMISSIONER
Facsimile No. 82-42-481-8578	Telephone No. 82-42-481-8109

Form PCT/ISA/220 (July 2017)

* Attention

Copies of the documents cited in the international search report can be searched in the following Korean Intellectual Property Office English website for six months(expire date : **2022.01.15**) from the date of mailing of the international search report.

http://www.kipo.go.kr/en/ => PCT ISA Portal => PCT Status

ID : PCT international application number

PW : **JF84PHM3&**

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PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference **20110-0024WOU1**		**FOR FURTHER ACTION** see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. **PCT/IB2021/052972**	International filing date *(day/month/year)* **09 April 2021**	(Earliest) Priority Date *(day/month/year)* **10 April 2020**
Applicant **JINA PHARMACEUTICALS, INC.**		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of **3** sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of:

   ☑ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

   b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

   c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II).

3. ☐ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

   ☑ the text is approved as submitted by the applicant.

   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   ☑ the text is approved as submitted by the applicant.

   ☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

   a. the figure of the **drawings** to be published with the abstract is Figure No. _____

   ☐ as suggested by the applicant.

   ☐ as selected by this Authority, because the applicant failed to suggest a figure.

   ☐ as selected by this Authority, because this figure better characterizes the invention.

   b. ☐ none of the figures is to be published with the abstract.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/052972

A. CLASSIFICATION OF SUBJECT MATTER

A61K 31/138(2006.01)i; **A61P 25/18**(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K 31/138(2006.01); A61K 31/00(2006.01); A61K 31/135(2006.01); A61K 31/4196(2006.01); A61K 31/7072(2006.01); A61K 9/06(2006.01); A61K 9/19(2006.01); A61P 25/24(2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & keywords: endoxifen, bipolar I disorder, dose, periods, manic, depression

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2019-0231687 A1 (JINA PHARMACEUTICALS, INC.) 01 August 2019 (2019-08-01) claims 1, 3, 6, 7, 9, 14; and paragraphs [0009], [0057], [0170]	1-5
A	AHMAD, A. et al., 'Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of Endoxifen', Clin. Transl. Sci., 2016, Vol.9, pp.252-259 the whole document	1-5
A	US 2012-0201908 A1 (MILLER, K. P.) 09 August 2012 (2012-08-09) the whole document	1-5
A	WO 2009-152430 A2 (REPLIGEN CORPORATION) 17 December 2009 (2009-12-17) the whole document	1-5
A	WO 2008-048194 A1 (YESILOGLUJ, A. Y.) 24 April 2008 (2008-04-24) the whole document	1-5

☐ Further documents are listed in the continuation of Box C. ☑ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 July 2021	**15 July 2021**
Name and mailing address of the ISA/KR **Korean Intellectual Property Office** **189 Cheongsa-ro, Seo-gu, Daejeon** **35208, Republic of Korea** Facsimile No. **+82-42-481-8578**	Authorized officer **Jung, Da Won** Telephone No. **+82-42-481-5373**

Form PCT/ISA/210 (second sheet) (July 2019)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2021/052972

Patent document cited in search report			Publication date (day/month/year)	Patent family member(s)			Publication date (day/month/year)
US	2019-0231687	A1	01 August 2019	CA	2669913	A1	12 June 2008
				CA	2669913	C	18 September 2012
				CA	2757838	A1	25 November 2010
				CA	2757838	C	17 December 2013
				DK	2101731	T3	16 April 2018
				EP	2101731	A2	23 September 2009
				EP	2101731	A4	20 April 2011
				EP	2101731	B1	31 January 2018
				EP	2432462	A2	28 March 2012
				EP	2432462	A4	13 November 2013
				ES	2665917	T3	30 April 2018
				HU	E037109	T2	28 August 2018
				IN	139MUN2014	A	19 June 2015
				JP	2010-510327	A	02 April 2010
				JP	2012-527484	A	08 November 2012
				MX	2011012409	A	14 March 2012
				PL	2101731	T3	31 July 2018
				PT	2101731	T	18 April 2018
				US	10376479	B2	13 August 2019
				US	2009-0291134	A1	26 November 2009
				US	2010-0112041	A1	06 May 2010
				US	2012-0164075	A1	28 June 2012
				US	2016-0346230	A1	01 December 2016
				US	9333190	B2	10 May 2016
				WO	2008-070463	A2	12 June 2008
				WO	2008-070463	A3	06 November 2008
				WO	2008-070463	A9	18 September 2008
				WO	2010-135703	A2	25 November 2010
				WO	2010-135703	A3	13 January 2011
US	2012-0201908	A1	09 August 2012	WO	2011-022292	A2	24 February 2011
				WO	2011-022292	A3	14 July 2011
WO	2009-152430	A2	17 December 2009	AU	2009-257353	A1	17 December 2009
				CA	2727546	A1	17 December 2009
				EP	2303284	A2	06 April 2011
				US	2011-0160158	A1	30 June 2011
				WO	2009-152430	A3	18 March 2010
WO	2008-048194	A1	24 April 2008	None			

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PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
KAVATHEKAR, Amol H.

Hamre, Schumann, Mueller & Larson, P.C. 45 South Seventh Street, Suite 2700 Minneapolis, Minnesota 55402 USA

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	**15 July 2021**
Applicant's or agent's file reference	**FOR FURTHER ACTION** See paragraph 2 below
20110-0024WOU1	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2021/052972	**09 April 2021**	**10 April 2020**

International Patent Classification (IPC) or both national classification and IPC
A61K 31/138(2006.01)i; **A61P 25/18**(2006.01)i

Applicant
JINA PHARMACEUTICALS, INC.

1. This opinion contains indications relating to the following items:

- [x] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [x] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability: citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/KR	Date of completion of this opinion	Authorized officer
Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon, 35208	**15 July 2021**	**Jung, Da Won**
Facsimile No. **+82-42-481-8578**		Telephone No. **+82-42-481-5373**

Form PCT/ISA/237 (Cover sheet) (revised January 2019)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2021/052972

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
   - [x] the international application in the language in which it was filed.
   - [ ] a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. [ ] This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(b)).

3. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
   - a. [ ] forming part of the international application as filed:
     - [ ] in the form of an Annex C/ST.25 text file.
     - [ ] on paper or in the form of an image file.
   - b. [ ] furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
   - c. [ ] furnished subsequent to the international filing date for the purposes of international search only:
     - [ ] in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).
     - [ ] on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. [ ] In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Atossa Therapeutics, Inc. Exhibit 1002
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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2021/052972

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-5	YES
	Claims	NONE	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-5	NO
Industrial applicability (IA)	Claims	1-5	YES
	Claims	NONE	NO

2. Citations and explanations :

Reference is made to the following document:

D1: US 2019-0231687 A1 (JINA PHARMACEUTICALS, INC.) 1 August 2019

(※ Claims 1-5 pertain to methods comprising a step of direct medical procedure for the human body. Nevertheless, based on the alleged effects of the compound or composition, the search has been performed and statement on novelty and inventive step has been established.)

I. Novelty and Inventive Step [PCT Article 33(2) and (3)]

1. Claim 1

D1 discloses a method of treating a cell for the treatment of bipolar disorder comprising exposing said cell to a composition comprising an effective amount of a complex comprising endoxifen or its salt, wherein said endoxifen salt includes endoxifen citrate, and wherein the endoxifen is formulated in an enteric coated tablet (see claims 1, 3, 6, 7, 9, 14).

Claim 1 differs from D1 in that the claim defines the method for maintaining a therapeutically effective concentration of endoxifen by administering a dose of 2-16 mg of endoxifen citrate for at least 21 days, wherein the patient is not administered rescue medication during the treatment.

However, D1 also mentions that the dose may be optimized in each patient, depending on individual responses (see paragraph [0170]), and it is considered that a person skilled in the art can adjust the dose and the duration of endoxifen administration by routine experiments, and the condition to not to administer rescue medication can be matched by said adjustment.

Moreover, it is not considered that said limitations present any unexpected effects of properties in relation to the rest of range in simply maintaining the concentration of endoxifen.

Therefore, clam 1 lacks an inventive step as being obvious over D1.

2. Claims 2-5

The features of claims 2-5 are well-known symptoms of bipolar disorder, and D1 also teaches that endoxifen can be used for the subject having manic disorder or depression signs (see paragraphs [0009], [0057]).

Therefore, claims 2-5 lack an inventive step as being obvious over D1.

II. Industrial Applicability [PCT Article 33(4)]

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Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**

Claims 1-5 are industrially applicable.

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PGR2026-00015
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Electronic Acknowledgement Receipt

EFS ID:	43470027
Application Number:	17226671
International Application Number:	
Confirmation Number:	1772
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Customer Number:	52835
Filer:	Masako Yoshida/Peggy Kerkhove
Filer Authorized By:	Masako Yoshida
Attorney Docket Number:	20110.0024USU1
Receipt Date:	10-AUG-2021
Filing Date:	09-APR-2021
Time Stamp:	13:06:38
Application Type:	Utility under 35 USC 111(a)

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	Information Disclosure Statement (IDS) Form (SB08)	US_Form_SB08_0024.pdf	1034422 0fc0cb83009a06734dea959a9130e24757d adf74	no	4

Warnings:

Information:					
2	Patent Term Adjustment Stmt Under 37CFR1.704(d)	30-day_Statement_0024.pdf	266600 17e453f521721b1afc33f2469f9b89352d7ca38d4	no	2
Warnings:					
Information:					
3	Foreign Reference	FR1_WO2009152430A2.pdf	2138626 4efb83aac7a6703ce50f925aed2e61f96cd205a6	no	45
Warnings:					
Information:					
4	Foreign Reference	FR2_WO2008048194A1.pdf	1118922 4357e04ee578aece128675473b6fe108585b55e6	no	27
Warnings:					
Information:					
5	Other Reference-Patent/App/Search documents	NPL1_ISR_0024.pdf	537367 55c39717fd92c01adb4789145a8d834bfd1255950	no	9
Warnings:					
Information:					
		Total Files Size (in bytes):	5095937		

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.

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
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1

CONFIRMATION NO. 1772

PUBLICATION NOTICE

52835
HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

OC000000129101075

Title:ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Publication No.US-2021-0315845-A1
Publication Date:10/14/2021

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently https://portal.uspto.gov/pair/PublicPair. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

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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.
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1	1772

52835 7590 04/28/2022

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
04/28/2022	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOMail@hsml.com

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
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Office Action Summary	Application No. 17/226,671	Applicant(s) AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	Art Unit 1611	AIA (FITF) Status Yes

-- 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 MONTHS 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 _____.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

3)☐ 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.

4)☐ 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*

5) ☑ Claim(s) 1-5 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-5 is/are rejected.

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

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

* If any claims have been determined allowable, 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.**

Application Papers

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

11)☐ 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).

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).

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)).

** 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) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date 8/10/21 & 7/13/21.

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

4) ☐ Other: _____.

Atossa Therapeutics, Inc. Exhibit 1002
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Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Receipt of IDS dated 7/13/21 is acknowledged.

Claims 1-5 are pending.

Claim Objections

Claim 5 is objected to because it is grammatically incomplete, as it lacks a verb, such as "is" or "has". Appropriate correction is required.

Claim Rejections - 35 USC § 102

1. In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention.

3. Claim(s) 1-5 are rejected under 35 U.S.C. 102(a)(1) as being anticipated by Ahmad et al (2016, cited on IDS).

Instant claims are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days.

Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BP) with current manic or mixed episode.

Ahmad states that several drugs have been approved such as lithium, valproate, carbamazepine, and atypical antipsychotics for the treatment of acute bipolar mania, which while providing relief for many individuals with BP, significant issues with tolerability and efficacy still remain. Ahmad describes that adherence to the treatment is affected by adverse effects such as sedation and weight gain, and that there is an urgent need to develop novel and more effective treatments for BP (p 252). Ahmad teaches enteric coated endoxifen citrate salt ("CgHgO7" is citric acid, see figure 1 and page 253, col. 2- Methodology) (claim 1). The results were expressed as Young Mania Rating Scale (YMRS) total score (≥50% decrease from baseline). Secondary end points were mean change from baseline to the end of treatment in the Montgomery–Åsberg Depression Rating Scale (MADRS) total score, Clinical Global Impressions–Severity of Illness Scale (CGI-S) score, and Columbia–Suicide Severity Rating Scale (C-SSRS) score, shown in Table 1. Ahmad teaches that a switch to depression remains a concern in all treatments of bipolar mania, depressive symptoms were assessed with the MADRS score throughout the trial. Ahmad teaches effectiveness of endoxifen 4 mg and 8 mg in alleviating depressive symptoms of mixed episode of BPD similar to that of divalproex (p 256, col.1 & Table 2) (claim 1). Further, the administration of endoxifen (4

mg and 8 mg) provides a steady state plasma concentration of endoxifen for 14 and also 20 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect (which can be construed as without mixed episode) or mixed episodes patients of endoxifen (p 258). In a double-blind, active-controlled study, 84 subjects with BPD I were randomly assigned to receive endoxifen (4 mg/day or 8 mg/day) or divalproex in a 2:1 ratio. Patients orally administered 4 mg/day or 8 mg/day endoxifen showed significant improvement in mania assessed by the Young Mania Rating Scale as early as 4 days. The effect remained significant throughout the 21-day period. At study end point, response rates were 44.44% and 64.29% at 4 mg/day and 8 mg/day of endoxifen treatment, respectively (abstract). Thus, Ahmad teaches endoxifen has been shown as a promising novel antimanic or mood stabilizing agent, as seen by significantly improved YMRS scale at almost every treatment evaluation.

Instant claims recite the limitation that "the patient is not administered rescue medication during the said treatment". Instant specification defines "rescue medication" as additional medication necessary to treat breakthrough or recurring symptoms (p 4, last para). Ahmad teaches concomitant medications such as lorazepam have been discontinued before treatment and thus meet the instant claim limitation. Thus, Ahmad anticipates instant claims.

Double Patenting

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 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); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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 nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may

be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

2. Claims 1-5 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 11291640. Although the claims at issue are not identical, they are not patentably distinct from each other. Instant claims as well as the copending claims are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Instant claims recite the limitation that "the patient is not administered rescue medication during the said treatment". Instant specification defines "rescue medication" as additional medication necessary to treat breakthrough or recurring symptoms (p 4, last para). Patented claims do not recite any additional medication and therefore meet the claim limitation "the patient is not administered rescue medication during the said treatment". Both instant and patented claims recite the that the patient has manic episodes without mixed features, with mixed features, the patient has depression and also depressive episodes. Thus, patented claims anticipate instant claims.

3. Claims 1-5 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10376479 in view of Ahmad et al (2016, cited on IDS).

Patented claims are directed to a method of delivering endoxifen to the plasma of a subject, comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver and the endoxifen is a synthetic endoxifen that is at least 80% z-endoxifen and in the form of a citrate salt.

Patented claims do not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patented claims also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5.

The teachings of Ahmad have been discussed above and incorporated here with. Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BPD I) with current manic or mixed episode.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (patented claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. A skilled artisan would have been motivated because Ahmad teaches administering endoxifen 4 mg and 8 mg for alleviating depressive symptoms of mixed episode of BPD similar to that of divalproex, with a steady state plasma concentration of endoxifen for 14 and also 21 days, and that

doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect or mixed episodes patients of endoxifen (p 258).

4. Claims 1-5 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over the claims of copending Application No. 17/023208 in view of Ahmad et al (2016, cited on IDS).

Copending claims are directed to a method of inhibiting protein kinase C by administering an enteric coated tablet comprising endoxifen citrate. However, a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Copending claims lack the amounts of endoxifen citrate, for the duration of 21 days, and also lacks instant claims 4-5.
The teachings of Ahmad have been discussed above and incorporated here with. Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BPD I) with current manic or mixed episode.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (copending claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. A skilled artisan would have been motivated because Ahmad teaches administering endoxifen 4 mg and 8 mg for

alleviating depressive symptoms of mixed episode of BPD similar to that of divalproex, with a steady state plasma concentration of endoxifen for 14 and also 21 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect or mixed episodes patients of endoxifen (p 258).

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

5. Claims 1-5 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over the claims of copending Application No. 17/226,651 filed on the same day as that of the instant application, and 17/226,703. Although the claims at issue are not identical, they are not patentably distinct from each other because they claim methods of treating bipolar | disorder with endoxifen. This is a provisional nonstatutory double-patenting rejection because the patentably indistinct claims have not, in fact, been patented. Both instant and copending claim sets recite the that the patient has manic episodes without mixed features, with mixed features, the patient has depression and also depressive episodes.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKSHMI SARADA CHANNAVAJJALA whose

telephone number is (571)272-0591. The examiner can normally be reached Generally M- F 9 AM to 6 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Notice of References Cited	Application/Control No. 17/226,671	Applicant(s)/Patent Under Reexamination AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	Art Unit 1611	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-10376479-B2	08-2019	Ahmad; Ateeq	A61K9/48	1/1
*	B	US-11291640-B2	04-2022	Ahmad; Ateeq	A61K9/28	1/1
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

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Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

CPC - Searched*		
Symbol	Date	Examiner
classification- attached	04/23/2022	LC

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
PE2E search history- all data bases- inventor, classification, text- attached	04/23/2022	LC
google scholar	04/23/2022	LC

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Endoxifen: a new, protein kinase C inhibitor to treat acute and **mixed** mania associated with **bipolar** I **disorder**
A Ahmad, S Sheikh, MA Khan, A Chaturvedi ... - ... disorders, 2021 - Wiley Online Library
... **Endoxifen** is a protein kinase C inhibitor. The objective of the present phase III study was to demonstrate the safety and efficacy of **endoxifen** in treating **bipolar** I **disorder** ... **Bipolar disorder** ...
☆ Save 99 Cite Cited by 3 Related articles All 7 versions

Efficacy of **Endoxifen**, a Protein kinase C inhibitor for acute and **mixed** mania: Some concerns worth considering
A Ghosh, S Rani, S Grover - **Bipolar disorders**, 2021 - europepmc.org
... acute manic episodes with/without **mixed** features. However, we are ... The efficacy endpoints briefly mentioned "**endoxifen** was ... of non-inferiority between **endoxifen** and divalproex in the ...
☆ Save 99 Cite Cited by 1 Related articles All 4 versions »

Endoxifen is a new potent inhibitor of PKC: a potential therapeutic agent for **bipolar disorder**
SM Ali, A Ahmad, S Shahabuddin, MU Ahmad ... - Bioorganic & Medicinal ..., 2010 - Elsevier
... results in symptoms related to **bipolar disorder**. Tamoxifen, a widely ... **endoxifen**, a tamoxifen active metabolite and compared its PKC inhibitory activity with that of tamoxifen. **Endoxifen** ...
☆ Save 99 Cite Cited by 27 Related articles All 9 versions

Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of **Endoxifen**
A Ahmad, S Sheikh, T Sheth, MS Reddy ... - Clinical and ..., 2016 - Wiley Online Library
... for **bipolar disorder** (BP) patients. In this study we show for the first time the antimanic properties of **endoxifen** in patients with **bipolar** I **disorder** (BPD I) with current manic or **mixed** ...
☆ Save 99 Cite Cited by 11 Related articles All 7 versions »

Endoxifen: A new hope for **Bipolar Disorder**
M Amin, A Sharique, MY Hafiz - 2021 - scommons.aku.edu
... of **Endoxifen**. A multicentre, double-blind, active-controlled study was conducted using **Endoxifen** ... in the treatment of acute mania and **mixed** mania.One of the many advantages include ...
☆ Save 99 Cite Related articles All 8 versions

Endoxifen, an estrogen receptor targeted therapy: From bench to bedside
S Jayaraman, JM Reid, JR Hawse, MP Goetz - Endocrinology, 2021 - academic.oup.com
... characterized by the occurrence of acute mania or **mixed** episodes of shifts in mood, ... **endoxifen** in **bipolar disorder** and calls for further exploration of **endoxifen** actions in this **disease**...
☆ Save 99 Cite Cited by 3 Related articles All 5 versions »

Therapeutic Approaches to **Bipolar Disorder**
MU Ahmad, SM Ali, S Sheikh, A Ahmad ... - Psychiatric Disorders, 2012 - books.google.com
... lithium for treating mania, rapid cycling **bipolar disorder** or **mixed** states. However, it is not ... as **endoxifen** (Figure 13.5) may provide better opportunity for the treatment of **bipolar disorder** ...
☆ Save 99 Cite Related articles All 3 versions »

Omega 3 fatty acids in **bipolar disorder**: a preliminary double-blind, placebo-controlled trial
AL Stoll, **WE** Severus, MP Freeman, S Rueter, ... - Archives of general psychiatry - 1999 - jamanetwork.com
[PDF] jamanetwork.com

Omega-3 fatty acids and **bipolar disorder**: a review
AL Stoll, CA Locke, LB Marangell, WE Severus - Prostaglandins, Leukotrienes and Esse... - 1999 - sciencedirect.com
[PDF] planktonholland.de

Initial evidence for the role of CACNA1C on subcortical brain morphology in patients with **bipolar disorder**
E Ferrier, F Pompei, G Ruberto, E Vassos, D ... - European Psychiatry - 2011 - cambridge.org
[PDF] academia.edu

Tamoxifen for **bipolar disorder**: Systematic review and meta-analysis
J Palacios, A Yildiz, AH Young ... - Journal of ..., 2019 - journals.sagepub.com
... as a potential treatment for **bipolar disorder**. Tamoxifen acts to ... in the treatment of **bipolar disorder** and synthesise their ... in the treatment of **bipolar disorder** and synthesise their results ...
☆ Save 99 Cite Cited by 26 Related articles All 4 versions »

A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute **bipolar** mania
PE Keck Jr, P Marcus, S Tourkodimitris ... - American Journal of ..., 2003 - Am Psychiatric Assoc
... manic or **mixed** episode of **bipolar disorder**. METHOD: This 3-week, multicenter, double-blind study randomly assigned 262 **bipolar disorder** patients in an acute manic or **mixed** episode ...
☆ Save 99 Cite Cited by 600 Related articles All 10 versions »

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Antipsychotic switching in **bipolar disorders**: a systematic review

I Grover, M Bernardo, J Bobes... - International Journal ..., 2014 - academic.oup.com

... With the increasingly widespread use of antipsychotics in **bipolar disorder** (BD), switching ... published but also recruitment in most studies included **mixed** samples of patients. In general, ...

☆ Save 99 Cite Cited by 35 Related articles All 14 versions »

Related searches

omega 3 fatty acids bipolar disorder
relapse prevention in bipolar disorder
aripiprazole in bipolar disorder
burden of bipolar disorder
patients with bipolar i disorder
bipolar i disorder **26 week trial**
bipolar disorders **antipsychotic switching**
potential therapeutic agent bipolar disorder
many facets bipolar disorder
fish oils bipolar disorder
therapeutic approaches bipolar disorder
meta analysis bipolar disorder
bipolar i disorder **3 week**
12 month clinical trial bipolar disorder
wave bd bipolar disorder
multinational longitudinal study bipolar disorder

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	1	"17226671"	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:01 PM
L2	308893	Jina Pharmaceuticals, Inc.	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:02 PM
L3	11231441	AHMAD, Ateeq; AHMAD, Imran; AHMAD, Moghisuddin; ALI, Shoukath M; SHEIKH, Saifuddin	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:02 PM
L4	152	(1 2) AND endoxifen	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:03 PM
L5	22	(1 2) AND endoxifen adj5 (citrate citrate)	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:04 PM
L6	13	(1 2) AND endoxifen adj5 (citrate citrate) AND enteric adj5 coated	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:04 PM
L7	13	endoxifen adj5 (citrate citrate) AND enteric adj5 coated	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:20 PM
L8	13	endoxifen SAME (citrate citrate) AND enteric adj5 coated	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:20 PM
L9	44	endoxifen SAME (citrate citrate) AND tablet	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L10	0	endoxifen SAME (citrate citrate) AND tablet AND enteral	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L11	30	endoxifen SAME (citrate citrate) AND tablet AND intestine	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L12	17	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated)	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L13	4	12 NOT 8	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:22 PM
L14	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated) AND bipolar	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:31 PM
L15	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:32 PM

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		coated) AND bipolar AND (depression depressive manic mania)					
L16	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated) AND bipolar AND (depression depressive manic mania) AND features	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:32 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.S.C/

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. 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	17226671
Filing Date	2021-04-09
First Named Inventor	AHMAD
Art Unit	1615
Examiner Name	
Attorney Docket Number	20110.0024USU1

U.S.PATENTS Remove

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	9,333,190		2016-05-10	Ahmad, et al.	
	2	10,376,479		2019-08-13	Ahmad, et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

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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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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	2014/141292	WO		2014-09-18			

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Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00182

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17226671
	Filing Date	2021-04-09
	First Named Inventor	AHMAD
	Art Unit	1615
	Examiner Name	
	Attorney Docket Number	20110.0024USU1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.S.C/

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	Ahmad, et al., "Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of Endoxifen", Clin Transl Sci (2016) 9, 252–259	
	2	Ali, et al., "Endoxifen is a new potent inhibitor of PKC: A potential therapeutic agent for bipolar disorder", Bioorganic & Medicinal Chemistry Letters 20 (2010) 2665–2667	

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Examiner Signature	/LAKSHMI S CHANNAVAJJALA/	Date Considered	04/23/2022

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[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or 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.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Art Unit	1615
Examiner Name	
Attorney Docket Number	20110.0024USU1

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

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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.

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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	/Masako Yoshida/	Date (YYYY-MM-DD)	2021-07-13
Name/Print	Masako Yoshida	Registration Number	70,057

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.**

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00184

Privacy Act Statement

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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.

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PTO/SB/08a (02-18)
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Application Number	17226671
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Attorney Docket Number	20110.0024USU1

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	1	20120201908		2012-08-09	Miller	
	2	20190231687		2019-08-01	Ahmad, et al.	

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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	2009/152430	WO		2009-12-17			
	2	2008/048194	WO		2008-04-24			

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	First Named Inventor	AHMAD
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	Examiner Name	
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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	International Search Report and Written Opinion issued in International Application No. PCT/IB2021/052972, July 15, 2021, 9 pages	

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EXAMINER SIGNATURE

Examiner Signature	/LAKSHMI S CHANNAVAJJALA/	Date Considered	04/23/2022

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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.

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Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00189

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	1	"17226671"	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:01 PM
L2	308893	Jina Pharmaceuticals, Inc.	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:02 PM
L3	11231441	AHMAD, Ateeq; AHMAD, Imran; AHMAD, Moghisuddin; ALI, Shoukath M; SHEIKH, Saifuddin	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:02 PM
L4	152	(1 2) AND endoxifen	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:03 PM
L5	22	(1 2) AND endoxifen adj5 (citrate citrate)	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:04 PM
L6	13	(1 2) AND endoxifen adj5 (citrate citrate) AND enteric adj5 coated	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:04 PM
L7	13	endoxifen adj5 (citrate citrate) AND enteric adj5 coated	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:20 PM
L8	13	endoxifen SAME (citrate citrate) AND enteric adj5 coated	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:20 PM
L9	44	endoxifen SAME (citrate citrate) AND tablet	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L10	0	endoxifen SAME (citrate citrate) AND tablet AND enteral	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L11	30	endoxifen SAME (citrate citrate) AND tablet AND intestine	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L12	17	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated)	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L13	4	12 NOT 8	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:22 PM
L14	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated) AND bipolar	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:31 PM
L15	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:32 PM

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PGR2026-00015
Page 00190

		coated) AND bipolar AND (depression depressive manic mania)					
L16	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated) AND bipolar AND (depression depressive manic mania) AND features	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:32 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00191

Endoxifen: a new, protein kinase C inhibitor to treat acute and **mixed** mania associated with **bipolar I disorder**

A Ahmad, S Sheikh, MA Khan, A Chaturvedi, ... - ... disorders, 2021 - Wiley Online Library

... In this study, **endoxifen** was effective and generally well tolerated in the treatment of acute manic or **mixed episodes** associated with BPD I. The change in total YMRS score at day 21 ...

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Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of **Endoxifen**

A Ahmad, S Sheikh, T Shah, MS Reddy ... - Clinical and ..., 2016 - Wiley Online Library

... may be an innovative medicine for **bipolar disorder** (BP) patients. In this study we show for ... of **endoxifen** in patients with **bipolar** I **disorder** (BPD I) with current manic or **mixed episode**. In ...

☆ Save 99 Cite Cited by 11 Related articles All 7 versions »

Efficacy of **Endoxifen**, a Protein kinase C inhibitor for acute and **mixed** mania: Some concerns worth considering

A Ghosh, S Rani, S Grover - Bipolar disorders, 2021 - europepmc.org

... that **endoxifen** is efficacious and safe in patients with acute manic **episodes** with/without **mixed** ... The efficacy endpoints briefly mentioned "**endoxifen** was considered non-inferior to ...

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Endoxifen: A new hope for **Bipolar Disorder**

M Amin, A Shafique, MY Hafiz - 2021 - ecommons.aku.edu

... , literature reports breakthrough **episodes** in treated groups ranging ... have reported that **bipolar disorder** is associated with ... Research has shown promise in effectiveness of **Endoxifen**. ...

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Endoxifen, an estrogen receptor targeted therapy: From bench to bedside

S Jayaraman, JM Reid, JR Hawse, MP Goetz - Endocrinology, 2021 - academic.oup.com

... characterized by the occurrence of acute mania or **mixed episodes** of shifts in mood, ... **endoxifen** in **bipolar disorder** and calls for further exploration of **endoxifen** actions in this **disease**...

☆ Save 99 Cite Cited by 3 Related articles All 5 versions »

Therapeutic Approaches to **Bipolar Disorder**

MU Ahmad, SM Ali, S Sheikh, A Ahmad ... - ... Psychiatric Disorders, 2012 - books.google.com

... -term prophylaxis or prevention of new **episodes** of **bipolar disorder**. The three most effective ... **endoxifen** (Figure 13.5) may provide better opportunity for the treatment of **bipolar disorder** ...

☆ Save 99 Cite Related articles All 3 versions »

A placebo-controlled, double-blind study of the efficacy and safety of aripiprazole in patients with acute **bipolar** mania

PE Keck Jr, P Marcus, S Tourkodimitris ... - American Journal of ..., 2003 - Am Psychiatric Assoc

... or **mixed episode** of **bipolar disorder**. METHOD: This 3-week, multicenter, double-blind study randomly assigned 262 **bipolar disorder** patients in an acute manic or **mixed episode** to ...

☆ Save 99 Cite Cited by 600 Related articles All 10 versions »

The Use of Tamoxifen as a Potential Treatment for **Bipolar Disorder**

N Bagdadi, AN Azab, ... - PSYCHIATRY ..., 2021 - psychiatry-psychopharmacology ...

... mania or **mixed state** were treated for 21 days with **endoxifen** (4 ... **endoxifen** group from day 4 of treatment. The effect remained significant throughout 21 days. The efficcacy of **endoxifen** ...

☆ Save 99 Cite Related articles All 3 versions »

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00192

Tamoxifen for **bipolar disorder**: Systematic review and meta-analysis

J Palacios, A Yildiz, AH Young... - Journal of ..., 2019 - journals.sagepub.com

... There were no trials in the treatment of **episodes** of **bipolar depression**, or for relapse prevention. The studies of mania treatment were of between three and six weeks duration. ...

☆ Save 99 Cite Cited by 26 Related articles All 4 versions »

Antipsychotic switching in **bipolar disorders**: a systematic review

I Grande, M Bernardo, J Bobes, ... - International Journal ..., 2014 - academic.oup.com

... logic algorithms were ['**bipolar disorder**' AND (switch OR ...)] as well as ['**bipolar disorder**' AND (switch OR switching OR ... **episode** as well as an elevated mood **episode** or depressive ...

☆ Save 99 Cite Cited by 35 Related articles All 14 versions »

Related searches

omega 3 fatty acids bipolar disorder

bipolar i disorder episodes **in patients**

relapse prevention in bipolar disorder

treatments for bipolar disorder

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bipolar disorders **antipsychotic switching**

potential therapeutic agent bipolar disorder

many facets bipolar disorder

fish oils bipolar disorder

therapeutic approaches bipolar disorder

use of tamoxifen bipolar disorder

meta analysis bipolar disorder

acute manic or mixed episodes

bipolar i disorder **3 week**

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L2	308893	Jina Pharmaceuticals, Inc.	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:02 PM
L3	11231441	AHMAD, Ateeq; AHMAD, Imran; AHMAD, Moghisuddin; ALI, Shoukath M; SHEIKH, Saifuddin	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:02 PM
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L9	44	endoxifen SAME (citrate citrate) AND tablet	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L10	0	endoxifen SAME (citrate citrate) AND tablet AND enteral	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
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L12	17	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated)	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:21 PM
L13	4	12 NOT 8	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:22 PM
L14	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated) AND bipolar	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:31 PM
L15	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:32 PM

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Page 00194

		coated) AND bipolar AND (depression depressive manic mania)					
L16	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated) AND bipolar AND (depression depressive manic mania) AND features	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 08:32 PM
L17	1	"17226671" AND rescue	(US-PGPUB; USPAT)	OR	ON	ON	2022/04/23 09:34 PM
L18	362490	(A61K31/138 or A61K9/0053 or A61K9/28 or A61P25/18 or A61K9/2833).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/04/23 11:32 PM
L19	100	(A61K31/138).cpc. AND (A61K9/0053 OR A61K9/28).cpc. AND (A61P25/18).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/04/23 11:33 PM
L20	13	endoxifen AND (A61K9/0053 OR A61K9/28).cpc. AND (A61P25/18).cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL,	OR	ON	ON	2022/04/23 11:33 PM

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00195

			PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	5	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	USPAT	OR	ON	2022/04/23 20:02
S2	12	("9333190" "10376479" "11261151" "11291640").pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2022/04/23 20:33
S3	11	endoxifen SAME (citrate citrate) AND tablet AND intestine SAME (coat coating coated) and bipolar and (depression depressive manic mania) and features	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2022/04/23 20:33
S4	2	17/226628	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2022/04/23 21:49
S5	1	17/226671	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2022/04/23 21:52

EAST Search History (Interference)

<This search history is empty>

4/23/2022 11:37:24 PM

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HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

Courtesy Reminder for Application Serial No: 17/226,671

Attorney Docket No: 20110.0024USU1
Customer Number: 52835
Date of Electronic Notification: 04/28/2022

This is a courtesy reminder that new correspondence is available for this application. If you have not done so already, please review the correspondence. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

An email notification regarding the correspondence was sent to the following email address(es) associated with your customer number:
PTOMail@hsml.com

To view your correspondence online or update your email addresses, please visit us anytime at **https://ppair-my.uspto.gov/pair/PrivatePair.**
If you have any questions, please email the Electronic Business Center (EBC) at EBC@uspto.gov or call 1-866-217-9197.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	PAPER
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION.
I hereby certify that this paper is being transmitted by EFS Web to the United States Patent & Trademark Office on July 21, 2022.

By: ___/asako nakauchi/____
Name: Asako Nakauchi

AMENDMENT AND RESPONSE

Mail Stop: AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the Office Action issued April 28, 2022, please amend the above-identified application as follows:

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

Remarks begin on page 3 of this paper.

The requisite fee of $170, set forth in 37 CFR 1.20(d), is being paid herewith.

The Commissioner is hereby authorized to charge any deficiency of fees and credit any overpayments to Deposit Account Number 50-3478.

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) A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from [[of]] 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days[[;]],

wherein no ~~the patient is not administered~~ rescue medication is administered to the patient during the [[said]] treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient.

2. (Original) The method of claim 1, wherein the patient has manic episodes with mixed features.

3. (Original) The method of claim 1, wherein the patient has manic episodes without mixed features.

4. (Original) The method of claim 1, wherein the patient has depression.

5. (Currently Amended) The method of claim 1, wherein the patient ~~associated with~~ has depressive episodes.

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REMARKS

Favorable reconsideration of this application is requested in view of the above amendments and the following remarks.

Claims 1 and 5 have been amended editorially.

Claim Objections

Claim 5 has been objected to for informalities. Claim 5 has been amended editorially as suggested by the Examiner, and thus this objection should be withdrawn. Applicant respectfully requests withdrawal of the objection.

Claim Rejections - 35 U.S.C. § 102

Claims 1-5 have been rejected under 35 U.S.C. §102(a)(1) as being anticipated by Ahmad et al. *"Endoxifen, a New Treatment Option for Mania..."* (Clin. Transl. Sci. 9(5), 252-259 (2016), Ahmad (2016)). Applicant respectfully traverses this rejection.

Claim 1 is directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2-16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Claim 1 recites that no rescue medication is administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient.

The rejection states that Ahmad (2016) teaches concomitant medications such as lorazepam for treating the bipolar I disorder and then discontinued them before the treatment to avoid efficacy or safety overlap with the endoxifen (see page 4 of the Office Action issued April 28, 2022). Applicant respectfully disagrees.

Ahmad (2016) discloses "[a]ll psychotropic medications except benzodiazepines (lorazepam/diazepam only) were discontinued at least 2 days before randomization. Benzodiazepines...were allowed as adjunctive medications as needed...from 2 days prior to randomization but not beyond the first 10 days of investigational medicinal product dosing" (see "Concomitant medications" section at left coln. on page 254 (emphases added)).

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As per the claimed invention, the inventors found that there is no need to administer other medications (i.e. lorazepam) during a period of the treatment of the bipolar I disorder by maintaining the therapeutically effective concentration of endoxifen in the patient, which is achieved by administering endoxifen citrate to the patient as recited in claim 1 (see "Clinical study data" and "Design of the study" sections on page 6 of the present specification).

In contrast, as discussed above, Ahmad (2016) allows to administer benzodiazepines to the patient to whom endoxifen is administered, up to 10 days from starting administering of endoxifen, and Ahmad (2016) does not disclose that no rescue medication is administered to the patient during the treatment of the bipolar I disorder by maintaining the therapeutically effective concentration of endoxifen in the patient, as claim 1 recites.

Accordingly, claim 1 and its dependent claims 2-5 are distinguished from Ahmad (2016), and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Double Patenting

Claims 1-5 have been rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 11,291,640 (Ahmad '640). Applicant respectfully traverses this rejection.

Claim 1 of the Ahmad '640 is directed to the method by which the patient has an early response time to the treatment in at least 2 days from starting the administration and a remission time that is not more than 4 days. Claims 1-6 of Ahmad '640 do not disclose or suggest that no rescue medication is administered to the patient during the treatment of the bipolar I disorder by maintaining the therapeutically effective concentration of endoxifen in the patient, as recited in present claim 1. In fact, the rejection states that the claims of Ahmad '640 are not identical to those of the present application (see page 6 of the Office Action).

Without conceding this rejection stating that the pending claims are patentably indistinct over the cited pending applications, but in order to expedite prosecution of the subjected application, Applicant submits herewith a terminal disclaimer over U.S. Patent No. 11,291,640.

Accordingly, this rejection is moot and should be withdrawn

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Claims 1-5 have been rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 (Ahmad '479) in the view of Ahmad et al. *"Endoxifen, a New Treatment Option for Mania..."* (Clin. Transl. Sci. 9(5), 252-59 (2016), Ahmad (2016)). Applicant respectfully traverses this rejection.

Claim 1 of Ahmad '479 is directed to a method of delivering endoxifen to the plasma of a subject. Claim 1 of Ahmad '479, however, does not disclose that no rescue medication is administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient, as present claim 1 recites.

As discussed above, Ahmad '479 and Ahmad (2016) do not disclose the feature of administering no rescue medication to the patient during the treatment of the bipolar I disorder by maintaining the therapeutically effective concentration of endoxifen in the patient, as present claim 1 recites.

Accordingly, present claim 1 and its dependent claims 2-5 are distinguished from claim 1 of Ahmad '479 in view of Ahmad (2016), and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Claims 1-5 have been provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims of copending Application No. 17/023,208 (US '208) in view of Ahmad et al. *"Endoxifen, a New Treatment Option for Mania..."* (Clin. Transl. Sci. 9(5), 252-59 (2016) Ahmad (2016)). Applicant respectfully traverses this rejection.

Claims of US '208 are directed to a method of inhibiting protein kinase C (PKC) in a subject, or a method of inhibiting protein kinase C (PKC) in a subject by delivering endoxifen to the plasma of the subject. The claims of US '208 and Ahmad (2016) do not disclose or suggest that no rescue medication is administered to the patient during the treatment of the bipolar I disorder by maintaining the therapeutically effective concentration of endoxifen in the patient, as present claim 1 recites.

Accordingly, present claim 1 and its dependent claims 2-5 are distinguished from claims of US '208 in view of Ahmad (2016), and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

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Claims 1-5 have been provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims of copending Application No. 17/226,703; and claims of copending Application No. 17/226,651. Applicant submits herewith a terminal disclaimer over co-pending application Nos. 17/226,703 and 17/226,651. Accordingly, this rejection is moot and should be withdrawn. Applicant does not concede the correctness of this rejection.

In view of the above, Applicant requests reconsideration of the application in the form of a Notice of Allowance.

Respectfully submitted,

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683
(612) 455-3814

Dated: July 21, 2022

By: /Masako Yoshida/
Masako Yoshida
Reg. No. 70,057
MY/an

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00204

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	PAPER
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION
I hereby certify that this paper is being transmitted by EFS Web to the United States Patent & Trademark Office on July 21, 2022.

By: /asako nakauchi/
Name: Asako Nakauchi

TERMINAL DISCLAIMER

Mail Stop: AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

Petitioner, JINA PHARMACEUTICALS, INC., the owner of the entire right, title and interest in the above identified application, U.S. Patent No. 11,291,640 issued from U.S. patent Application No. 17/226,628, and U.S. Patent Application Nos. 17/226,703 and 17/226,651, through the undersigned attorney of record, hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the above-identified application that would extend beyond the expiration date of the full statutory term of U.S. Patent No. 11,291,640 and patents granted on U.S. Patent Application Nos. 17/226,703 and 17/226,651, and hereby agrees that any patent so granted on the above-identified application shall be enforceable only for and during such period that said patent and U.S. Patent No. 11,291,640 and patents granted on U.S. Patent Application Nos. 17/226,703 and 17/226,651, shall be commonly owned, this agreement to run with any patent granted on the above-identified application and to be binding upon the grantee, its successors, or assigns.

In making the above disclaimer, Petitioner does not disclaim the terminal part of any patent granted on the above-identified application that would extend to the full statutory term as presently shortened by any terminal disclaimer of U.S. Patent No. 11,291,640 and patents granted on U.S. Patent Application Nos. 17/226,703 and 17/226,651, in the event that U.S. Patent No. 11,291,640 or a patent granted on U.S. Patent Application Nos. 17/226,703 and 17/226,651 expires for failure to pay a maintenance fee, is held unenforceable, is found invalid, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321(a), has all claims cancelled by a reexamination certification, or is otherwise terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer, except for the separation of ownership stated above.

The requisite fee of $170, set forth in 37 CFR 1.20(d), is being paid herewith.

Respectfully submitted,

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 S. 7th St., Suite 2700
Minneapolis, MN 55402
(612) 455-3814

Dated: July 21, 2022

By: /Masako Yoshida/
Masako Yoshida
Reg. No.: 70,057
MY/an

Electronic Patent Application Fee Transmittal

Application Number:	17226671
Filing Date:	09-Apr-2021
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Filer:	Masako Yoshida/Asako Nakauchi
Attorney Docket Number:	20110.0024USU1

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

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($)
Miscellaneous:				
STATUTORY OR TERMINAL DISCLAIMER	1814	1	170	170
		Total in USD ($)		**170**

Electronic Acknowledgement Receipt

EFS ID:	46241141
Application Number:	17226671
International Application Number:	
Confirmation Number:	1772
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Customer Number:	52835
Filer:	Masako Yoshida/Asako Nakauchi
Filer Authorized By:	Masako Yoshida
Attorney Docket Number:	20110.0024USU1
Receipt Date:	21-JUL-2022
Filing Date:	09-APR-2021
Time Stamp:	12:37:17
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$170
RAM confirmation Number	E20227KC37432990
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		Amendment.pdf	153392 d7d80ca2d586c78d2215ecaadbeba3d508 20a910	yes	6
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Amendment/Request for Reconsideration-After Non-Final Rejection		1	1	
	Claims		2	2	
	Applicant Arguments/Remarks Made in an Amendment		3	6	
Warnings:					
Information:					
2	Terminal Disclaimer Filed	Terminal_Disclaimer.pdf	74173 28442526c1cdde5d0a7c7bc2dd792f64e51 4caad	no	2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	37915 8be3b5d7da002223f059193112173f24bec 81458	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	265480		

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)
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 17/226,671	Filing Date 04/09/2021	☐ 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 $100 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $480 =	
☐ 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	07/21/2022	(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))	* 5	Minus	** 20	= 0		x $100 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0		x $480 =	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 $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ 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.	SLIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/ANISSA D DEVLIN/
*** 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.	

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.

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
* 17/226,671 *	17/226,671	AHMAD et al.	
	Examiner	Art Unit	
	CHANNAVAJJALA, LAKSHMI SARADA	1611	

Document Code - DISQ	Internal Document - DO NOT MAIL

TERMINAL DISCLAIMER	☑ APPROVED	☐ DISAPPROVED
Date Filed: 21 July 2022	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:

/KIMBERLY R WHITE/

Technology Center: OPLC

Telephone: (571)272-6179

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00213

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1	1772

52835 7590 11/08/2022

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
11/08/2022	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOMail@hsml.com

Atossa Therapeutics, Inc. Exhibit 1002
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Office Action Summary	Application No. 17/226,671	Applicant(s) AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	Art Unit 1611	AIA (FITF) Status Yes

-- 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 MONTHS 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 _____.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

3)☐ 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.

4)☐ 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*

5) ☑ Claim(s) 1-5 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-5 is/are rejected.

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

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

* If any claims have been determined allowable, 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.**

Application Papers

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

11)☐ 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).

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).

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)).

** 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) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

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

4) ☐ Other: _____.

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Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Receipt of amendment and response dated 7/21/22 is acknowledged.

Claims 1-5 are pending.

Terminal Disclaimer

The terminal disclaimer filed on 7/21/22 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 11,291,640, copending applications 17/226,651 and 17/226,703. has been reviewed and is accepted. The terminal disclaimer has been recorded.

In response to the amendment, the previous rejection of record has been replaced with the following new rejection:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claim(s) 1-5 are is/are rejected under 35 U.S.C. 102((a)(1)) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Ahmad et al (2016, cited on IDS).

Instant claims are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days.

Claim 1 has been amended to recite "wherein no rescue medication is administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient".

Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BP) with current manic or mixed episode.

Ahmad states that several drugs have been approved such as lithium, valproate, carbamazepine, and atypical antipsychotics for the treatment of acute bipolar mania, which while providing relief for many individuals with BP, significant issues with tolerability and efficacy still remain. Ahmad describes that adherence to the treatment is affected by adverse effects such as sedation and weight gain, and that there is an urgent need to develop novel and more effective treatments for BP (p 252). Ahmad teaches enteric coated endoxifen citrate salt ("CgHgO7" is citric acid, see figure 1 and page 253, col. 2- Methodology) (claim 1). The results were expressed as Young Mania Rating Scale (YMRS) total score (≥50% decrease from baseline). Secondary end points were mean change from baseline to the end of treatment in the Montgomery–Åsberg Depression Rating Scale (MADRS) total score, Clinical Global Impressions–Severity of Illness Scale (CGI-S) score, and Columbia–Suicide Severity Rating Scale (C-SSRS) score, shown in Table 1. Ahmad teaches that a switch to depression remains a concern in all treatments of bipolar mania, depressive symptoms were assessed with the

MADRS score throughout the trial. Ahmad teaches effectiveness of endoxifen 4 mg and 8 mg in alleviating depressive symptoms of mixed episode of BPD similar to that of divalproex (p 256, col.1 & Table 2) (claim 1). Further, the administration of endoxifen (4 mg and 8 mg) provides a steady state plasma concentration of endoxifen for 14 and also 20 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect (which can be construed as without mixed episode) or mixed episodes patients of endoxifen (p 258). In a double-blind, active-controlled study, 84 subjects with BPD I were randomly assigned to receive endoxifen (4 mg/day or 8 mg/day) or divalproex in a 2:1 ratio. Patients orally administered 4 mg/day or 8 mg/day endoxifen showed significant improvement in mania assessed by the Young Mania Rating Scale as early as 4 days. The effect remained significant throughout the 21-day period. At study end point, response rates were 44.44% and 64.29% at 4 mg/day and 8 mg/day of endoxifen treatment, respectively (abstract). Thus, Ahmad teaches endoxifen has been shown as a promising novel antimanic or mood stabilizing agent, as seen by significantly improved YMRS scale at almost every treatment evaluation.

The newly added limitation excludes administering any rescue medication during the treatment so as to maintain a therapeutically effective concentration of endoxifen. Ahmad teaches concomitant medications such as lorazepam have been discontinued before treatment and thus meet the instant claim limitation. Ahmad teaches that the plasma concentration of endoxifen is maintained at 14 and 20 days, indicating steady state of the endoxifen (fig.4). Ahmad also teaches monotherapy trials of drugs for the treatment of bipolar disorder (table 3 and 4b).

Thus, the monotherapy in Table 3 of Ahmad (administering only endoxifen (4 mg or 8 mg)) meets the instant claimed "no rescue medication is administered", and thus Ahmad anticipates instant method of administration. This is further evidenced from the study design (fig. 2) of Ahmad wherein the design does **not** include any benzodiazepines. Further, with respect to maintaining the therapeutically effective concentration of endoxifen in the patient, Ahmad teaches that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen).

Alternatively, if Applicants argue that Ahmad does not explicitly state not administering rescue medication for maintaining the therapeutically effective concentration of endoxifen in the patient, Ahmad also teaches that benzodiazepines are allowed as adjunctive medication as needed at the discretion of the investigator (p 254). Thus, Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen. Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen without any other medication such as benzodiazepines because Ahmad suggests benzodiazepines only as needed and further Ahmad shows that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2-pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen). One of an ordinary skill in the art would have expected only endoxifen citrate to be effective in treating BD and also main therapeutically effective plasma concentration because Ahmad teaches a study design without any concomitant

medication and yet providing endoxifen concentration for up to 21 days. Further, Ahmad teaches 4 mg and 8 mg/day endoxifen citrate and for the same dosage regimen. Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of a rescue medication.

Double Patenting

2. Claims 1-5 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 in view of Ahmad et al (2016, cited on IDS).

Patented claims are directed to a method of delivering endoxifen to the plasma of a subject, comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver and the endoxifen is a synthetic endoxifen that is at least 80% z-endoxifen and in the form of a citrate salt.

Patented claims do not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patented claims also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5.

The teachings of Ahmad have been discussed above and incorporated here with. Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BPD I) with current manic or mixed episode.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (patented claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. A skilled artisan would have been motivated because Ahmad teaches administering endoxifen 4 mg and 8 mg for alleviating depressive symptoms of mixed episode of BPD similar to that of divalproex, with a steady state plasma concentration of endoxifen for 14 and also 21 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect or mixed episodes patients of endoxifen (p 258).

The newly added limitation excludes administering any rescue medication during the treatment so as to maintain a therapeutically effective concentration of endoxifen.

Ahmad teaches concomitant medications such as lorazepam have been discontinued before treatment and thus meet the instant claim limitation. Ahmad teaches that the plasma concentration of endoxifen is maintained at 14 and 20 days, indicating steady state of the endoxifen (fig.4). Ahmad also teaches monotherapy trials of drugs for the treatment of bipolar disorder (table 3 and 4b).

Thus, the monotherapy in Table 3 of Ahmad (administering only endoxifen (4 mg or 8 mg)) meets the instant claimed "no rescue medication is administered. This is further evidenced from the study design (fig. 2) of Ahmad wherein the design does not include

any benzodiazepines. Further, with respect to maintaining the therapeutically effective concentration of endoxifen in the patient, Ahmad teaches that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen).

In the alternative, Ahmad also teaches that benzodiazepines are allowed as adjunctive medication as needed at the discretion of the investigator (p 254). Thus, Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen. Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to modify the patented claims to administer only endoxifen without any other medication such as benzodiazepines because Ahmad suggests benzodiazepines only as needed and further Ahmad shows that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen).

3. Claims 1-5 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over the claims of copending Application No. 17/023208 in view of Ahmad et al (2016, cited on IDS).

Copending claims are directed to a method of inhibiting protein kinase C by administering an enteric coated tablet comprising endoxifen citrate. However, a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a

patient with bipolar I disorder. Copending claims lack the amounts of endoxifen citrate, for the duration of 21 days, and also lacks instant claims 4-5.

The teachings of Ahmad have been discussed above and incorporated here with. Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BPD I) with current manic or mixed episode.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (copending claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. A skilled artisan would have been motivated because Ahmad teaches administering endoxifen 4 mg and 8 mg for alleviating depressive symptoms of mixed episode of BPD similar to that of divalproex, with a steady state plasma concentration of endoxifen for 14 and also 21 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect or mixed episodes patients of endoxifen (p 258).

The newly added limitation excludes administering any rescue medication during the treatment so as to maintain a therapeutically effective concentration of endoxifen.

Ahmad teaches concomitant medications such as lorazepam have been discontinued before treatment and thus meet the instant claim limitation. Ahmad teaches that the plasma concentration of endoxifen is maintained at 14 and 20 days,

indicating steady state of the endoxifen (fig.4). Ahmad also teaches monotherapy trials of drugs for the treatment of bipolar disorder (table 3 and 4b).

Thus, the monotherapy in Table 3 of Ahmad (administering only endoxifen (4 mg or 8 mg)) meets the instant claimed "no rescue medication is administered. This is further evidenced from the study design (fig. 2) of Ahmad wherein the design does not include any benzodiazepines. Further, with respect to maintaining the therapeutically effective concentration of endoxifen in the patient, Ahmad teaches that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen).

In the alternative, Ahmad also teaches that benzodiazepines are allowed as adjunctive medication as needed at the discretion of the investigator (p 254). Thus, Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen. Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to modify the patented claims to administer only endoxifen without any other medication such as benzodiazepines because Ahmad suggests benzodiazepines only as needed and further Ahmad shows that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2-pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen).

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed 7/21/22 have been fully considered but they are not persuasive.

With respect to each of the rejections under 35 USC 103 and the Double Patenting rejections over US Patent 10376479, copending application 17/023208, Applicants arguments have been considered but not found persuasive.

Applicants argue that Ahmad teaches psychotropic medications except benzodiazepines (lorazepam/diazepam only) were discontinued at least 2 days before randomization. It is argued that the inventors found that, according to the instant invention, there is no need to administer other medications (i.e. lorazepam) during a period of the treatment of the bipolar I disorder by maintaining the therapeutically effective concentration of endoxifen in the patient, which is achieved by administering endoxifen citrate to the patient as recited in claim 1 (see "Clinical study data" and "Design of the study" sections on page 6 of the present specification). It is argued that in contrast, Ahmad (2016) allows to administer benzodiazepines to the patient to whom endoxifen is administered, up to 10 days from starting administering of endoxifen, and Ahmad (2016) does not disclose that no rescue medication is administered to the patient during the treatment of the bipolar I disorder by maintaining the therapeutically effective concentration of endoxifen in the patient, as claim 1 recites.

Applicants' arguments are not persuasive because Ahmad teaches concomitant medications such as lorazepam have been discontinued before treatment. Ahmad

teaches that the plasma concentration of endoxifen is maintained at 14 and 20 days, indicating steady state of the endoxifen (fig.4). Ahmad also teaches monotherapy trials of drugs for the treatment of bipolar disorder and (table 3 and 4b). Thus, Ahmad teaches administering endoxifen composition that is same as the claimed enteric coated tablet comprising endoxifen citrate, administered with amounts that falls within the claimed ranges and also for the claimed duration. According to Ahmad treatment of bipolar disorder (BD), as described in Tables 3 and 4b, does not include any rescue medication. From the study design, endoxifen treated patient population does not include any treat

Alternatively, if Applicants argue that Ahmad does not explicitly state not administering rescue medication for maintaining the therapeutically effective concentration of endoxifen in the patient, Ahmad also teaches that benzodiazepines are allowed as adjunctive medication as needed at the discretion of the investigator (p 254). Thus, Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen. Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen without any other medication such as benzodiazepines because Ahmad suggests benzodiazepines only as needed and further Ahmad shows that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2-pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen). One of an ordinary skill in the art would have expected only endoxifen citrate to be effective in treating BD and also main therapeutically effective plasma

concentration because Ahmad teaches a study design without any concomitant medication and yet providing endoxifen concentration for up to 21 days. Further, Ahmad teaches 4 mg and 8 mg/day endoxifen citrate and for the same dosage regimen. Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of a rescue medication.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKSHMI SARADA CHANNAVAJJALA whose

telephone number is (571)272-0591. The examiner can normally be reached Generally M- F 9 AM to 6 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

CPC - Searched*		
Symbol	Date	Examiner
classification- attached	04/23/2022	LC

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
PE2E search history- all data bases- inventor, classification, text- attached	04/23/2022	LC
google scholar	04/23/2022	LC
PE2E search history- all data bases- inventor, classification, text- attached	11/03/2022	LC
google scholar	11/03/2022	LC

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	2	"17226671"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/01 02:38 PM
L2	1	"17/226671"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/01 02:40 PM
L3	6	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2022/11/03 10:14 AM
L4	136	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 10:14 AM
L5	18	L4 AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 10:17 AM
L6	388	endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 10:18 AM

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L7	46	endoxifen SAME (plasma OR pharmacokinetic) SAME (effective OR concentration)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 10:19 AM
L8	3	endoxifen SAME (plasma OR pharmacokinetic) SAME (effective OR concentration) SAME bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 10:19 AM
L9	21	endoxifen SAME (plasma OR pharmacokinetic) SAME (effective OR concentration) AND bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 10:19 AM
L10	21	endoxifen SAME (plasma OR pharmacokinetic) SAME (effective OR concentration) AND tablet AND bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 11:27 AM
L11	6	endoxifen SAME (plasma OR pharmacokinetic) SAME (effective OR concentration) SAME tablet AND bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 11:27 AM
L12	22	endoxifen SAME tablet AND bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 11:27 AM
L13	10	endoxifen SAME tablet SAME bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/11/03 11:27 AM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

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Endoxifen, a new treatment option for **mania**: a double-blind, active-controlled trial demonstrates the antimanic efficacy of **endoxifen**

A Ahmad, S Sheikh, T Shah, MS Reddy ... - Clinical and ..., 2016 - Wiley Online Library

... , respectively, whereas for **endoxifen** at 8 mg/day ... **plasma** AUC. We have shown in our earlier single-dose study13 that AUC and maximum **plasma concentration** (C max) for **endoxifen** ...

☆ Save 99 Cite Cited by 15 Related articles All 7 versions »

Endoxifen, an estrogen receptor targeted therapy: From bench to bedside

S Jayaraman, JM Reid, JR Hawse, MP Goetz - Endocrinology, 2021 - academic.oup.com

... of oral **Z-endoxifen** resulted in **plasma concentrations** of **Z-endoxifen** reaching as high as ... Bipolar I disorder is a chronic mental illness characterized by the occurrence of acute **mania** ...

☆ Save 99 Cite Cited by 7 Related articles All 6 versions »

Orally administered **endoxifen** inhibits tumor growth in melanoma-bearing mice

P Chen, S Sheikh, A Ahmad, SM Ali ... - Cellular & ..., 2018 - cmbl.biomedcentral.com

... **plasma concentration** (C max) of 34 ng/ml and the **endoxifen** was found to accumulate in the **plasma** ... **plasma** and other tissues, like the lungs, and in lung-associated melanoma lesions. ...

☆ Save 99 Cite Cited by 4 Related articles All 11 versions »

Cancer diagnosis in people with severe mental illness: practical and ethical issues

LM Howard, EA Barley, S Davies, A Rigg, H Lempp... - The lancet oncology, 2010 - Elsevier

... **mania**) and on others mood is lowered and energy and activity decreased (depression). Repeated episodes of hypomania or **mania** ... to lower **plasma concentrations** of **endoxifen**. There ...

☆ Save 99 Cite Cited by 183 Related articles All 13 versions

Use of antidepressants in patients with breast cancer taking tamoxifen

SH Kim, MR Lee, KC Lee, JH Lee... - Journal of Breast ..., 2010 - synapse.koreamed.org

... the illness, anti-**manic** effects of tamoxifen in ... on **endoxifen plasma concentrations**. They found that the CYP2D6 genoptypes are highly associated with **endoxifen plasma concentrations** ...

☆ Save 99 Cite Cited by 5 Related articles All 24 versions »

Therapeutic Approaches to Bipolar Disorder

MU Ahmad, SM Ali, S Sheikh, A Ahmad... - Drug Discovery for ..., 2012 - books.google.com

... **concentration** of lamotrigine in the blood. Valproate doubles the **plasma level** of lamotrigine, and the **level** of ... with tamoxifen in acute **mania**, and very recently **endoxifen**, which exhibited ...

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Therapeutic Drug Monitoring and Toxicology of Anticancer Drugs

S Kohli, LK Conway - Recent Advances in Therapeutic Drug Monitoring and ..., 2022 - Springer

... **endoxifen plasma concentration**. Therefore, TDM of tamoxifen is based on the monitoring of **endoxifen plasma concentrations**, ... The **plasma concentration** of the metabolite **endoxifen** can ...

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Ziprasidone in the treatment of acute bipolar **mania**: a three-week, placebo-controlled, double-blind, randomized trial

..., Ziprasidone in Mania Study Group - American Journal of ..., 2003 - Am Psychiatric Assoc

... the treatment of adult patients with acute bipolar **mania**. METHOD: Patients with a primary DSM-IV diagnosis of bipolar I disorder and a current **manic** or mixed episode (confirmed by the ...

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Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00232

Rapid antimanic effect of risperidone monotherapy: a 3-week multicenter, double-blind, placebo-controlled trial

PMA Hirschfeld, PE Keck Jr, M Kramer ... - American journal of ..., 2004 - Am Psychiatric Assoc

... **mania**. METHOD: Patients with DSM-IV bipolar I disorder experiencing an acute **manic** episode (baseline Young **Mania** ... Among men, the mean **plasma** prolactin **levels** increased from ...

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Valproate for acute **mania**

J Jochim, RP Rifkin-Zybutz, J Geddes ... - Cochrane Database ..., 2019 - cochranelibrary.com

... Ahmad 2016 compared valproate with two different doses of **endoxifen** (4 mg versus 8 mg), which we merged for our purposes. Bowden 1994 compared valproate, lithium, and placebo. ...

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HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

Courtesy Reminder for
Application Serial No: 17/226,671

Attorney Docket No: 20110.0024USU1
Customer Number: 52835
Date of Electronic Notification: 11/08/2022

This is a courtesy reminder that new correspondence is available for this application. If you have not done so already, please review the correspondence. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

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P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

ACKNOWLEDGEMENT OF CHANGE TO SMALL ENTITY STATUS

APPLICATION #	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET #	REQUEST ID
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1	62398

The entity status change request below filed through Patent Center on 02/03/2023 has been accepted.

Certifications

APPLICANT ASSERTING SMALL ENTITY STATUS. See 37CFR 1.27.

Signature

I certify, in accordance with 37 CFR 1.4(d)(4), that I am one of the signatories making the entity status change.

Signature	Name	Registration #
/Masako Yoshida/	Masako Yoshida	70057

Doc Code: A.NE.AFCP
Document Description: After Final Consideration Program Request

PTO/SB/434 (3-22)

CERTIFICATION AND REQUEST FOR CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0

Practitioner Docket No.:	Application No.:	Filing Date:
20110.0024USU1	17/226,671	2021-04-09
First Named Inventor:	**Title:**	
AHMAD, Ateeq	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0 (AFCP 2.0) OF THE ACCOMPANYING RESPONSE UNDER 37 CFR 1.116.

1. The above-identified application is (i) an original utility, plant, or design nonprovisional application filed under 35 U.S.C. 111(a) [a continuing application (*e.g.*, a continuation or divisional application) is filed under 35 U.S.C. 111(a) and is eligible under (i)], or (ii) an international application that has entered the national stage in compliance with 35 U.S.C. 371(c).
2. The above-identified application contains an outstanding final rejection.
3. Submitted herewith is a response under 37 CFR 1.116 to the outstanding final rejection. The response includes an amendment to at least one independent claim, and the amendment does not broaden the scope of the independent claim in any aspect.
4. This certification and request for consideration under AFCP 2.0 is the only AFCP 2.0 certification and request filed in response to the outstanding final rejection.
5. Applicant is willing and available to participate in any interview requested by the examiner concerning the present response.
6. This certification and request is being filed electronically using the USPTO's patent electronic filing system.
7. Any fees that would be necessary consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, extension of time fees, are being concurrently filed herewith. [There is no additional fee required to request consideration under AFCP 2.0.]
8. By filing this certification and request, applicant acknowledges the following:
   - Reissue applications and reexamination proceedings are not eligible to participate in AFCP 2.0.
   - The examiner will verify that the AFCP 2.0 submission is compliant, *i.e.*, that the requirements of the program have been met (see items 1 to 7 above). For compliant submissions:
     - The examiner will review the response under 37 CFR 1.116 to determine if additional search and/or consideration (i) is necessitated by the amendment and (ii) could be completed within the time allotted under AFCP 2.0. If additional search and/or consideration is required but cannot be completed within the allotted time, the examiner will process the submission consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, by mailing an advisory action.
     - If the examiner determines that the amendment does not necessitate additional search and/or consideration, or if the examiner determines that additional search and/or consideration is required and could be completed within the allotted time, then the examiner will consider whether the amendment places the application in condition for allowance (after completing the additional search and/or consideration, if required). If the examiner determines that the amendment does not place the application in condition for allowance, then the examiner will contact the applicant and request an interview.
       - The interview will be conducted by the examiner, and if the examiner does not have negotiation authority, a primary examiner and/or supervisory patent examiner will also participate.
       - If the applicant declines the interview, or if the interview cannot be scheduled within ten (10) calendar days from the date that the examiner first contacts the applicant, then the examiner will proceed consistent with current practice concerning responses after final rejection under 37 CFR 1.116.

Signature	Date	Practitioner Registration No.
/Masako Yoshida/	February 8, 2023	70,057
Name (Print/Typed)	**Telephone Number**	
Masako Yoshida	(612) 455-3814	

***Note**: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.*

☐ * Total of _____ forms are submitted.

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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.
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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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	CHANNAVAJJALA
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION.
I hereby certify that this paper is being transmitted by EFS Web to the United States Patent & Trademark Office on February 8, 2023.

By: /Maria Wait/
Name: Maria Wait

AMENDMENT AND RESPONSE

Mail Stop: AF
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the Office Action issued November 8, 2022, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims as marked copy that begins on page 2.

Remarks begin on page 3 of this paper.

After Final Consideration Pilot request is filed with this paper.

The Commissioner is hereby authorized to charge any deficiency of fees and credit any overpayments to Deposit Account Number 50-3478.

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) A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days,

wherein no rescue medication is required to be administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient, wherein the rescue medicine is at least one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics.

2. (Original) The method of claim 1, wherein the patient has manic episodes with mixed features.

3. (Original) The method of claim 1, wherein the patient has manic episodes without mixed features.

4. (Original) The method of claim 1, wherein the patient has depression.

5. (Previously Presented) The method of claim 1, wherein the patient has depressive episodes.

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REMARKS

Favorable reconsideration of this application is requested in view of the above amendments and the following remarks. The amendments to claim 1 are supported by the original disclosure, for example, by page 4, last paragraph of the specification as filed.

Claim Rejections - 35 U.S.C. § 102/103

Claims 1-5 have been rejected under 35 U.S.C. §102(a)(1) as being anticipated by, or, in the alternative, obvious over Ahmad et al. *"Endoxifen, a New Treatment Option for Mania..."* Clin. Transl. Sci. 9(5), 252-59 (2016) Ahmad (2016). Applicant respectfully traverses this rejection.

Claim 1 is directed to a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Claim 1 recites that no rescue medication is required to be administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient, wherein the rescue medicine is at least one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics.

The rejection admits that Ahmad teaches concomitant medications such as lorazepam have been discontinued before the treatment to avoid efficacy or safety overlap with the endoxifen, but contends that it would have been obvious to achieve the features of claim 1 (see page 4 of the Office Action issued November 8, 2022). Applicant respectfully disagrees.

In particular, Ahmad's study focuses on the evaluation of the efficacy and safety of endoxifen in BPD I patients with current manic or mixed episode (see, e.g., page 253 of Ahmad (2016)). On the other hand, claim 1 recites that no rescue medication is required to be administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient.

It is noted that there are many combination therapies available for bipolar I disorder (BPD I) as reserved as a subsequent choice or for severe cases. However, such drugs for treatment of BPD I are generally known to have many possible side effects. Moreover, in

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routine practice, monotherapy is often not sufficiently effective for acute and/or maintenance therapy. As a consequence, most patients are given combination therapies. Claim 1 on the other hand recites a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with BPD I, and further recites that no rescue medication is required to be administered to the patient during the treatment of the BPD I by the maintaining the therapeutically effective concentration of endoxifen in the patient.

Furthermore, Ahmad (2016) describes the following:

"All psychotropic medications except benzodiazepines (lorazepam/diazepam only) were discontinued at least 2 days before randomization. Benzodiazepines (lorazepam/diazepam only) (up to 5 mg/day, preferably in divided doses) were allowed as adjunctive medication as needed at the discretion of the investigator from 2 days prior to randomization but not beyond the first 10 days of investigational medicinal product dosing. Benzodiazepines were avoided within 12 h of scheduled mania rating." (see page 254 of Ahmad (2016)).

That is to say, during Ahmad's study, benzodiazepines (i.e., lorazepam/diazepam) were allowed to be administered as concomitant medicines. Further, benzodiazepines were allowed to be administered for 2 days prior to the study and continued to be administered for the first 10 days of the study. According to Ahmad's study, benzodiazepines were avoided within 12 hours of mania rating only. As such, administering benzodiazepines (i.e., lorazepam/diazepam) that is recited in claim 1 as a rescue medicine is not excluded from the medication in Ahmad. It is important to note that Ahmad's study mentions that the investigator is allowed to administer concomitant medicines (as rescue medicines) if the patient showed undue excitement (see "Concomitant medications" section on page 254 of Ahmad (2016)). This implies that the investigator had to monitor the patients continuously to investigate whether the rescue medication would be required for each and every patient undergoing the treatment according to Ahmad's study. On the other hand, claim 1 recites that no rescue medication is required to be administered to the patient during the treatment of the BPD I by the maintaining the therapeutically effective concentration of endoxifen in the patient, wherein the rescue medicine is at least one selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics.

As per the claimed invention, the rescue medication is not administered during a period of maintaining the therapeutically effective concentration of endoxifen in the patient, and there is

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no need to administer other rescue medications taught by Ahmad, namely, benzodiazepines, lorazepam, to the patient undergoing the endoxifen treatment according to the claimed invention. Accordingly, claim 1 and its dependent claims 2-5 are distinguished from Ahmad (2016), and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Double Patenting

Claims 1-5 have been rejected on the ground of non-statutory double patenting as being unpatentable over claims 1 of U.S. Patent No. 10,376,479 (Ahmad '479) in view of Ahmad (2016). Applicant respectfully traverses this rejection.

Claim 1 of the Ahmad '479 is directed to a method of delivering endoxifen to the plasma of a subject, and recites "[a method of delivering endoxifen to the plasma of a subject comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver endoxifen to the plasma of the subject, wherein : i) said preparation of endoxifen is at least 80% z-endoxifen; and ii) said synthetic preparation of endoxifen is in the form of a citrate salt.

Claim 1 of Ahmad '479 does not disclose or suggest maintaining a therapeutically effective concentration of endoxifen in a patient undergoing treatment of bipolar I disorder (BPD I) by administering 2-16 mg/once a day of endoxifen citrate in an enteric coated tablet for at least 21 days to the patient, as present claim 1 recites. In fact, the rejection admits that the patented claim 1 of Ahmad '479 does not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with BPD I, and also lacks the claimed amounts of endoxifen citrate and the period of administration (see page 6 of the Office Action). Even further, claim 1 of Ahmad '479 does not disclose or suggest that no rescue medication is required to be administered to the patient during the treatment of the BPD I by the maintaining the therapeutically effective concentration of endoxifen in the patient, wherein the rescue medicine is at least one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics, as recited in present claim 1. Thus, claim 1 of US '479 is distinguished from present claim 1.

Ahmad (2016) does not remedy the deficiencies of claim 1 of Ahmad '479. As discussed above, Ahmad (2016) teaches benzodiazepines (i.e. lorazepam/diazepam) is allowed as a

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concomitant treatment with endoxifen therapy for BPD I (page 254 of Ahmad (2016)). As such, during Ahmad (2016)'s study, the investigator is allowed to administer concomitant medicine(s) (as rescue medicines) if the patient shows undue excitement (see "Concomitant medications" section on page 254). This implies that the investigator has to monitor the patients continuously to investigate whether the rescue medication would be required for each and every patient undergoing the treatment according to Ahmad's study. On the other hand, present claim 1 recites that no rescue medication is required to be administered to the patient during the treatment of the BPD I by the maintaining the therapeutically effective concentration of endoxifen in the patient, wherein the rescue medicine is at least one selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics. Thus, the monitoring of the patients necessary in Ahmad (2016) is not necessary in the method of claim 1.

In view of the above, Applicant submits that present claim 1 and its dependent claims 2-5 are distinguished from claim 1 of Ahmad '479 in view of Ahmad (2016), and this rejection should be withdrawn.

Claims 1-5 are provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims of co-pending Application No. 17/023208 (US '208) in view of Ahmad (2016). Applicant respectfully traverses this rejection.

Applicant notes that the 17/023208 application has claims 26-28. Applicant respectfully requests that the claims in US '208 cited in this rejection be clarified. In case that all claims 26-28 of US '208 are cited, which Applicant does not concede, Applicant will discuss claims 26-28 below.

Claims 26-28 of US '208 are directed to a method of inhibiting protein kinase C (PKC) in a subject by delivering endoxifen to the plasma of the subject. Claims 26-28 of US '208, however, do not disclose or suggest maintaining of a therapeutically effective concentration of endoxifen in a patient undergoing a treatment of bipolar I disorder (BPD I) by administering of endoxifen citrate to the patient in an amount of 2-16 mg/once a day in an enteric coated tablet for at least 21 days, wherein the rescue medication is not require to administered during a period of the maintaining the therapeutically effective concentration of endoxifen in the patient, and wherein the rescue medicine is at least one selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics. as claim 1 recites. In fact, the

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rejection admits that claims 26-28 of US '208 lack the teaching of the amounts of endoxifen citrate for the duration of 21 days as recited in claim 1 of the present application (see page 9 of the Office Action).

Ahmad (2016) does not remedy the deficiencies of claims 26-28 of US '208. In particular, as discussed above, Ahmad (2016) teaches the inclusion of benzodiazepines (i.e. lorazepam/diazepam) as a concomitant treatment with endoxifen therapy for BPD. As such, during Ahmad (2016)'s study, the investigator is allowed to administer a concomitant medicine(s) (as rescue medicines) if the patient shows undue excitement (see "Concomitant medications" section on page 254). This implies that the investigator has to monitor the patients continuously to investigate whether the rescue medication would be required for each and every patient undergoing the treatment according to Ahmad (2016)'s study. On the other hand, present claim 1 recites that no rescue medication is required to be administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient, wherein the rescue medicine is at least one selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics. Thus, the monitoring of the patients necessary in Ahmad (2016) is not necessary in the method of present claim 1.

In view of the above, Applicant submits that present claim 1 and its dependent claims 2-5 are distinguished from claims 26-28 of US '208 in view of Ahmad (2016), and this rejection should be withdrawn.

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In view of the above, Applicant requests reconsideration of the application in the form of a Notice of Allowance.

Respectfully submitted,

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683
(612) 455-3814

Dated: February 8, 2023

By: /Masako Yoshida/
Masako Yoshida
Reg. No. 70,057
MY/YM/mw

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
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Electronic Acknowledgement Receipt

EFS ID:	47501353
Application Number:	17226671
International Application Number:	
Confirmation Number:	1772
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Customer Number:	52835
Filer:	Masako Yoshida/Maria Zamorano
Filer Authorized By:	Masako Yoshida
Attorney Docket Number:	20110.0024USU1
Receipt Date:	08-FEB-2023
Filing Date:	09-APR-2021
Time Stamp:	14:29:36
Application Type:	Utility under 35 USC 111(a)

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	After Final Consideration Program Request	REQUEST_FOR_CONSIDERATION_UNDER_AFCP.pdf	256522 accance419c148c9457a13d46835010c39e873c1	no	2
Warnings:					

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2		AMENDMENT.pdf	163475 e8e63d3c7a25431cf1e69bd7736e08f1e68da112e	yes	8

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Claims	2	2
Applicant Arguments/Remarks Made in an Amendment	3	8

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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.

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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
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	CHANNAVAJJALA
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION
I hereby certify that this paper is being transmitted by EFS Web to the United States Patent & Trademark Office on February 8, 2023.

By: /Maria Wait/
Name: Maria Wait

AMENDMENT AND RESPONSE

Mail Stop: AF
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the Office Action issued November 8, 2022, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims as marked copy that begins on page 2.

Remarks begin on page 3 of this paper.

After Final Consideration Pilot request is filed with this paper.

The Commissioner is hereby authorized to charge any deficiency of fees and credit any overpayments to Deposit Account Number 50-3478.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1	1772

52835 7590 02/22/2023

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
02/22/2023	ELECTRONIC

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

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOMail@hsml.com

Atossa Therapeutics, Inc. Exhibit 1002
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Advisory Action Before the Filing of an Appeal Brief	**Application No.** 17/226,671	**Applicant(s)** AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	**Art Unit** 1611	**AIA (FITF) Status** Yes

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

THE REPLY FILED 08 February 2023 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

NO NOTICE OF APPEAL FILED

1. ☑ The reply was filed after a final rejection. No Notice of Appeal has been filed. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114 if this is a utility or plant application. Note that RCEs are not permitted in design applications. The reply must be filed within one of the following time periods:
   a) ☑ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action; or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   c) ☐ A prior Advisory Action was mailed more than 3 months after the mailing date of the final rejection in response to a first after-final reply filed within 2 months of the mailing date of the final rejection. The current period for reply expires ____ months from the mailing date of *the prior Advisory Action* or SIX MONTHS from the mailing date of the final rejection, whichever is earlier.
   Examiner Note: If box 1 is checked, check either box (a), (b) or (c). ONLY CHECK BOX (b) WHEN THIS ADVISORY ACTION IS THE FIRST RESPONSE TO APPLICANTS FIRST AFTER-FINAL REPLY WHICH WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. ONLY CHECK BOX (c) IN THE LIMITED SITUATION SET FORTH UNDER BOX (c). See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) or (c) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37CFR 41.37(a).

AMENDMENTS

3. ☑ The proposed amendments filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   a) ☑ They raise new issues that would require further consideration and/or search (see NOTE below);
   b) ☐ They raise the issue of new matter (see NOTE below);
   c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: See Continuation Sheet (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☑ For purposes of appeal, the proposed amendment(s):(a) ☑ will not be entered, or (b) ☐ will be entered, and an explanation of how the new or amended claims would be rejected is provided below or appended.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____
9. ☐ The affidavit or other evidence filed after final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
10. ☐ The affidavit or other evidence filed after the date of filing the Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
11. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

12. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
13. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
14. ☑ Other: PTO-2323; PTO-413.

STATUS OF CLAIMS

15. The status of the claim(s) is (or will be) as follows:
    Claim(s) allowed: _____.
    Claim(s) objected to: _____.
    Claim(s) rejected: 1-5.
    Claim(s) withdrawn from consideration: _____.

/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Continuation of 3. NOTE: the newly added limitations require further consideration and possibly new search because the new limitations have not been presented before.

Examiner-Initiated Interview Summary	**Application No.** 17/226,671	**Applicant(s)** AHMAD et al.		
	Examiner LAKSHMI S CHANNAVAJJALA	**Art Unit** 1611	**AIA (First Inventor to File) Status** Yes	**Page** 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	**Title**	**Type**
LAKSHMI S CHANNAVAJJALA	Primary Examiner	Telephonic
Yuhgo Maruta	Attorney of Record	

Date of Interview: 15 February 2023

Issues Discussed:

Other

Examiner informed the attorney of record that the newly added limitations require further consideration because the limitations have not been presented before.Further, Examiner informed the Attorney that the new limitations do not exclude administering the rescue medications prior to the administration of endoxifen (of Ahmad et al). Examiner informed that the double patenting rejections will be maintained for the above reasons. Attorney informed that Applicants will consider filing RCE and consider further amending claims to exclude the rescue medication prior to administering endoxifen.

	/LAKSHMI S CHANNAVAJJALA/ Primary Examiner, Art Unit 1611

Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04
Please further see:
MPEP 713.04
Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b)
37 CFR § 1.2 Business to be transacted in writing

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.

Atossa Therapeutics, Inc. Exhibit 1002
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AFCP 2.0 Decision	Application No.	Applicant(s)	
	17/226,671	AHMAD et al.	
	Examiner	Art Unit	AIA (FITF) Status
	LAKSHMI S CHANNAVAJJALA	1611	Yes

This is in response to the After Final Consideration Pilot request filed 08 February 2023.

1. **Improper Request** – The AFCP 2.0 request is improper for the following reason(s) and the after final amendment submitted with the request will be treated under pre-pilot procedure.

   ☐ An AFCP 2.0 request form PTO/SB/434 (or equivalent document) was not submitted.

   ☐ A non-broadening amendment to at least one independent claim was not submitted.

   ☐ The request is not the first proper AFCP 2.0 request submitted in response to the most recent final rejection.

   ☐ Other: _____

2. **Proper Request**

   A. After final amendment submitted with the request will not be treated under AFCP 2.0.
   The after final amendment cannot be reviewed and a search conducted within the guidelines of the pilot program.

   ☐ The after final amendment will be treated under pre-pilot procedure.

   B. Updated search and/or completed additional consideration.
   The examiner performed an updated search and/or completed additional consideration of the after final amendment within the time authorized for the pilot program. The result(s) of the updated search and/or completed additional consideration are:

   ☐ 1. All of the rejections in the most recent final Office action are overcome and a Notice of Allowance is issued herewith.

   ☐ 2. The after final amendment would not overcome all of the rejections in the most recent final Office action . See attached interview summary for further details.

   ☑ 3. The after final amendment was reviewed, and it raises a new issue(s). See attached interview summary for further details.

   ☐ 4. The after final amendment raises new issues, but would overcome all of the rejections in the most recent final Office action. A decision on determining allowability could not be made within the guidelines of the pilot. See attached interview summary for further details, including any newly discovered prior art.

   ☐ 5. Other: _____

   Examiner Note: Please attach an interview summary when necessary as described above.

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DO NOT ENTER: /L.S.C/

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	CHANNAVAJJALA
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION
I hereby certify that this paper is being transmitted by EFS Web to the United States Patent & Trademark Office on February 8, 2023.

By: /Maria Wait/
Name: Maria Wait

AMENDMENT AND RESPONSE

Mail Stop: AF
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the Office Action issued November 8, 2022, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims as marked copy that begins on page 2.

Remarks begin on page 3 of this paper.

After Final Consideration Pilot request is filed with this paper.

The Commissioner is hereby authorized to charge any deficiency of fees and credit any overpayments to Deposit Account Number 50-3478.

PTO/SB/30EFS (01-22)
Approved for use through 05/31/2024. 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	17/226,671	Filing Date	2021-04-09	Docket Number (if applicable)	20110.0024USU1	Art Unit	1611
First Named Inventor	AHMAD			Examiner Name	CHANNAVAJJALA		

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 orde 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 one-month extension of time ($88 small entity)

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 _____

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

X Patent Practitioner Signature

Applicant Signature

PTO/SB/30EFS (01-22)
Approved for use through 05/31/2024. 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	/Masako Yoshida/	Date (YYYY-MM-DD)	2023-03-07
Name	Masako Yoshida	Registration Number	70057

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 l 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 estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Tim will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions f 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 informatio 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 ma 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.

Atossa Therapeutics, Inc. Exhibit 1002
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PTO/SB/22 (12-22)
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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.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional): 20110.0024USU1

Application Number: 17/226,671

Filed: April 9, 2021

For: ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Art Unit: 1611

Examiner: CHANNAVAJJALA

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))	$220	$88	$44	$ 88
☐	Two months (37 CFR 1.17(a)(2))	$640	$256	$128	$
☐	Three months (37 CFR 1.17(a)(3))	$1,480	$592	$296	$
☐	Four months (37 CFR 1.17(a)(4))	$2,320	$928	$464	$
☐	Five months (37 CFR 1.17(a)(5))	$3,160	$1,264	$632	$

☑ 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 503478.

☑ 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 70,057.

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____.

/Masako Yoshida/
Signature

March 7, 2023
Date

Masako Yoshida
Typed or printed name

(612) 455-3814
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 1 forms are submitted.

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0031. Public burden for this form is estimated to average 6 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **If filing this completed form by mail, 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.

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. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013). https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf

Routine uses of the information in this record may include disclosure to: 1) law enforcement, in the event that the system of records indicates a violation or potential violation of law; 2) a Federal, state, local, or international agency, in response to its request; 3) a contractor of the USPTO having need for the information in order to perform a contract; 4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record; 5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record; 6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations; 7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals; 8) 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)); 9) the Office of Personnel Management (OPM) for personnel research purposes; and 9) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Additional Uses

Additional USPTO uses of the information in this record may include disclosure to: 1) the International Bureau of the World Intellectual Property Organization, if the record is related to an international application filed under the Patent Cooperation Treaty; 2) the public i) after publication of the application pursuant to 35 U.S.C. 122(b), ii) after issuance of a patent pursuant to 35 U.S.C. 151, iii) 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, or iv) without publication of the application or patent under the specific circumstances provided for by 37 CFR 1.14(a)(1)(v)-(vii); and/or 3) the National Archives and Records Administration, for inspection of records.

Electronic Patent Application Fee Transmittal

Application Number:	17226671
Filing Date:	09-Apr-2021
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Filer:	Masako Yoshida/Maria Zamorano
Attorney Docket Number:	20110.0024USU1

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

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($)
Extension - 1 month with $0 paid	2251	1	88	88
Miscellaneous:				
RCE- 1ST REQUEST	2801	1	544	544
		Total in USD ($)		**632**

Electronic Acknowledgement Receipt

EFS ID:	47643291
Application Number:	17226671
International Application Number:	
Confirmation Number:	1772
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Customer Number:	52835
Filer:	Masako Yoshida/Maria Zamorano
Filer Authorized By:	Masako Yoshida
Attorney Docket Number:	20110.0024USU1
Receipt Date:	07-MAR-2023
Filing Date:	09-APR-2021
Time Stamp:	14:36:26
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$632
RAM confirmation Number	E202337E37016200
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)	REQUEST_FOR_CONTINUED_EXAMINATION.pdf	1667164 8ed0f2a34ba00cc0f8dfc99278391cf34[illegible]62f	no	3
Warnings:					
Information:					
2	Extension of Time	PETITION_FOR_EXTENSION_OF_TIME.pdf	461984 fb22d833ba324e396c1b3dcea022f0d49641254a	no	2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	40559 2196341ba67484c0752 1a6d25068c9c171acc65f	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	2169707		

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)
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 17/226,671	Filing Date 04/09/2021	☐ 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 $50 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $240 =	
☐ 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	03/07/2023	(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))	* 5	Minus	** 20	= 0		x $40 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0		x $192 =	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 $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ 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.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/YOLANDA CHADWICK/
*** 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.	

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.**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1	1772

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
03/30/2023	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOMail@hsml.com

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00265

Office Action Summary	Application No. 17/226,671	Applicant(s) AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	Art Unit 1611	AIA (FITF) Status Yes

-- 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 MONTHS 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 3/7/23.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

3)☐ 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.

4)☐ 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*

5) ☑ Claim(s) 1-5 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-5 is/are rejected.

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

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

* If any claims have been determined allowable, 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.**

Application Papers

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

11)☐ 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).

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).

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)).

** 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) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

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

4) ☐ Other: _____.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/7/21 has been entered.

Receipt of amendment and response dated 3/7/21 is acknowledged.

Claims 1-5 are pending.

In response to the amendment, the following new rejection has been applied:

2. Claims 1-5 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

Instant claim 1 on one hand recites "wherein no rescue medication is required to be administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient" and also recites "wherein the rescue medicine is at least one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics". The claim as presented is confusing because it is unclear if the

claimed method excludes all of the rescue medications or just one of the medicines selected from lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics. Instant specification does not describe any more than what is present in the above claim and hence it is unclear as to the meets and bounds of the claimed exclusion.

For examination purposes, the claim is interpreted as excluding any one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics.

Clarification and correction is requested.

The following rejection of record has been maintained:

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claim(s) 1-5 are is/are rejected under 35 U.S.C. 102((a)(1)) as anticipated by Ahmad et al (2016, cited on IDS).

Instant claims are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days.

Claim 1 has been amended to recite "wherein the rescue medicine is at least one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics".

Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BP) with current manic or mixed episode. Ahmad teaches that protein kinase C family of kinases play a vital role in cell signaling pathways including mood regulation; and PKC is a target for treating bipolar disorder (pa 252). Ahmad describes that adherence to the treatment is affected by adverse effects such as sedation and weight gain, and that there is an urgent need to develop novel and more effective treatments for BP (p 252). Ahmad states that several drugs have been approved such as lithium, valproate, carbamazepine, and atypical antipsychotics for the treatment of acute bipolar mania, which while providing relief for many individuals with BP, significant issues with tolerability and efficacy still remain, whereas endoxifen shows 4-fold higher potency in inhibiting PKC activity. Ahmad teaches enteric coated endoxifen citrate salt ("CgHgO7" is citric acid, see figure 1 and page 253, col. 2- Methodology) (claim 1). The results were expressed as Young Mania Rating Scale (YMRS) total score (≥50% decrease from baseline). Secondary end points were mean change from baseline to the end of treatment in the Montgomery–Åsberg Depression Rating Scale (MADRS) total score, Clinical Global Impressions–Severity of Illness Scale (CGI-S) score, and Columbia–Suicide Severity Rating Scale (C-SSRS) score, shown in Table 1. Ahmad teaches that a switch to depression remains a concern in all treatments of bipolar mania, depressive symptoms were assessed with the MADRS score throughout the trial. Ahmad teaches effectiveness of endoxifen 4 mg and 8 mg in alleviating depressive symptoms of mixed episode of BPD similar to that of divalproex (p 256, col.1 & Table 2) (claim 1). Further, the administration of endoxifen (4 mg and 8 mg) provides a steady state plasma concentration of endoxifen for 14 and also 21 days, and that doubling of the dose from 4

to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect (which can be construed as without mixed episode) or mixed episodes patients of endoxifen (p 258). In a double-blind, active-controlled study, 84 subjects with BPD I were randomly assigned to receive endoxifen (4 mg/day or 8 mg/day) or divalproex in a 2:1 ratio. Patients orally administered 4 mg/day or 8 mg/day endoxifen showed significant improvement in mania assessed by the Young Mania Rating Scale as early as 4 days. The effect remained significant throughout the 21-day period. At study end point, response rates were 44.44% and 64.29% at 4 mg/day and 8 mg/day of endoxifen treatment, respectively (abstract). Thus, Ahmad teaches endoxifen has been shown as a promising novel antimanic or mood stabilizing agent, as seen by significantly improved YMRS scale at almost every treatment evaluation.

Ahmad teaches that the plasma concentration of endoxifen is maintained at 14 and 20 days, indicating steady state of the endoxifen (fig.4). Ahmad also teaches monotherapy trials of drugs for the treatment of bipolar disorder (table 3 and 4b). Thus, the monotherapy in Table 3 of Ahmad (administering only endoxifen (4 mg or 8 mg)) meets the instant claimed "no rescue medication is administered", and thus Ahmad anticipates instant method of administration. This is further evidenced from the study design (fig. 2) of Ahmad wherein the design does **not** include any benzodiazepines. Further, with respect to maintaining the therapeutically effective concentration of endoxifen in the patient, Ahmad teaches that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen).

Claim 1 excludes administering any rescue medication during the treatment so as to maintain a therapeutically effective concentration of endoxifen and yet states rescue medication "is at least one medicine selected from the group consisting of lithium, valproate, lamotrigine, benzodiazepine and anticholinergics". As explained above, claim 1 is interpreted as excluding any one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics. Ahmad teaches all concomitant psychotropic medications except benzodiazepines (such as lorazepam) have been discontinued before treatment and thus meet the instant claimed new limitation any one medicine is excluded.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-5 are rejected under 35 U.S.C. 103 as being unpatentable over Ahmad et al (2016, cited on IDS) in view of Ali et al (Ali, cited on IDS dated 7/13/21).

The teachings of Ahmad have been discussed above and incorporated herewith in entirety. Should Applicants argue that Ahmad does not anticipate instant claims because Ahmad does not explicitly state not administering rescue medication for maintaining the therapeutically effective concentration of endoxifen in the patient,

Ahmad also teaches that benzodiazepines are allowed as adjunctive medication as needed at the discretion of the investigator (p 254). Thus, Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen.

Ali teaches endoxifen as a potent inhibitor of PKC, and its use in treating bipolar disorder for reducing the excessive activity of PKC (abstract). Ali teaches endoxifen inhibited PKC activity in concentration dependent manner, with 12% to 78% inhibition at a concentration of 0.025 nM to 0.2 nM; and that endoxifen shows 4-fold higher potency in inhibiting PKC activity (p 2666, col. 2). Ali suggests that endoxifen is a superior candidate for treating bipolar disorder (fig. 2) because daily oral administration of 4 mg and 8 mg doses for 28 days does not result in any toxicity (p 2667). Ali does not teach or suggest combining other PKC inhibiting or bipolar disorder treating medications (tamoxifen or any other conventional medication) with endoxifen. Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen without any other medication such as benzodiazepines in the teachings of Ahmad because while Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Ali also demonstrates endoxifen alone for effectively inhibiting PKC and therefore effective bipolar disorder. One of an ordinary skill in the art would have expected only endoxifen citrate to be effective in treating BD and also main therapeutically effective plasma concentration because Ahmad the same dosage

regimen claimed for providing endoxifen concentration for up to 21 days and Ali suggests 4 or 8 mg endoxifen (falls within the claimed range of 2-16 mg as well as that taught by Ahmad et al) does not cause toxicity for up to 28 days. Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of any or all of the rescue medications such as those excluded in the instant claims.

Double Patenting

5. Claims 1-5 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 in view of Ahmad et al (2016, cited on IDS) and Ali et al (Ali).

Patented claims are directed to a method of delivering endoxifen to the plasma of a subject, comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver and the endoxifen is a synthetic endoxifen that is at least 80% z-endoxifen and in the form of a citrate salt.

Patented claims do not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patented claims also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5.

The teachings of Ahmad and Ali have been discussed above and incorporated herewith, in full.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (patented claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. Further one would be motivated because Ali suggests that endoxifen is a superior candidate for treating bipolar disorder (fig. 2) because daily oral administration of 4 mg and 8 mg doses for 28 days does not result in any toxicity (p 2667). Ali does not teach or suggest combining other PKC inhibiting or bipolar disorder treating medications (tamoxifen or any other conventional medication) with endoxifen. Further, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen without any other medication such as benzodiazepines in the patented claims because while Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Ali also demonstrates endoxifen alone for effectively inhibiting PKC and therefore effective bipolar disorder. One of an ordinary skill in the art would have expected only endoxifen citrate to be effective in treating BD and also main therapeutically effective plasma concentration because Ahmad the same dosage regimen claimed for providing

endoxifen concentration for up to 21 days and Ali suggests 4 or 8 mg endoxifen (falls within the claimed range of 2-16 mg as well as that taught by Ahmad et al) does not cause toxicity for up to 28 days. Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of any or all of the rescue medications such as those excluded in the instant claims.

6. Claims 1-5 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over the claims 26-28 of copending Application No. 17/023208 in view of Ahmad et al (2016, cited on IDS).

Copending claims are directed to a method of inhibiting protein kinase C by administering an enteric coated tablet comprising endoxifen citrate. However, a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Copending claims lack the amounts of endoxifen citrate, for the duration of 21 days, and also lacks instant claims 4-5.
The teachings of Ahmad and Ali have been discussed above and incorporated herewith, in full.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (of the copending claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients

and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. Further one would be motivated because Ali suggests that endoxifen is a superior candidate for treating bipolar disorder (fig. 2) because daily oral administration of 4 mg and 8 mg doses for 28 days does not result in any toxicity (p 2667). Ali does not teach or suggest combining other PKC inhibiting or bipolar disorder treating medications (tamoxifen or any other conventional medication) with endoxifen. Further, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen without any other medication such as benzodiazepines in the patented claims because while Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Ali also demonstrates endoxifen alone for effectively inhibiting PKC and therefore effective bipolar disorder. One of an ordinary skill in the art would have expected only endoxifen citrate to be effective in treating BD and also main therapeutically effective plasma concentration because Ahmad the same dosage regimen claimed for providing endoxifen concentration for up to 21 days and Ali suggests 4 or 8 mg endoxifen (falls within the claimed range of 2-16 mg as well as that taught by Ahmad et al) does not cause toxicity for up to 28 days. Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of any or all of the rescue medications such as those excluded in the instant claims.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed 3/7/23 have been fully considered but they are not persuasive.

Rejections under 35 USC 102 & 103:

Applicants argue that instant claims now exclude the administration of rescue medication during the treatment of bipolar I disorder, wherein the rescue medicine is at least one medicine selected from the group consisting of lithium, valproate, lamotripigine, benzodiazepine and anticholinergics. It is argued that Ahmad et al teaches benzodiazepine such as lorazepam was allowed to be administered as concomitant medicine, that lorazepam was administered for 2 days prior to the study and continued for the first 10 days, and that lorazepam was avoided within 12 hours of mania rating only. It is argued instant claim excludes lorazepam of Ahmad, whereas the reference allows the same should patient be unduly excited i.e., that the patient has to be monitored continuously to decide if a rescue medication is required for each and every patient undergoing the treatment. It is argued that instant claims distinguish over that of Ahmad.

Applicants' arguments are considered but not found persuasive because as explained in the new rejection under 35 USC 112, 2nd paragraph, instant claims have been

interpreted as excluding any one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics. Accord to Ahmad all the other medications other than lorazepam (benzodiazepine) are stopped before treatment with endoxifen. Thus, Ahmad teaches the instant claimed exclusion. Ahmad also teaches monotherapy trials of drugs for the treatment of bipolar disorder (table 3 and 4b). YMRS scores from the monotherapy in Table 3 of Ahmad (administering only endoxifen (4 mg or 8 mg)) meets the instant claimed "no rescue medication is administered", and thus Ahmad anticipates instant method of administration. This is further evidenced from the study design (fig. 2) of Ahmad wherein the design does not include any benzodiazepines, and further Ahmad teaches that the administration of lorazepam is determined as needed. With respect to the argument that Ahmad allows lorazepam should patient be unduly excited and that the patient has to be monitored continuously to decide if a rescue medication is required for each and every patient undergoing the treatment, instant claims do not exclude the condition that patient(s) need not be monitored during the treatment. Applicants have not provided evidence on record that excluding any or all of the rescue medications listed in claim 1 avoids monitoring the patient(s) undergoing the treatment by excluding rescue medications and/or administering the claimed endoxifen.

Alternatively, the present rejection also relies on additional teachings of Ali et al. Ali et al shows endoxifen alone (the methods and description of Ali does not include any other medication) provides more effective inhibition of PKC that is highly implied in the treatment of bipolar disorders (similar to Ahmad et al as well as instant specification). Ali teaches that the same amounts of endoxifen (4 and 8 mg) as that of Ahmad as being

not toxic for 28 days. Thus, one of an ordinary skill in the art before the effective filing date of the instant invention would have been motivated to employ endoxifen alone in Ahmad and still expect to provide effective PKC inhibition and hence effective treatment of bipolar disorder, without the aid of other rescue medications. As explained above, Ahmad also teaches that benzodiazepines are allowed as adjunctive medication as needed at the discretion of the investigator (p 254). Thus, Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen. Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen, without any other medication such as benzodiazepines, because Ali teaches endoxifen alone and Ahmad suggests benzodiazepines only as needed and further Ahmad shows that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen). Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of a rescue medication.

Rejections under 35 USC 103 and the Double Patenting rejections over US Patent 10376479, copending application 17/023208:

Applicants argue that Claim 1 of the Ahmad '479 is directed to a method of delivering endoxifen to the plasma of a subject but does not disclose or suggest maintaining a therapeutically effective concentration of endoxifen in a patient undergoing treatment of bipolar I disorder (BPD I) by administering 2-16 mg/once a day

of endoxifen citrate in an enteric coated tablet for at least 21 days to the patient, as present claim 1 recites. It is argued that claim 1 of Ahmad '479 does not disclose or suggest excluding rescue medication as recited in present claim 1. It is argued that Ahmad et al does not cure the deficiencies of the patented claims and presented the same arguments regarding Ahmad et al (as above). Applicants' arguments are not found persuasive because the present rejection relies additionally on Ali et al to show that endoxifen also provides effective inhibition of PKC that is strongly implied in the treatment of bipolar disorder (Ali as well as Ahmad). Hence one of an ordinary skill in the art would have been motivated to modify the endoxifen composition of patented claims to include the claimed amounts (Ahmad as well as Ali) and use for effective treatment of bipolar disorder. Applicants arguments regarding the teachings of Ahmad et al and particularly regarding exclusion of rescue medication have been addressed above and incorporated herewith in entirety, hence the rejection is deemed proper.

Applicants' argument regarding the double patenting rejection over the copending claims (17/023208) have been considered but not found persuasive because copending claims are directed to inhibiting PKC but does not suggest maintaining a therapeutically effective concentration of endoxifen in a patient undergoing BPD I disorder. It is argued copending claims do not teach instant composition and instant exclusion of rescue medication. It is argued that Ahmad et al does not cure the deficiencies of the patented claims and presented the same arguments regarding Ahmad et al (as above). Applicants' arguments are not found persuasive because the present rejection relies additionally on Ali et al to show that endoxifen also provides effective inhibition of PKC that is strongly implied in the treatment of bipolar disorder (Ali

as well as Ahmad). Hence one of an ordinary skill in the art would have been motivated to modify the endoxifen composition of patented claims to include the claimed amounts (Ahmad as well as Ali) and use for effective treatment of bipolar disorder. Applicants arguments regarding the teachings of Ahmad et al and particularly regarding exclusion of rescue medication have been addressed above and incorporated herewith in entirety, hence the rejection is deemed proper.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKSHMI SARADA CHANNAVAJJALA whose telephone number is (571)272-0591. The examiner can normally be reached Generally M- F 9 AM to 6 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

CPC - Searched*		
Symbol	Date	Examiner
classification- attached	04/23/2022	LC
classification- attached	03/25/2023	

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
PE2E search history- all data bases- inventor, classification, text- attached	04/23/2022	LC
google scholar	04/23/2022	LC
PE2E search history- all data bases- inventor, classification, text- attached	11/03/2022	LC
google scholar	11/03/2022	LC
google scholar	03/25/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	03/25/2023	LC

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Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

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Correlates of **suicide** attempt history in **bipolar disorder**: a stress-diathesis perspective
MF Grunebaum, SR Ramsay, HC Galfalvy, ... - ... **disorders**, 2006 - Wiley Online Library
... **Manic** symptoms were assessed with the **Young Mania** Rating Scale (20). Global psychopathology was measured with ... Lifetime **suicide** attempt history was gathered with the ...
☆ Save 99 Cite Cited by 111 Related articles All 7 versions

Reduced lateral orbitofrontal cortex volume and **suicide** behavior in **youth** with **bipolar disorder**
RS Huber, P Subramaniam, DG Kondo, X Shi, ... - ... **Disorders**, 2019 - Wiley Online Library
... ideation and behavior were examined using the **Columbia Suicide** Severity ... **Depression** Rating Scale (MADRS)32 was used to assess depressive symptoms and the **Young Mania** ...
☆ Save 99 Cite Cited by 28 Related articles All 3 versions

Clinical features, impulsivity, temperament and functioning and their role in **suicidality** in patients with **bipolar disorder**
E Jiménez, B Arias, M Mitjans, ... - Acta Psychiatrica ..., 2016 - Wiley Online Library
... **-suicidal** (NS) **bipolar** patients (BP), BP reporting only **suicidal** ideation (SI) and BP **suicide** attempters according to **Columbia–Suicide** ... prone to present a **manic** onset of the **illness** (P = ...
☆ Save 99 Cite Cited by 43 Related articles All 7 versions

Detailed assessment of **suicidal** ideation in **youth** with **bipolar disorder** verses major depressive **disorder**
RS Huber, D Soxer, CJ Smith, PF Renshaw, ... - ... **disorders**, 2023 - Wiley Online Library
... Lifetime symptoms of SI and SA were assessed using the **Columbia Suicide** Severity Rating ... the **Young Mania** Rating Scale(YMRS)32 was administered to assess symptoms of **mania**. ...
☆ Save 99 Cite Related articles All 5 versions

... effects of quetiapine extended-release formulation: an open-label, non-controlled extension study in Japanese patients with **bipolar depression**
S Kanba, M Murasaki, T Koyama, M Takeuchi, ... - BMC psychiatry, 2019 - Springer
... Scale, **Young Mania** Rating Scale, and the **Columbia Suicide** Severity Rating Scale. ... that greatly affected the patient's current mental status; a **Young Mania** Rating Scale (YMRS) total ...
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Suicidal ideation and insomnia in **bipolar disorders**: Ideation suicidaire et insomnie dans les troubles bipolaires
L Bertrand, C Bourgouin, ... - The Canadian ..., 2020 - journals.sagepub.com
... Rating Scale (MADRS)21 and the peak severity of **manic** symptoms using the **Young Mania** ... We complemented the survey with the **Columbia Suicide** Severity Rating Scale (C-SSRS)—...
☆ Save 99 Cite Cited by 3 Related articles All 6 versions

Elevated interleukin-17 and reduced testosterone in **bipolar disorder**. Relation with **suicidal** behaviour
N Keshri, H Nandeesha, S Kattimani - Asian journal of psychiatry, 2018 - Elsevier
... in **bipolar disorder** in remission and these were not associated with ... **Columbia suicide** severity rating scale ... BD cases in remission and those with **Youngs mania** rating score (YMRS...
☆ Save 99 Cite Cited by 17 Related articles All 3 versions

Ketamine versus midazolam in **bipolar depression** with **suicidal** thoughts: A pilot midazolam-controlled randomized clinical trial
MF Grunebaum, SP Ellis, JG Keilp, VK Mollra, ... - ... **disorders**, 2017 - Wiley Online Library
... **Manic** symptoms were assessed with the **Young Mania** Rating Scale (YMRS).24 Anxiety ... Mental Hygiene for commercial use of the **Columbia Suicide** Severity Rating Scale, which was ...
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A feasibility study of varenicline for smoking cessation in **bipolar** patients with subsyndromal **depression**

MA Frye, JO Ebbert, CA Prince... - Journal of clinical ..., 2013 - journals.lww.com

... **bipolar disorder** with tobacco dependence have higher rates of mixed episodes, **suicide** ... , history of a serious **suicide** attempt, or current **mania** or severe **depression**. Sixteen people ...

☆ Save 99 Cite Cited by 17 Related articles All 4 versions »

... of borderline personality **disorder** and features to **suicide** risk in psychiatric inpatients with **bipolar disorder**, major **depression** and schizoaffective **disorder**

R Zeng, LJ Cohen, T Tanis, A Gizlibash, Y Lopatyuk... - Psychiatry ..., 2015 - Elsevier

... SCID I and II, and the **Columbia Suicide** Severity Rating Scale. Logistic regression analyses ... regressed number of both **manic** and depressive episodes onto past **suicide** attempts, only ...

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Related searches

suicidal **behavior** bipolar disorder

smoking cessation in bipolar disorder

suicide **attempts** bipolar disorder

japanese patients with bipolar depression

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suicide **mortality in** bipolar disorder

suicide **events patients with** bipolar disorder

bipolar depression suicidal **thoughts**

correlates of suicide bipolar disorder

bipolar depression **quetiapine extended release formulation**

young **adults with** bipolar disorder

youth bipolar disorder **self harm**

suicidal **ideation patients with** bipolar disorder

suicidal **acts** bipolar disorder

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	136	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 11:13 AM
L2	6	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2023/03/24 11:13 AM
L8	217	bipolar ADJ disorder AND (columbia adj2 suicide OR young ADJ mania)	(USPAT)	OR	ON	ON	2023/03/24 12:06 PM
L9	19	bipolar ADJ disorder SAME (columbia adj2 suicide OR young ADJ mania)	(USPAT)	OR	ON	ON	2023/03/24 12:06 PM
L10	470	bipolar ADJ disorder SAME suicid$4	(USPAT)	OR	ON	ON	2023/03/24 02:37 PM
L11	1	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) adj5 (risk OR occurence OR occur OR probability)	(USPAT)	OR	ON	ON	2023/03/24 02:38 PM
L12	32	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) SAME (risk OR occurence OR occur OR probability)	(USPAT)	OR	ON	ON	2023/03/24 02:39 PM
L13	0	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) SAME (risk OR occurence OR occur OR probability) AND A61K31/138.cpc.	(USPAT)	OR	ON	ON	2023/03/24 02:41 PM
L14	133	bipolar ADJ disorder AND A61K31/138.cpc.	(USPAT)	OR	ON	ON	2023/03/24 02:41 PM
L15	32	bipolar ADJ disorder	(USPAT)	OR	ON	ON	2023/03/24

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		AND A61K31/138.cpc. AND A61P25/18.cpc.					02:42 PM
L16	0	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. AND 4-OH-tamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L17	32	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. andtamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L18	1	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. AND tamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L19	3	"17023208"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 06:07 PM
L20	1	"17/023208"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 06:07 PM
L21	3	"20090291134"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK,	OR	ON	ON	2023/03/24 10:10 PM

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			TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)				
L22	2	"20090291134" AND (patient o rhuman)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 10:10 PM
L23	3	"20090291134" AND (patient OR human)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 10:10 PM
L24	1	17/226628	(USPAT)	OR	ON	ON	2023/03/24 11:44 PM
L25	455	(endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen))	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 11:47 PM
L26	18	(endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen)) AND L2	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 11:47 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N1	17	(endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen))	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:49 PM

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		AND L2					
N2	90	L1	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:49 PM
N3	3	bipolar ADJ disorder SAME suicid$4 AND I25	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:50 PM
N4	90	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:50 PM
N5	17	N4 AND (endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen))	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:51 PM
N6	24911	A61P25/18.cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:52 PM
N7	3911	A61K31/138.cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:52 PM
N8	313	N6 AND N7	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:53 PM
N9	9	N6 AND N7 AND N1	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:53 PM

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	136	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin")))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 11:13 AM
L2	6	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2023/03/24 11:13 AM
L8	217	bipolar ADJ disorder AND (columbia adj2 suicide OR young ADJ mania)	(USPAT)	OR	ON	ON	2023/03/24 12:06 PM
L9	19	bipolar ADJ disorder SAME (columbia adj2 suicide OR young ADJ mania)	(USPAT)	OR	ON	ON	2023/03/24 12:06 PM
L10	470	bipolar ADJ disorder SAME suicid$4	(USPAT)	OR	ON	ON	2023/03/24 02:37 PM
L11	1	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) adj5 (risk OR occurence OR occur OR probability)	(USPAT)	OR	ON	ON	2023/03/24 02:38 PM
L12	32	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) SAME (risk OR occurence OR occur OR probability)	(USPAT)	OR	ON	ON	2023/03/24 02:39 PM
L13	0	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) SAME (risk OR occurence OR occur OR probability) AND A61K31/138.cpc.	(USPAT)	OR	ON	ON	2023/03/24 02:41 PM
L14	133	bipolar ADJ disorder AND A61K31/138.cpc.	(USPAT)	OR	ON	ON	2023/03/24 02:41 PM
L15	32	bipolar ADJ disorder	(USPAT)	OR	ON	ON	2023/03/24

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		AND A61K31/138.cpc. AND A61P25/18.cpc.					02:42 PM
L16	0	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. AND 4-OH-tamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L17	32	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. andtamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L18	1	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. AND tamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L19	3	"17023208"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 06:07 PM
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			TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)				
L22	2	"20090291134" AND (patient o rhuman)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 10:10 PM
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L24	1	17/226628	(USPAT)	OR	ON	ON	2023/03/24 11:44 PM
L25	455	(endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen))	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 11:47 PM
L26	18	(endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen)) AND L2	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 11:47 PM
L27	143	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO,	OR	ON	ON	2023/03/25 09:10 AM

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			NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
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L30	100	(endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen)) SAME (PKC OR protein adj2 kinase OR plama adj5 therapeutic)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/03/25 09:13 AM
L31	78	(endoxifen OR (hydroxy NEAR desmethyltamoxifen)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY,	OR	ON	ON	2023/03/25 09:13 AM

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		OR (desmethyl near2 hydroxytamoxifen)) SAME (PKC OR protein adj2 kinase OR plama adj5 therapeutic)	CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L32	222	(endoxifen OR (hydroxy NEAR desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen)) AND (PKC OR protein adj2 kinase OR plama adj5 therapeutic)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/03/25 09:15 AM
L33	3	(endoxifen OR (hydroxy NEAR desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen)) AND (PKC OR protein adj2 kinase OR plama adj5 therapeutic) SAME enteric	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2023/03/25 09:15 AM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N1	17	(endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen)) AND L2	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:49 PM

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N2	90	L1	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:49 PM
N3	3	bipolar ADJ disorder SAME suicid$4 AND I25	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:50 PM
N4	90	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:50 PM
N5	17	N4 AND (endoxifen OR (hydroxy near2 desmethyltamoxifen) OR (desmethyl near2 hydroxytamoxifen))	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:51 PM
N6	24911	A61P25/18.cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:52 PM
N7	3911	A61K31/138.cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:52 PM
N8	313	N6 AND N7	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:53 PM
N9	9	N6 AND N7 AND N1	(US-PGPUB; USPAT)	OR	ON	ON	2023/03/24 11:53 PM

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Endoxifen: a new, protein kinase C inhibitor to treat acute and mixed mania associated with **bipolar** I **disorder**

A Ahmad, S Sheikh, MA Khan, A Chaturvedi . - ... Disorders, 2021 - Wiley Online Library

... **Endoxifen** is a protein kinase C inhibitor. The objective of the ... efficacy of **endoxifen** in treating **bipolar** I **disorder** (BPD I) patients. ... for **bipolar disorders**, which include type one **bipolar** and ...

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Endoxifen is a new potent inhibitor of PKC: a potential therapeutic agent for **bipolar disorder**

SM Ali, A Ahmad, S Shahabuddin, MU Ahmad . - Bioorganic & Medicinal ..., 2010 - Elsevier

... results in symptoms related to **bipolar disorder**. Tamoxifen, a widely ... **endoxifen**, a tamoxifen active metabolite and compared its PKC inhibitory activity with that of tamoxifen. **Endoxifen** ...

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Endoxifen, a new treatment option for mania: a double-blind, active-controlled trial demonstrates the antimanic efficacy of **endoxifen**

A Ahmad, S Sheikh, T Shah, MS Reddy... - Clinical and ..., 2016 - Wiley Online Library

... **disorders** and PKC inhibitors such as **endoxifen** may be an innovative medicine for **bipolar disorder** ... time the antimanic properties of **endoxifen** in patients with **bipolar** I **disorder** (BPD I) ...

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Endoxifen, an estrogen receptor targeted therapy: From bench to bedside

S Jayaraman, JM Reid, JP Hawse, MP Goetz - Endocrinology, 2021 - academic.oup.com

... in bone, as well as its emerging role as an antimanic agent in **bipolar disorder**. In total, ... **endoxifen** in **bipolar disorder** and calls for further exploration of **endoxifen** actions in this **disease**...

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Endoxifen Approval for **Bipolar Disorder** in India: A Premature or a Pragmatic Decision?

P Gupta, S Singh - Journal of Clinical Psychopharmacology, 2022 - journals.lww.com

... Both Tamoxifen and **Endoxifen** have been investigated for their role in treating manic ... enzyme implicated in the pathogenesis of **Bipolar Disorder** (BD). **Endoxifen** has been found to be ...

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Real-World Long-Term Experience on **Endoxifen** in **Bipolar Disorder** with Psychotic Symptoms

V Thanvi - Case Reports in Psychiatry, 2022 - hindawi.com

... role in the treatment of **bipolar** affective **disorder** (BPAD). **Endoxifen**, an active metabolite of ... Treatment with **endoxifen** 8mg once a day showed improvement in manic symptoms with a ...

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Efficacy of **endoxifen**, a protein kinase C inhibitor for acute and mixed mania: Some concerns worth considering.

A Ghosh, S Rani, S Grover - Bipolar Disorders, 2021 - europepmc.org

... **Endoxifen**: A new, protein kinase C inhibitor to treat acute and mixed mania associated with **bipolar** I **disorder**.... inhibitor to treat acute and mixed mania associated with **bipolar** I **disorder**." ...

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Endoxifen: A new hope for **Bipolar Disorder**

M Amin, A Chaliqua, MY Hafiz - 2021 - ecommons.aku.edu

... Advances in molecular neuropsychiatry have reported that **bipolar disorder** is associated ... **Endoxifen**. A multicentre, double-blind, active-controlled study was conducted using **Endoxifen** ...

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Long-Term Effectiveness and Safety Of **Endoxifen** In The Treatment Of Acute **Bipolar** Mania: A Case Report

A CHAKLADAR, N KUMAR, R VERMA, MK SPAR - 2022 - researchsquare.com

... of **endoxifen** at present are limited. We present a case demonstrating the e cacy of **endoxifen** in the management of acute **bipolar** ... **endoxifen** was successfully given for such a duration. ...

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Long-Term Effectiveness and Safety Of **Endoxifen** In The Treatment Of Acute **Bipolar** Mania: A Case Report

B MK - 2022 - europepmc.org

... -term use of **endoxifen**. Here we describe a case of acute **bipolar** mania not able to tolerate clozapine therapy, efficaciously controlled with long-term use (9-weeks) of **endoxifen** 8 mg, ...

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	136	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 11:13 AM
L2	6	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2023/03/24 11:13 AM
L8	217	bipolar ADJ disorder AND (columbia adj2 suicide OR young ADJ mania)	(USPAT)	OR	ON	ON	2023/03/24 12:06 PM
L9	19	bipolar ADJ disorder SAME (columbia adj2 suicide OR young ADJ mania)	(USPAT)	OR	ON	ON	2023/03/24 12:06 PM
L10	470	bipolar ADJ disorder SAME suicid$4	(USPAT)	OR	ON	ON	2023/03/24 02:37 PM
L11	1	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) adj5 (risk OR occurence OR occur OR probability)	(USPAT)	OR	ON	ON	2023/03/24 02:38 PM
L12	32	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) SAME (risk OR occurence OR occur OR probability)	(USPAT)	OR	ON	ON	2023/03/24 02:39 PM
L13	0	bipolar ADJ disorder SAME suicid$4 adj5 (high OR increased OR elevated OR major) SAME (risk OR occurence OR occur OR probability) AND A61K31/138.cpc.	(USPAT)	OR	ON	ON	2023/03/24 02:41 PM
L14	133	bipolar ADJ disorder AND A61K31/138.cpc.	(USPAT)	OR	ON	ON	2023/03/24 02:41 PM
L15	32	bipolar ADJ disorder	(USPAT)	OR	ON	ON	2023/03/24

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		AND A61K31/138.cpc. AND A61P25/18.cpc.					02:42 PM
L16	0	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. AND 4-OH-tamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L17	32	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. andtamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L18	1	bipolar ADJ disorder AND A61K31/138.cpc. AND A61P25/18.cpc. AND tamoxifen	(USPAT)	OR	ON	ON	2023/03/24 02:43 PM
L19	3	"17023208"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 06:07 PM
L20	1	"17/023208"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2023/03/24 06:07 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

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Endoxifen, a new treatment option for **mania**: a double-blind, active-controlled trial demonstrates the antimanic efficacy of **endoxifen**

A Ahmad, S Sheikh, T Shah, MS Reddy... - Clinical and ..., 2018 - Wiley Online Library

... such as **endoxifen** may be an innovative **medicine** for bipolar ... the antimanic properties of **endoxifen** in patients with bipolar ... evaluates **combined** safety and efficacy of the **medication**. At ...

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Endoxifen: a new, protein kinase C inhibitor to treat acute and mixed **mania** associated with bipolar I disorder

A Ahmad, S Sheikh, MA Khan, A Chaturvedi ... - Bipolar ..., 2021 - Wiley Online Library

... to concomitant **medication** in the outcome of the **endoxifen** is ... The time to remission was 14 days with the **combination** of ... Furthermore, weight gain with the use of antipsychotic **drugs** ...

☆ Save 99 Cite Cited by 10 Related articles All 3 versions

Long-Term Effectiveness and Safety Of **Endoxifen** In The Treatment Of Acute Bipolar **Mania**: A Case Report

A CHAKLADAR, N KUMAR, R VERMA, MK BRAR - 2022 - researchsquare.com

... **endoxifen** 8 mg in **combination** with clozapine 350 mg and lithium 1200 mg, for acute symptomatic control of **mania**... safety of any **drug** in bipolar **mania**, the two available clinical trials on ...

☆ Save 99 Cite Related articles »

Endoxifen is a new potent inhibitor of PKC: a potential therapeutic agent for bipolar disorder

SM Ali, A Ahmad, S Shahabuddin, MU Ahmad ... - Bioorganic & Medicinal ..., 2010 - Elsevier

... Tamoxifen, a widely used breast cancer **drug** is known to inhibit ... treatment of acute **mania** showed anti-**manic** effects compared to ... Briefly, 50 µl of a reaction **mix** containing Kinase Assay ...

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Long-Term Effectiveness and Safety Of **Endoxifen** In The Treatment Of Acute Bipolar **Mania**: A Case Report

S MK - 2022 - europepmc.org

... **drugs** and mood stabilizers as mono or **combination** therapy are first-line agents in the treatment of the **manic** phase ... Here we describe a case of acute bipolar **mania** not able to tolerate ...

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Endoxifen Approval for Bipolar Disorder in India: A Premature or a Pragmatic Decision?

R Gupta, S Singh - Journal of Clinical Psychopharmacology, 2022 - journals.lww.com

... of **Endoxifen** for the treatment of acute **mania** by the **drug** regulatory ... to approve **Endoxifen** for the treatment of **mania** is premature ... For example, the recent FDA-approved **combination** of ...

☆ Save 99 Cite Related articles All 4 versions »

Endoxifen, an estrogen receptor targeted therapy: From bench to bedside

S Jayaraman, JM Reid, JR Hawse, MP Goetz - Endocrinology, 2021 - academic.oup.com

... the development of **endoxifen** as a novel **drug** was pursued to ... by the occurrence of acute **mania** or mixed episodes of shifts in ... whether **endoxifen** and CDK 4/6i **combinations** provide ...

☆ Save 99 Cite Cited by 10 Related articles All 6 versions »

Real-World Long-Term Experience on **Endoxifen** in Bipolar Disorder with Psychotic Symptoms

V Thanvi - Case Reports in Psychiatry, 2022 - hindawi.com

... Treatment with **endoxifen** 8mg once a day showed improvement in **manic** symptoms with a YMRS score of 4 ... Long-term treatment with **endoxifen** is safe and effective in severe BPAD. ...

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Existing and emerging pharmacological approaches to the treatment of **mania**: A critical overview

G Sparacino, N Verdolini, E Viela... - Translational Psychiatry, 2022 - nature.com

... On the other hand, the use of SGAs in **combination** with ... who were symptomatic on their SGA **medication**, but results of the ... efficacy of **endoxifen** in reducing **manic** symptoms and faster ...

☆ Save 99 Cite Cited by 3 Related articles All 5 versions »

Valproate for acute **mania**

J Jochim, RP Rifkin-Zybutz, J Geddes ... - Cochrane Database ..., 2019 - cochranelibrary.com

... and other **drugs** in the treatment of acute **manic** episodes in ... depressive episodes in **combination** with full **manic** episodes (... valproate with two different doses of **endoxifen** (4 mg versus ...

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	CHANNAVAJJALA
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION
I hereby certify that this paper is being transmitted by EFS Web to the United States Patent & Trademark Office on June 30, 2023.

By: /Maria K. Z. Wait/
Name: Maria K. Z. Wait

AMENDMENT AND RESPONSE

Mail Stop: AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the Office Action issued March 30, 2023, please amend the above-identified application as follows:

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

Remarks begin on page 3 of this paper.

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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) A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for ~~at least~~ up to 21 days,

~~wherein no rescue medication is required to be administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient, wherein the rescue medicine is at least one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics.~~

wherein no rescue medication is required for the treatment of the bipolar I disorder.

2. (Original) The method of claim 1, wherein the patient has manic episodes with mixed features.

3. (Original) The method of claim 1, wherein the patient has manic episodes without mixed features.

4. (Original) The method of claim 1, wherein the patient has depression.

5. (Previously Presented) The method of claim 1, wherein the patient has depressive episodes.

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REMARKS

Favorable reconsideration of this application is requested in view of the above amendments and the following remarks. The amendments to claim 1 are supported by the original disclosure, for example, by page 4, first full paragraph and last paragraph of the specification as filed. Claims 1-5 are pending. No new matter has been added.

Claim Rejections - 35 U.S.C. § 112

Claims 1-5 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

The present claims do not recite "wherein no rescue medication is required to be administered to the patient during the treatment of the bipolar I disorder by the maintaining the therapeutically effective concentration of endoxifen in the patient, wherein the rescue medicine is at least one medicine selected from a group consisting of lithium, valproate, lamotrigine, benzodiazepines, and anticholinergics". Thus, the rejection is rendered moot. Applicant does not concede the correctness of the rejection. Withdrawal of the rejection is requested.

Claim Rejections - 35 U.S.C. § 102

Claims 1-5 have been rejected under 35 U.S.C. §102(a)(1) as being anticipated "Endoxifen, a New Treatment Option for Mania..." Clin. Transl. Sci. 9(5), 252-59 (2016), Ahmad (2016). Applicant respectfully traverses this rejection.

Claim 1 is directed to a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder. The method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days. Claim 1 further recites that no rescue medication is required for the treatment of the bipolar I disorder. That is to say, no rescue medication is required to the patient during the treatment of the bipolar I disorder at the time of maintaining the therapeutically effective concentration of endoxifen in the patient.

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The rejection admits that Ahmad (2016) teaches concomitant medications such as lorazepam have been discontinued before the treatment to avoid efficacy or safety overlap with the endoxifen, but contends that it would have been obvious to achieve the features of claim 1 (see page 6 of the Office Action issued March 30, 2023). Applicant respectfully disagrees.

In particular, Ahmad (2016)'s study focuses on the evaluation of the efficacy and safety of endoxifen in BPD I patients with current manic or mixed episode (see, e.g., page 253 of Ahmad (2016)). On the other hand, claim 1 recites that no rescue medication is required for the treatment of the bipolar I disorder.

That is to say, **during Ahmad (2016)'s study, benzodiazepines (i.e., lorazepam/diazepam) were allowed to be administered as concomitant medicines** (see page 254 of Ahmad (2016)). Further, benzodiazepines were allowed to be administered for 2 days prior to the study and continued to be administered for the first 10 days of the study (*Id.*). As such, administering benzodiazepines (i.e., lorazepam/diazepam) as a rescue medicine is not excluded from the medication in Ahmad (2016). It is important to note that Ahmad (2016)'s study mentions that the investigator **is allowed to administer concomitant medicines (as rescue medicines) if the patient showed undue excitement** (see "Concomitant medications" section on page 254 of Ahmad (2016)). This implies that the investigator had to monitor the patients continuously to investigate whether the rescue medication would be required for each and every patient undergoing the treatment according to Ahmad (2016)'s study. In summary, Ahmed teaches that, if needed, benzodiazepines were allowed for at least the first 10 days. On the other hand, claim 1 recites that no rescue medication is required for the treatment of the bipolar I disorder.

Further, according to the rejection on page 5 of the Office Action, Ahmad (2016) teaches monotherapy trials of drugs for the treatment of bipolar disorders as per Fig. 4(b) and Table 3 on pages 257-8 of Ahmad (2016). However, Table 3 provides data on "Baseline Young Mania Rating Scale score" and "Onset of action" in days, which does not provide any clarity as to the results of the treatment itself. Further, Fig 4(b) refers to the Pharmacokinetic–pharmacodynamics relationship, which also does not provide any clarify as to the exact results of the treatment.

It is noted that it is generally understood in the art that there are many combination therapies available for BPD I as reserved as a subsequent choice or for severe cases. However,

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such drugs for treatment of BPD I are generally known to have many possible side effects. Moreover, in routine practice, monotherapy is often not sufficiently effective for acute and/or maintenance therapy. As a consequence, most patients are given combination therapies. Claim 1 on the other hand recites a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with BPD I, and further recites that no rescue medication is required for the treatment of the bipolar I disorder.

Further, Ahmad (2016) also shows that during their study, they observed many adverse events in many numbers of patients (see under "Safety and tolerability" on page 256 of Ahmad (2016)). According to Ahmad (2016)'s study, they provided additional medication to the patients to overcome adverse events, e.g., rescue medicine if patients showed undue excitement as indicated above. Further, Ahmad (2016) indicates the following in the Discussion section on page 258: "However, longer studies are needed to determine the efficacy and tolerability of endoxifen." This indicates that according to Ahmad (2016)'s study, the results were not optimum.

On the other hand, claim 1 recites that no rescue medication is required for the treatment of the bipolar I disorder. That is to say, the method does not require the administration of rescue medications as taught by Ahmad (2016), namely, benzodiazepines, to the patient undergoing the endoxifen treatment according to the claimed invention. Accordingly, claim 1 and its dependent claims 2-5 are distinguished from Ahmad (2016), and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Claim Rejections - 35 U.S.C. § 103

Claims 1-5 have been rejected under 35 U.S.C. 103 as being unpatentable over Ahmad et al (2016, cited on IDS) in view of Ali et al (Ali, cited on IDS dated 7/13/21). Applicant respectfully traverses this rejection.

As discussed above, claim 1 is directed to a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder. The method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days. Claim 1 further recites that no rescue medication is required for the treatment of the bipolar I disorder. That is to say, no rescue

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medication is required to the patient during the treatment of the bipolar I disorder at the time of maintaining the therapeutically effective concentration of endoxifen in the patient.

As is clear from the above discussion, in Ahmad (2016)'s study, endoxifen treatment requires concomitant medication to overcome adverse events (see page 254 of Ahmad (2016)). Ahmad (2016) also refers to such adverse events that happened during the treatment (see under "Safety and tolerability" on page 256 of Ahmad (2016)). Further, in the Discussion section on page 258, Ahmad (2016) indicates that a longer study is needed to determine the efficacy and tolerability of endoxifen. Thus, Ahmad (2016)'s study does not provide definitive results of their treatment, and the reference does not teach that no rescue medication is required for the treatment of the bipolar I disorder as recited in claim 1.

Further, as discussed above, Ahmed discloses that **benzodiazepines (i.e., lorazepam/diazepam) were allowed to be administered as concomitant medicines.** Further, benzodiazepines were allowed to be administered for 2 days prior to the study and continued to be administered for the first 10 days of the study. As such, administering benzodiazepines (i.e., lorazepam/diazepam) as a rescue medicine is not excluded from the medication in Ahmad (2016). It is important to note that Ahmad (2016)'s study mentions that the investigator **is allowed to administer concomitant medicines (as rescue medicines) if the patient showed undue excitement** (see "Concomitant medications" section on page 254 of Ahmad (2016)). This implies that the investigator had to monitor the patients continuously to investigate whether the rescue medication would be required for each and every patient undergoing the treatment according to Ahmad (2016)'s study. In summary, Ahmed teaches that, if needed, benzodiazepines were allowed for at least first 10 days. On the other hand, claim 1 recites that no rescue medication is required for the treatment of the bipolar I disorder.

As to Ali, this reference shows the results of endoxifen in the inhibition of PKC activity in a concentration dependent manner (page 2666, col. 2 of Ali). However, Ali's study was held in rat and mice, as opposed to human patients, and the reference does not provide any indication as to adverse events or side effects of synthesized endoxifen. In this regard, it is generally known that many combination therapies are available for bipolar I disorder (BPD I) as reserved as a subsequent choice or for severe cases.

Ali's study demonstrated that endoxifen is about four-fold more potent of a PKC inhibitor than that of tamoxifen (page 2666). However, there is no teaching or suggestion in

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Ali as to whether endoxifen in human patients would not require any concomitant medication for the treatment of bipolar I disorder. Ahmad (2016), as indicated above, teaches administration of concomitant medicine to human patients to overcome adverse effects.

In view of the above, it is clear that Ahmad (2016) and Ali do not teach or suggest the feature: "no rescue medication is required for the treatment of the bipolar I discorder" as recited in claim 1. Accordingly, claim 1 and its dependent claims 2-5 are patentable over Ahmad (2016) and Ali, and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Double Patenting

Claims 1-5 have been rejected on the ground of non-statutory double patenting as being unpatentable over claims 1 of U.S. Patent No. 10,376,479 (Ahmad '479) in view of Ahmad (2016) and Ali et al (Ali). Applicant respectfully traverses this rejection.

Claim 1 of Ahmad '479 is directed to a method of delivering endoxifen to the plasma of a subject, and recites "a method of delivering endoxifen to the plasma of a subject comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver endoxifen to the plasma of the subject, wherein : i) said preparation of endoxifen is at least 80% z-endoxifen; and ii) said synthetic preparation of endoxifen is in the form of a citrate salt."

Claim 1 of Ahmad '479 does not disclose or suggest maintaining a therapeutically effective concentration of endoxifen in a patient undergoing treatment of bipolar I disorder (BPD I) by administering 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days to the patient, as present claim 1 recites. In fact, claim 1 of Ahmad '479 does not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with BPD I, and also lacks the claimed amounts of endoxifen citrate and the period of administration. Even further, claim 1 of Ahmad '479 does not disclose or suggest that no rescue medication is required for the treatment of BPDI, as recited in present claim 1. Thus, claim 1 of the present application is distinguished from claim 1 of US '479.

Ahmad (2016) and Ali do not remedy the deficiencies of claim 1 of Ahmad '479. As discussed above, Ahmad (2016) teaches benzodiazepines (i.e. lorazepam/diazepam) is allowed

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as a concomitant treatment with endoxifen therapy for BPD I (page 254 of Ahmad (2016)). As such, during Ahmad (2016)'s study, the investigator is allowed to administer concomitant medicine(s) (as rescue medicines) if the patient shows undue excitement (see "Concomitant medications" section on page 254). This implies that the investigator has to monitor the patients continuously to investigate whether the rescue medication would be required for each and every patient undergoing the treatment according to Ahmad (2016)'s study. As to Ali, there is no teaching or suggestion in Ali as to whether endoxifen in human patients would not require any concomitant medication for the treatment of bipolar I disorder. On the other hand, claim 1 recites that no rescue medication is required for the treatment of the bipolar I disorder.

In view of the above, Applicant submits that present claim 1 and its dependent claims 2-5 are distinguished from claim 1 of Ahmad '479 in view of Ahmad (2016) and Ali, and this rejection should be withdrawn.

Claims 1-5 are provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims 26-28 of co-pending Application No. 17/023208 (US '208) in view of Ahmad (2016). Applicant respectfully traverses this rejection.

Ali was not included in the statement of the rejection. However, the substance of the rejection includes discussion of Ali, and as such, Ali will be addressed below.

Claims 26-28 of US '208 are directed to a method of inhibiting protein kinase C (PKC) in a subject by delivering endoxifen to the plasma of the subject. Claims 26-28 of US '208, however, do not disclose or suggest maintaining of a therapeutically effective concentration of endoxifen in a patient undergoing a treatment of bipolar I disorder (BPD I) by administering of endoxifen citrate to the patient in an amount of 2-16 mg/once a day in an enteric coated tablet for up to 21 days, wherein no rescue medication is required for the treatment of the bipolar I disorder, as claim 1 recites. In fact, the rejection admits that claims 26-28 of US '208 lack the teaching of the amounts of endoxifen citrate for the duration of 21 days as recited in claim 1 of the present application (see page 10 of the Office Action issued March 30, 2023).

Ahmad (2016) and Ali do not remedy the deficiencies of claims 26-28 of US '208. In particular, as discussed above, Ahmad (2016) teaches the inclusion of benzodiazepines (i.e. lorazepam/diazepam) as a concomitant treatment with endoxifen therapy for BPD. As such, during Ahmad (2016)'s study, the investigator is allowed to administer a concomitant

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medicine(s) (as rescue medicines) if the patient shows undue excitement (see "Concomitant medications" section on page 254). This implies that the investigator has to monitor the patients continuously to investigate whether the rescue medication would be required for each and every patient undergoing the treatment according to Ahmad (2016)'s study. As to Ali, there is no teaching or suggestion in Ali as to whether endoxifen in human patients would not require any concomitant medication for the treatment of bipolar I disorder. On the other hand, claim 1 recites that no rescue medication is required for the treatment of the bipolar I disorder.

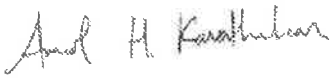
In view of the above, Applicant submits that present claim 1 and its dependent claims 2-5 are distinguished from claims 26-28 of US '208 in view of Ahmad (2016) and Ali, and this rejection should be withdrawn.

Applicants respectfully assert that the pending claims are in condition for allowance. If a telephone conference would be helpful in resolving any issues concerning this communication, please contact the undersigned attorney, Amol H. Kavathekar (Reg. No. 63,975), at (612) 455-3831.

Respectfully submitted,

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Dated: June 30, 2023

By: 

Amol H. Kavathakar
Reg. No.
AHK/YM/mw

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Electronic Acknowledgement Receipt

EFS ID:	48239453
Application Number:	17226671
International Application Number:	
Confirmation Number:	1772
Title of Invention:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER
First Named Inventor/Applicant Name:	Ateeq AHMAD
Customer Number:	52835
Filer:	Amol H. Kavathekar/Maria Zamorano
Filer Authorized By:	Amol H. Kavathekar
Attorney Docket Number:	20110.0024USU1
Receipt Date:	30-JUN-2023
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Application Type:	Utility under 35 USC 111(a)

Payment information:

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		AMENDMENT.pdf	156534 9f49a14c64a05fffe66c2347048a297bbed41604	yes	9

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment/Request for Reconsideration-After Non-Final Rejection	1	1
	Claims	2	2
	Applicant Arguments/Remarks Made in an Amendment	3	9
Warnings:			
Information:			
	Total Files Size (in bytes):	156534	

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
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 17/226,671	Filing Date 04/09/2021	☐ 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 $50 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $240 =	
☐ 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	06/30/2023	(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))	* 5	Minus	** 20	= 0		x $40 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0		x $192 =	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 $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ 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.	SLIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/Theresa OKON/
*** 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.	

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.**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1	1772

52835 7590 10/12/2023

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

EXAMINER
CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
10/12/2023	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOMail@hsml.com

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Office Action Summary	Application No. 17/226,671	Applicant(s) AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	Art Unit 1611	AIA (FITF) Status Yes

-- 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 MONTHS 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 6/30/23.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

3)☐ 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.

4)☐ 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*

5) ☑ Claim(s) 1-5 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-5 is/are rejected.

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

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

* If any claims have been determined allowable, 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.**

Application Papers

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

11)☐ 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).

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).

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)).

** 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) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

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

4) ☐ Other: _____.

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Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Receipt of amendment and response dated 6/30/20 is acknowledged.

Claims 1-5 are pending.

The following rejection of record has been maintained:

Claim Interpretation

Instant claim 1 has been amended to recite "no rescue medication is required". However, the claim term implies that the presence of a rescue medication is not positively eliminated from the instant treatment. Rather, the term "not required" implies that the rescue medication is optional, left to one's choice or discretion, and not mandatory, because instant claims do not recite "must not include rescue medication". Therefore, the claim is interpreted as "optional" for rescue medication.

Claim Rejections - 35 USC § 103

1. Claims 1-5 are rejected under 35 U.S.C. 103 as being unpatentable over Ahmad et al (2016, cited on IDS) in view of Ali et al (Ali, cited on IDS dated 7/13/21).

Instant claims are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Claim 1 has been amended

to recite "wherein no the rescue medicine is required for the treatment of the bipolar I disorder".

Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BP) with current manic or mixed episode. Ahmad teaches that protein kinase C family of kinases play a vital role in cell signaling pathways including mood regulation; and PKC is a target for treating bipolar disorder (pa 252). Ahmad describes that adherence to the treatment is affected by adverse effects such as sedation and weight gain, and that there is an urgent need to develop novel and more effective treatments for BP (p 252). Ahmad states that several drugs have been approved such as lithium, valproate, carbamazepine, and atypical antipsychotics for the treatment of acute bipolar mania, which while providing relief for many individuals with BP, significant issues with tolerability and efficacy still remain, whereas endoxifen shows 4-fold higher potency in inhibiting PKC activity.

Ahmad teaches enteric coated endoxifen citrate salt ("CgHgO7" is citric acid, see figure 1 and page 253, col. 2- Methodology) (claim 1). The results were expressed as Young Mania Rating Scale (YMRS) total score (≥50% decrease from baseline). Secondary end points were mean change from baseline to the end of treatment in the Montgomery–Åsberg Depression Rating Scale (MADRS) total score, Clinical Global Impressions–Severity of Illness Scale (CGI-S) score, and Columbia–Suicide Severity Rating Scale (C-SSRS) score, shown in Table 1. Ahmad teaches that a switch to depression remains a concern in all treatments of bipolar mania, depressive symptoms were assessed with the MADRS score throughout the trial. Ahmad teaches effectiveness of endoxifen 4 mg and 8 mg in alleviating depressive symptoms of mixed

episode of BPD similar to that of divalproex (p 256, col.1 & Table 2) (claim 1). Further, the administration of endoxifen (4 mg and 8 mg) provides a steady state plasma concentration of endoxifen for 14 and also 21 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect (which can be construed as without mixed episode) or mixed episodes patients of endoxifen (p 258). In a double-blind, active-controlled study, 84 subjects with BPD I were randomly assigned to receive endoxifen (4 mg/day or 8 mg/day) or divalproex in a 2:1 ratio. Patients orally administered 4 mg/day or 8 mg/day endoxifen showed significant improvement in mania assessed by the Young Mania Rating Scale as early as 4 days. The effect remained significant throughout the 21-day period. At study end point, response rates were 44.44% and 64.29% at 4 mg/day and 8 mg/day of endoxifen treatment, respectively (abstract). Thus, Ahmad teaches endoxifen has been shown as a promising novel antimanic or mood stabilizing agent, as seen by significantly improved YMRS scale at almost every treatment evaluation.

Ahmad teaches that the plasma concentration of endoxifen is maintained at 14 and 20 days, indicating steady state of the endoxifen (fig.4). Ahmad also teaches monotherapy trials of drugs for the treatment of bipolar disorder (table 3 and 4b).

Ahmad does not require that additional rescue medication is evident from the study design (fig. 2), wherein the design does not include any benzodiazepines. Further, with respect to maintaining the therapeutically effective concentration of endoxifen in the patient, Ahmad teaches that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen).

Instant claim 1 has been amended to recite "no rescue medication is required", which implies that the presence of a rescue medication is not positively eliminated from the instant treatment. Rather, the term "not required" implies that the rescue medication is optional, left to one's choice or discretion, and not mandatory.

Ahmad does not explicitly state "rescue medication is not required for the treatment of bipolar I disorder", Ahmad also teaches that benzodiazepines are allowed as adjunctive medication as needed at the discretion of the investigator (p 254). Thus, Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen.

Ali teaches endoxifen as a potent inhibitor of PKC, and its use in treating bipolar disorder for reducing the excessive activity of PKC (abstract). Ali teaches endoxifen inhibited PKC activity in concentration dependent manner, with 12% to 78% inhibition at a concentration of 0.025 nM to 0.2 nM; and that endoxifen shows 4-fold higher potency in inhibiting PKC activity (p 2666, col. 2). Ali suggests that endoxifen is a superior candidate for treating bipolar disorder (fig. 2) because daily oral administration of 4 mg and 8 mg doses for 28 days does not result in any toxicity (p 2667). Ali does not teach or suggest combining other PKC inhibiting or bipolar disorder treating medications (tamoxifen or any other conventional medication) with endoxifen. Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen without any other medication such as benzodiazepines in the teachings of Ahmad because while Ahmad

suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Ali also demonstrates endoxifen alone for effectively inhibiting PKC and therefore effective bipolar disorder. One of an ordinary skill in the art would have expected only endoxifen citrate to be effective in treating BD and also main therapeutically effective plasma concentration because Ahmad the same dosage regimen claimed for providing endoxifen concentration for up to 21 days and Ali suggests 4 or 8 mg endoxifen (falls within the claimed range of 2-16 mg as well as that taught by Ahmad et al) does not cause toxicity for up to 28 days. Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of any or all of the rescue medications such as those excluded in the instant claims.

Double Patenting

5. Claims 1-5 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 in view of Ahmad et al (2016, cited on IDS) and Ali et al (Ali).

Instant claim 1 has been amended to recite "no rescue medication is required", which implies that the presence of a rescue medication is not positively eliminated from the instant treatment. Rather, the term "not required" implies that the rescue medication is optional, left to one's choice or discretion, and not mandatory.

Patented claims are directed to a method of delivering endoxifen to the plasma of a subject, comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver and the endoxifen is a synthetic endoxifen that is at least 80% z-endoxifen and in the form of a citrate salt.

Patented claims do not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patented claims also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5.

The teachings of Ahmad and Ali have been discussed above and incorporated herewith, in full.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (patented claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. Further one would be motivated because Ali suggests that endoxifen is a superior candidate for treating bipolar disorder (fig. 2) because daily oral administration of 4 mg and 8 mg doses for 28 days does not result in any toxicity (p 2667). Ali does not teach or suggest combining other PKC inhibiting or bipolar disorder treating medications (tamoxifen or any other conventional

medication) with endoxifen. Further, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen without any other medication such as benzodiazepines in the patented claims because while Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Ali also demonstrates endoxifen alone for effectively inhibiting PKC and therefore effective bipolar disorder. One of an ordinary skill in the art would have expected only endoxifen citrate to be effective in treating BD and also main therapeutically effective plasma concentration because Ahmad the same dosage regimen claimed for providing endoxifen concentration for up to 21 days and Ali suggests 4 or 8 mg endoxifen (falls within the claimed range of 2-16 mg as well as that taught by Ahmad et al) does not cause toxicity for up to 28 days. Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of any or all of the rescue medications such as those excluded in the instant claims.

6. Claims 1-5 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over the claims 1-3 of US Patent 11672758 (same as copending Application No. 17/023208) in view of Ahmad et al (2016, cited on IDS).

Instant claim 1 has been amended to recite "no rescue medication is required", which implies that the presence of a rescue medication is not positively eliminated from the instant treatment. Rather, the term "not required" implies that the rescue medication is optional, left to one's choice or discretion, and not mandatory.

Patent claims are directed to a method of inhibiting protein kinase C by administering an enteric coated tablet comprising endoxifen citrate. However, a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patent claims lack the amounts of endoxifen citrate, for the duration of 21 days, and also lacks instant claims 4-5.
The teachings of Ahmad and Ali have been discussed above and incorporated herewith, in full.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (of the patent claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. Further one would be motivated because Ali suggests that endoxifen is a superior candidate for treating bipolar disorder (fig. 2) because daily oral administration of 4 mg and 8 mg doses for 28 days does not result in any toxicity (p 2667). Ali does not teach or suggest combining other PKC inhibiting or bipolar disorder treating medications (tamoxifen or any other conventional

medication) with endoxifen. Further, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen without any other medication such as benzodiazepines in the patented claims because while Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Ali also demonstrates endoxifen alone for effectively inhibiting PKC and therefore effective bipolar disorder. One of an ordinary skill in the art would have expected only endoxifen citrate to be effective in treating BD and also main therapeutically effective plasma concentration because Ahmad the same dosage regimen claimed for providing endoxifen concentration for up to 21 days and Ali suggests 4 or 8 mg endoxifen (falls within the claimed range of 2-16 mg as well as that taught by Ahmad et al) does not cause toxicity for up to 28 days. Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of any or all of the rescue medications such as those excluded in the instant claims.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Response to Arguments

In response to the amendment, the rejections have been withdrawn:

Claims 1-5 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

Claim(s) 1-5 are is/are rejected under 35 U.S.C. 102((a)(1)) as anticipated by Ahmad et al (2016, cited on IDS).

Applicant's arguments filed 6/30/23 have been fully considered but they are not persuasive.

Rejections under 35 USC 103:

Applicants argue that instant claims now exclude the administration of rescue medication during the treatment of bipolar I disorder, because claims recite "no rescue medication is required". However, the claim term implies that the presence of a rescue medication is not positively eliminated from the instant treatment. Rather, the term "not required" implies that the rescue medication is optional, left to one's choice or discretion, and not mandatory.

It is argued that Ahmad et al teaches benzodiazepine such as lorazepam was allowed to be administered as concomitant medicine, that lorazepam was administered for 2 days prior to the study and continued for the first 10 days, as a rescue medication.

It is argued instant claim excludes lorazepam of Ahmad, whereas the reference allows the same should patient be unduly excited i.e., that the patient has to be monitored continuously to decide if a rescue medication is required for each and every patient undergoing the treatment. Applicants argue that the monotherapy results (Table 3) and Fig 4b of Ahmad does not provide any clarity with regards to the results of the treatment. Applicants argue that it is generally understood from the prior art that there are many combinations of therapies for BPD I, and have many possible side effects. It is argued that in routine practice monotherapy is not sufficient for acute and/or maintenance therapy, and therefore require combination therapy. It is argued that Ahmad teaches many adverse effects (page 356) and hence suggests additional medication.

It is argued that Ali teaches the anti-PKC activity of endoxifen in rats and mice, as opposed to humans, and is silent regarding the adverse effects of synthesized endoxifen. Applicants' arguments are not found persuasive because the present action only includes an obviousness rejection over the teachings of Ahmad et al in view of Ali et al. Further, as explained from the claim interpretation above, the claim term "no rescue medication is required" implies that the presence of a rescue medication is not positively eliminated from the instant treatment. Rather, the term "not required" implies that the rescue medication is optional, left to one's choice or discretion, and not mandatory. Therefore, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to employ additional or concomitant administration of benzodiazepine only as needed, in the teachings of Ahmad, for treating BPD I. One of an ordinary skill in the art would have been motivated

to try only administering endoxifen citrate (of Ahmad et al) for treating BPD I not only because the second study design of Ahmad does not require any additional drug, instant claims allow additional rescue medication as an "option", Ahmad suggests inclusion of a concomitant medication "as needed".

The argument that Table 3 and fig 4 of Ahmad does not provide any clarity with regards to the results of the treatment is not persuasive because Ahmad clearly states the efficacy instant claimed composition, in the same dose and same duration of treatment, to be effective in treating BPD I with mixed or manic episodes (p 258, col. 1, abstract, table 3 and fig 4). Applicants have not explained why the results of monotherapy of Ahmad et al., are unclear. Ahmad provides mean trough plasma concentrations with 4 and 8 mg/day at 14 and 20 days after administration and states that the difference is not significant between 14 and 20 days. However, while Ahmad shows increased plasma levels at 8 mg dose, Ahmad no where states that the administration is insignificant or ineffective (p 256, col. 2- page 257).

Moreover, Ali teaches that endoxifen treatment not only for PKC inhibition but also for treating bipolar disorder. Ali clearly states that PKC is an important target, and probably the first mechanically distinct target for BPD, and hence endoxifen is a superior candidate for BPD treatment (col. 2, p 2666). The argument that Ali teaches in rats but not humans is not persuasive because Ali also suggests endoxifen for treating the same condition as in Ahmad., and one of an ordinary skill in the art would not require any additional evidence of the efficacy of endoxifen in humans.

Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen, without any other medication such as benzodiazepines, because Ali teaches endoxifen alone and Ahmad suggests benzodiazepines only as needed and further Ahmad shows that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen). Therefore, one of an ordinary skill in the art would have expected to provide the therapeutically effective concentration of endoxifen even in the absence of a rescue medication.

Double Patenting rejections:

Applicants presented the claims Ahmad '479 patents and the claims of 17/023208, now issued as patent US Patent 11672758, do not teach not teach instant claimed method, provide the same arguments regarding the teachings of Ahmad et al and Ali et al. However, Applicants' arguments regarding Ahmad et al and Ali et al have been addressed above and incorporated herewith. Hence, the rejections have been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKSHMI SARADA CHANNAVAJJALA whose telephone number is (571)272-0591. The examiner can normally be reached Generally M- F 9 AM to 6 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center,

visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

CPC - Searched*		
Symbol	Date	Examiner
classification- attached	04/23/2022	LC
classification- attached	03/25/2023	

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
PE2E search history- all data bases- inventor, classification, text- attached	04/23/2022	LC
google scholar	04/23/2022	LC
PE2E search history- all data bases- inventor, classification, text- attached	11/03/2022	LC
google scholar	11/03/2022	LC
google scholar	03/25/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	03/25/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	10/06/2023	LC

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Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	7	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2023/10/05 10:57 PM
L2	138	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 10:57 PM
L3	19	(1 OR 2) AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 10:58 PM
L4	10	(1 OR 2) AND endoxifen AND suicide	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 10:58 PM
L5	34	endoxifen AND suicide	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 10:59 PM
L6	12	endoxifen AND suicide SAME (reduc$5 OR alleviat$4 OR manag$5 OR control$5 OR prevent$5)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:01 PM
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L8	136	(A61K31/138).cpc. AND suicide SAME (reduc$5 OR alleviat$4 OR manag$5 OR control$5 OR prevent$5)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:04 PM
L9	6	(A61K31/138).cpc. AND suicide SAME (reduc$5 OR alleviat$4 OR manag$5 OR control$5 OR prevent$5) AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:04 PM
L10	2	17/023208	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:55 PM
L11	5	"9833489".pn.	(US-PGPUB; USPAT;	OR	ON	ON	2023/10/06

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			USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)				10:34 AM
L14	588	(A61K31/138).cpc. AND bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:20 PM
L15	15	(A61K31/138).cpc. AND bipolar adj4 disorder SAME endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:20 PM
L16	2	(17/226703 OR 17/226651)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:23 PM
L20	16	endoxifen SAME bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:54 PM
L21	3	(endoxifen SAME bipolar) NOT (rescue OR concomitant OR benzodiazepene OR lorazepam OR diazepam OR lithium opr valproate OR lamotrigine OR anticholinergic)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:55 PM
L22	2	(endoxifen SAME bipolar) SAME therapeutic NOT (rescue OR concomitant OR benzodiazepene OR lorazepam OR diazepam OR lithium opr valproate OR lamotrigine OR anticholinergic)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:56 PM
L23	114	(A61K31/138).cpc. AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:58 PM
L24	40	(A61K31/138).cpc. AND endoxifen SAME citrate	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:58 PM
L25	20	24 NOT (rescue OR concomitant OR benzodiazepene OR	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 02:58 PM

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		lorazepam OR diazepam OR lithium opr valproate OR lamotrigine OR anticholinergic)					
L26	9	24 NOT (rescue OR concomitant OR benzodiazepene OR lorazepam OR diazepam OR lithium opr valproate OR lamotrigine OR anticholinergic) AND bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/06 03:00 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	7	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2023/10/05 10:57 PM
L2	138	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 10:57 PM
L3	19	(1 OR 2) AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 10:58 PM
L4	10	(1 OR 2) AND endoxifen AND suicide	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 10:58 PM
L5	34	endoxifen AND suicide	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 10:59 PM
L6	12	endoxifen AND suicide SAME (reduc$5 OR alleviat$4 OR manag$5 OR control$5 OR prevent$5)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:01 PM
L7	0	endoxifen adj5 (citrate OR citric) AND suicide SAME (reduc$5 OR alleviat$4 OR manag$5 OR control$5 OR prevent$5)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:04 PM
L8	136	(A61K31/138).cpc. AND suicide SAME (reduc$5 OR alleviat$4 OR manag$5 OR control$5 OR prevent$5)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:04 PM
L9	6	(A61K31/138).cpc. AND suicide SAME (reduc$5 OR alleviat$4 OR manag$5 OR control$5 OR prevent$5) AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:04 PM
L10	2	17/023208	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2023/10/05 11:55 PM
L11	5	"9833489".pn.	(US-PGPUB; USPAT;	OR	ON	ON	2023/10/06

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			USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT)				10:34 AM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

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45 South Seventh Street
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Courtesy Reminder for

Application Serial No: 17226671

Attorney Docket No: 20110.0024USU1

Customer Number: 52835

Date of Electronic Notification: 2023-10-12

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FROM: noreply@uspto.gov
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SUBJECT: USPTO: Patent Electronic System - e-Postcard Notification for Customer Number 52835

Sat Oct 21 05:21:15 EDT 2023

Dear Patent Center Customer:

Correspondence Address:

HAMRE, SCHUMANN, MUELLER &LARSON, P.C.
45 South Seventh Street
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Minneapolis,MINNESOTA,55402-1683
UNITED STATES

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PTOMail@hsml.com

This is a courtesy reminder that new correspondence is available for the application. If you have not done so already, please review the correspondence listed below. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

Application	Document	Mailroom Date	Attorney Docket No.
17226671	CTFR	10/12/2023	20110.0024USU1

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Sincerely,

The Patent Center Team

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	CHANNAVAJJALA
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION
I hereby certify that this paper is being transmitted by Patent Center to the United States Patent & Trademark Office on January 12, 2024.

By: /Maria K. Z. Wait/
Name: Maria K. Z. Wait

AMENDMENT AND RESPONSE AFTER FINAL

Mail Stop: AF
Commissioner for
Patents P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the final Office Action issued October 12, 2023, please amend the above- identified application as follows:

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

Remarks begin on page 3 of this paper.

After Final Consideration Pilot request is filed with this paper.

The Commissioner is hereby authorized to charge any deficiency of fees and credit any overpayments to Deposit Account Number 50-3478.

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) A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days,

wherein [[no]] the method does not include a rescue medication ~~is required~~ for the treatment of the bipolar I disorder.

2. (Original) The method of claim 1, wherein the patient has manic episodes with mixed features.

3. (Original) The method of claim 1, wherein the patient has manic episodes without mixed features.

4. (Original) The method of claim 1, wherein the patient has depression.

5. (Previously Presented) The method of claim 1, wherein the patient has depressive episodes.

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REMARKS

Favorable reconsideration of this application is requested in view of the above amendments and the following remarks. The amendments to claim 1 are supported by the original disclosure, for example, at the last paragraph on page 4 of the specification as filed. Claims 1-5 are pending. No new matter has been added.

Claim Rejections - 35 U.S.C. § 103

Claims 1-5 were rejected under 35 U.S.C. 103 as being unpatentable over Ahmad et al. ("Endoxifen, a New Treatment Option for Mania…", Clin. Transl. Sci. 9(5), 252-59 (2016)) in view of Ali et al. ("Endoxifen is a new portent inhibitor of PKC…", Bioorganic & Medicinal Chemistry Letters, 20 (2010), 2665-2667). Applicant respectfully traverses this rejection.

Claim 1 is directed to a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days. Claim 1 further recites that the method does not include a rescue medication during the treatment of the bipolar I disorder.

On page 5 of the Office Action issued on October 12, 2023, the rejection states and acknowledges that Ahmad teaches that benzodiazepines are allowed as adjunctive medication **as needed** at the discretion of the investigator (the rejection's statement is reproduced below; see also p. 254 for Ahmad's teaching). Thus, Ahmad suggests that one can include benzodiazepines in the medication **whenever necessary,** and therefore the reference allows to include a rescue medication during the administration of endoxifen.

On the other hand, claim 1 recites that the method does not include a rescue medication during the treatment of the bipolar I disorder. That is to say, the method involves the complete removal of a rescue medication. Accordingly, claim 1 is distinguished from Ahmad.

Ali does not remedy the deficiencies of Ahmad. In particular, Ali describes experiments showing the *in vitro* effects of endoxifen on the inhibition of PKC (p. 2665). Ali provides the following description regarding the *in vivo* effects of endoxifen and its toxicity: "Repeated daily oral administration of endoxifen up to 4 mg/kg and 8 mg/kg body weight in rats and mice, respectively, for 28 days showed no signs of toxicity (unpublished observation).

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Efficacy studies with endoxifen will be the subject of further investigation." (p 2667 col. 1 (emphases added)). That is, Ali merely alleges, with no published data, that a repeated oral dose of endoxifen 4 mg/kg and 8 mg/kg in rats and mice shows no sign of toxicity. Moreover, Ali discusses the toxicity in rats and mice, but not in humans, much less a human patient with bipolar I disorder. Note that the term "toxicity" generally has been recognized in the art as the degree to which a chemical substance can damage an organism, and there is no reason to assume that the alleged toxicity data in rats and mice, can be extrapolated to humans, much less to human patients with bipolar I disorder, without substantiated data. Ali further indicates that efficacy studies of endoxifen shall be studied at a later time, which means that Ali does not provide any indication or guidance as to the efficacy of endoxifen for the treatment of bipolar I disorder. Even further, Ali merely suggests the use of endoxifen as a medication only due to its *in vitro* PKC inhibitory effect, and does not provide any *in vivo* data involving the administration of endoxifen. Thus, Ali merely provide a research project about efficacy of endoxifen. Contrary to the rejection's assertion, it would not have been obvious to combine Ahmad and Ali with a reasonable expectation of success in providing a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder, where the method does not include a rescue medication, as recited in claim 1.

In view of the above, it is clear that it would not have been obvious from the combination of Ahmad and Ali to achieve the feature: "wherein the method does not include a rescue medication for the treatment of bipolar I disorder", in a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, as recited in claim 1. Accordingly, claim 1 and its dependent claims 2-5 are patentable over Ahmad and Ali, and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Double Patenting

Claims 1-5 were rejected on the ground of non-statutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 (US '479) in view of Ahmad et al. (Clin. Transl. Sci. 9(5), 252-59 (2016)) (Ahmad) and Ali et al. (Bioorganic & Medicinal Chemistry Letters, 20 (2010), 2665-2667) (Ali). Applicant respectfully traverses this rejection. Claim 1 of the present application recites features indicated above. Claim 1 of US '479 is

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directed to a method of delivering endoxifen to the plasma of a subject, and recites "[a] method of delivering endoxifen to the plasma of a subject comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver endoxifen to the plasma of the subject, wherein : i) said preparation of endoxifen is at least 80% z-endoxifen; and ii) said synthetic preparation of endoxifen is in the form of a citrate salt."

The rejection states and acknowledges on page 7 of the Office Action issued on October 12, 2023, the following regarding claim 1of US '479: "Patented claims do not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patented claims also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5."

Moreover, US '479 does not disclose the feature "wherein the method does not include a rescue medication for the treatment of bipolar I disorder" as recited in claim 1 of the present application. Please note that a double patenting rejection compares the claim(s) of the cited patent reference with the claim(s) of the present application, rather than comparing the disclosure of the cited patent reference.

As discussed above, Ahmad and Ali also do not disclose the feature "wherein the method does not include a rescue medication for the treatment of bipolar I disorder" as recited in claim 1 of the present application. Thus, the combination of the cited references does not meet the features of claim 1 of the present application

In view of the above, Applicant submits that claim 1 and its dependent claims 2-5 of the present application are distinguished from claim 1 of US '479 in view of Ahmad and Ali, and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Claims 1-5 were provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims 1-3 of US Patent No. 11,672,758 (same as co-pending Application No. 17/023208) in view of Ahmad (Clin. Transl. Sci. 9(5), 252-59 (2016)). Applicant respectfully traverses this rejection.

Claims 1-3 of US' 758 are directed to a method of inhibiting protein kinase C by administering an enteric coated tablet comprising endoxifen citrate. However, claims 1-3 of

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US '758 do not disclose or suggest a method for maintaining a therapeutic effective concentration of endoxifen for the treatment of a patient with bipolar I disorder, wherein the method does not include a rescue medication during the treatment of the bipolar I disorder, as recited in claim 1 of the present application.

As discussed above, Ahmad and Ali also do not disclose the feature "wherein the method does not include a rescue medication for the treatment of bipolar I disorder" as recited in claim 1 of the present application. Thus, the combination of the references does not meet the features of claim 1 of the present application. In view of the above, claim 1 and its dependent claims 2-5 of the present application are distinguished from claims 1-3 of US '758 in view of Ahmad, and this rejection should be withdrawn.

Applicant respectfully asserts that the pending claims are in condition for allowance. If a telephone conference would be helpful in resolving any issues concerning this communication, please contact the undersigned attorney, Masako Yoshida (Reg. No. 70,057), at (612) 455-3814.

Respectfully submitted,

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 S. 7th St., Suite 2700
Minneapolis, MN 55402
(612) 455-3800

Dated: January 12, 2024

By: /Masako Yoshida/
Masako Yoshida
Reg. No.: 70,057
MY/YM/mkz

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Doc Code: A.NE.AFCP
Document Description: After Final Consideration Program Request

PTO/SB/434 (3-22)

CERTIFICATION AND REQUEST FOR CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0

Practitioner Docket No.:	Application No.:	Filing Date:
20110.0024USU1	17/226,671	April 9, 2021
First Named Inventor:	**Title:**	
AHMAD, Ateeq	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER	

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0 (AFCP 2.0) OF THE ACCOMPANYING RESPONSE UNDER 37 CFR 1.116.

1. The above-identified application is (i) an original utility, plant, or design nonprovisional application filed under 35 U.S.C. 111(a) [a continuing application (*e.g.*, a continuation or divisional application) is filed under 35 U.S.C. 111(a) and is eligible under (i)], or (ii) an international application that has entered the national stage in compliance with 35 U.S.C. 371(c).
2. The above-identified application contains an outstanding final rejection.
3. Submitted herewith is a response under 37 CFR 1.116 to the outstanding final rejection. The response includes an amendment to at least one independent claim, and the amendment does not broaden the scope of the independent claim in any aspect.
4. This certification and request for consideration under AFCP 2.0 is the only AFCP 2.0 certification and request filed in response to the outstanding final rejection.
5. Applicant is willing and available to participate in any interview requested by the examiner concerning the present response.
6. This certification and request is being filed electronically using the USPTO's patent electronic filing system.
7. Any fees that would be necessary consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, extension of time fees, are being concurrently filed herewith. [There is no additional fee required to request consideration under AFCP 2.0.]
8. By filing this certification and request, applicant acknowledges the following:
   - Reissue applications and reexamination proceedings are not eligible to participate in AFCP 2.0.
   - The examiner will verify that the AFCP 2.0 submission is compliant, *i.e.*, that the requirements of the program have been met (see items 1 to 7 above). For compliant submissions:
     - The examiner will review the response under 37 CFR 1.116 to determine if additional search and/or consideration (i) is necessitated by the amendment and (ii) could be completed within the time allotted under AFCP 2.0. If additional search and/or consideration is required but cannot be completed within the allotted time, the examiner will process the submission consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, by mailing an advisory action.
     - If the examiner determines that the amendment does not necessitate additional search and/or consideration, or if the examiner determines that additional search and/or consideration is required and could be completed within the allotted time, then the examiner will consider whether the amendment places the application in condition for allowance (after completing the additional search and/or consideration, if required). If the examiner determines that the amendment does not place the application in condition for allowance, then the examiner will contact the applicant and request an interview.
       - The interview will be conducted by the examiner, and if the examiner does not have negotiation authority, a primary examiner and/or supervisory patent examiner will also participate.
       - If the applicant declines the interview, or if the interview cannot be scheduled within ten (10) calendar days from the date that the examiner first contacts the applicant, then the examiner will proceed consistent with current practice concerning responses after final rejection under 37 CFR 1.116.

Signature	Date	Practitioner Registration No.
/Masako Yoshida/	January 12, 2024	70,057
Name (Print/Typed)	**Telephone Number**	
Masako Yoshida	(612) 455-3814	

***Note**: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.*

☐ * Total of _____ forms are submitted.

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	CHANNAVAJJALA
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION.
I hereby certify that this paper is being transmitted by Patent Center to the United States Patent & Trademark Office on January 12, 2024.

By: /Maria K. Z. Wait/
Name: Maria K. Z. Wait

AMENDMENT AND RESPONSE AFTER FINAL

Mail Stop: AF
Commissioner for
Patents P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the final Office Action issued October 12, 2023, please amend the above- identified application as follows:

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

Remarks begin on page 3 of this paper.

After Final Consideration Pilot request is filed with this paper.

The Commissioner is hereby authorized to charge any deficiency of fees and credit any overpayments to Deposit Account Number 50-3478.

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) A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days,

wherein [[no]] the method does not include a rescue medication ~~is required~~ for the treatment of the bipolar I disorder.

2. (Original) The method of claim 1, wherein the patient has manic episodes with mixed features.

3. (Original) The method of claim 1, wherein the patient has manic episodes without mixed features.

4. (Original) The method of claim 1, wherein the patient has depression.

5. (Previously Presented) The method of claim 1, wherein the patient has depressive episodes.

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REMARKS

Favorable reconsideration of this application is requested in view of the above amendments and the following remarks. The amendments to claim 1 are supported by the original disclosure, for example, at the last paragraph on page 4 of the specification as filed. Claims 1-5 are pending. No new matter has been added.

Claim Rejections - 35 U.S.C. § 103

Claims 1-5 were rejected under 35 U.S.C. 103 as being unpatentable over Ahmad et al. ("Endoxifen, a New Treatment Option for Mania…", Clin. Transl. Sci. 9(5), 252-59 (2016)) in view of Ali et al. ("Endoxifen is a new portent inhibitor of PKC…", Bioorganic & Medicinal Chemistry Letters, 20 (2010), 2665-2667). Applicant respectfully traverses this rejection.

Claim 1 is directed to a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days. Claim 1 further recites that the method does not include a rescue medication during the treatment of the bipolar I disorder.

On page 5 of the Office Action issued on October 12, 2023, the rejection states and acknowledges that Ahmad teaches that benzodiazepines are allowed as adjunctive medication **as needed** at the discretion of the investigator (the rejection's statement is reproduced below; see also p. 254 for Ahmad's teaching). Thus, Ahmad suggests that one can include benzodiazepines in the medication **whenever necessary,** and therefore the reference allows to include a rescue medication during the administration of endoxifen.

On the other hand, claim 1 recites that the method does not include a rescue medication during the treatment of the bipolar I disorder. That is to say, the method involves the complete removal of a rescue medication. Accordingly, claim 1 is distinguished from Ahmad.

Ali does not remedy the deficiencies of Ahmad. In particular, Ali describes experiments showing the *in vitro* effects of endoxifen on the inhibition of PKC (p. 2665). Ali provides the following description regarding the *in vivo* effects of endoxifen and its toxicity: "Repeated daily oral administration of endoxifen up to 4 mg/kg and 8 mg/kg body weight in rats and mice, respectively, for 28 days showed no signs of toxicity (unpublished observation).

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Efficacy studies with endoxifen will be the subject of further investigation." (p 2667 col. 1 (emphases added)). That is, Ali merely alleges, with no published data, that a repeated oral dose of endoxifen 4 mg/kg and 8 mg/kg in rats and mice shows no sign of toxicity. Moreover, Ali discusses the toxicity in rats and mice, but not in humans, much less a human patient with bipolar I disorder. Note that the term "toxicity" generally has been recognized in the art as the degree to which a chemical substance can damage an organism, and there is no reason to assume that the alleged toxicity data in rats and mice, can be extrapolated to humans, much less to human patients with bipolar I disorder, without substantiated data. Ali further indicates that efficacy studies of endoxifen shall be studied at a later time, which means that Ali does not provide any indication or guidance as to the efficacy of endoxifen for the treatment of bipolar I disorder. Even further, Ali merely suggests the use of endoxifen as a medication only due to its *in vitro* PKC inhibitory effect, and does not provide any *in vivo* data involving the administration of endoxifen. Thus, Ali merely provide a research project about efficacy of endoxifen. Contrary to the rejection's assertion, it would not have been obvious to combine Ahmad and Ali with a reasonable expectation of success in providing a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder, where the method does not include a rescue medication, as recited in claim 1.

In view of the above, it is clear that it would not have been obvious from the combination of Ahmad and Ali to achieve the feature: "wherein the method does not include a rescue medication for the treatment of bipolar I disorder", in a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, as recited in claim 1. Accordingly, claim 1 and its dependent claims 2-5 are patentable over Ahmad and Ali, and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Double Patenting

Claims 1-5 were rejected on the ground of non-statutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 (US '479) in view of Ahmad et al. (Clin. Transl. Sci. 9(5), 252-59 (2016)) (Ahmad) and Ali et al. (Bioorganic & Medicinal Chemistry Letters, 20 (2010), 2665-2667) (Ali). Applicant respectfully traverses this rejection. Claim 1 of the present application recites features indicated above. Claim 1 of US '479 is

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directed to a method of delivering endoxifen to the plasma of a subject, and recites "[a] method of delivering endoxifen to the plasma of a subject comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver endoxifen to the plasma of the subject, wherein : i) said preparation of endoxifen is at least 80% z-endoxifen; and ii) said synthetic preparation of endoxifen is in the form of a citrate salt."

The rejection states and acknowledges on page 7 of the Office Action issued on October 12, 2023, the following regarding claim 1of US '479: "Patented claims do not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patented claims also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5."

Moreover, US '479 does not disclose the feature "wherein the method does not include a rescue medication for the treatment of bipolar I disorder" as recited in claim 1 of the present application. Please note that a double patenting rejection compares the claim(s) of the cited patent reference with the claim(s) of the present application, rather than comparing the disclosure of the cited patent reference.

As discussed above, Ahmad and Ali also do not disclose the feature "wherein the method does not include a rescue medication for the treatment of bipolar I disorder" as recited in claim 1 of the present application. Thus, the combination of the cited references does not meet the features of claim 1 of the present application

In view of the above, Applicant submits that claim 1 and its dependent claims 2-5 of the present application are distinguished from claim 1 of US '479 in view of Ahmad and Ali, and this rejection should be withdrawn. Applicant does not concede the correctness of this rejection.

Claims 1-5 were provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims 1-3 of US Patent No. 11,672,758 (same as co-pending Application No. 17/023208) in view of Ahmad (Clin. Transl. Sci. 9(5), 252-59 (2016)). Applicant respectfully traverses this rejection.

Claims 1-3 of US' 758 are directed to a method of inhibiting protein kinase C by administering an enteric coated tablet comprising endoxifen citrate. However, claims 1-3 of

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US '758 do not disclose or suggest a method for maintaining a therapeutic effective concentration of endoxifen for the treatment of a patient with bipolar I disorder, wherein the method does not include a rescue medication during the treatment of the bipolar I disorder, as recited in claim 1 of the present application.

As discussed above, Ahmad and Ali also do not disclose the feature "wherein the method does not include a rescue medication for the treatment of bipolar I disorder" as recited in claim 1 of the present application. Thus, the combination of the references does not meet the features of claim 1 of the present application. In view of the above, claim 1 and its dependent claims 2-5 of the present application are distinguished from claims 1-3 of US '758 in view of Ahmad, and this rejection should be withdrawn.

Applicant respectfully asserts that the pending claims are in condition for allowance. If a telephone conference would be helpful in resolving any issues concerning this communication, please contact the undersigned attorney, Masako Yoshida (Reg. No. 70,057), at (612) 455-3814.

Respectfully submitted,

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(612) 455-3800

Dated: January 12, 2024

By: /Masako Yoshida/
Masako Yoshida
Reg. No.: 70,057
MY/YM/mkz

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UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/226,671	**01/12/2024 04:01:11 PM Z ET**	**20110.0024USU1**

Title of Invention

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1772	FILED BY	Maria Zamorano
PATENT CENTER #	63940948	FILING DATE	04/09/2021
CUSTOMER #	52835	FIRST NAMED INVENTOR	Ateeq AHMAD
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Masako Yoshida

Documents

TOTAL DOCUMENTS: 4

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
AMENDMENT_AFTER_FINAL.pdf		6	-	147 KB
AMENDMENT_AFTER_FINAL-A.NE.pdf	(1-1)	1	Response After Final Action	79 KB
AMENDMENT_AFTER_FINAL-CLM.pdf	(2-2)	1	Claims	78 KB
AMENDMENT_AFTER_FINAL-REM.pdf	(3-6)	4	Applicant Arguments/Remarks Made in an Amendment	139 KB
REQUEST_FOR_CONSIDERATION_UNDER_AFCP.pdf		2	After Final Consideration Program Request	257 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
AMENDMENT_AFTER_FINAL.pdf	A261C7B37D87A7B782255F6BDD432BE580A05EAA9B25FB6DBA3A3D45CA63E8B5F192D7085BB6157B6182311F87CDA7844DC78D0FF4296F38125DADBE1E1E4DC4
AMENDMENT_AFTER_FINAL-A.NE.pdf	D957C4933633D476747C83973B1E361856D0758942F4E1C6C9C91529270163EA491A0A34BDDF0A5FEE6807C7103F75C0E1956D9730C380A2EBBA21A078148639
AMENDMENT_AFTER_FINAL-CLM.pdf	51FCF73A0A1A455269D0F96819A5922DBB8F69B832297B4C6C1839FD1EE6D761F87BEC41DAAB517C36A3986630315 53C65D772948DD5C669B7E7B7B40A41E12B
AMENDMENT_AFTER_FINAL-REM.pdf	F8A0E8EBBEAD8FFF35FCC08E9A760D6364C54A325FC8D86F2698102599CC7988194F01292BCDB3D3DE1E18FA481BE8A2646154225AE7336A7127303A7E50B819
REQUEST_FOR_CONSIDERATION_UNDER_AFCP.pdf	3241221F36FA22B8EC4D99FB030C64682740D7837BCBFAA8C06CCA529C792A8F5CEF7C3EA880869957746 6E363C1733CFCE66DAEFB7694E4BEDE03600F7D62F3

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 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 17/226,671	Filing Date 04/09/2021	☐ 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 $50 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $240 =	
☐ 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	01/12/2024	(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))	* 5	Minus	** 20	= 0		x $40 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0		x $192 =	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 $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ 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.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/LISA THOMAS/
*** 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.	

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	CHANNAVAJJALA
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION.
I hereby certify that this paper is being transmitted by Patent Center to the United States Patent & Trademark Office on January 12, 2024.

By: /Maria K. Z. Wait/
Name: Maria K. Z. Wait

AMENDMENT AND RESPONSE AFTER FINAL

Mail Stop: AF
Commissioner for
Patents P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the final Office Action issued October 12, 2023, please amend the above- identified application as follows:

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

Remarks begin on page 3 of this paper.

After Final Consideration Pilot request is filed with this paper.

The Commissioner is hereby authorized to charge any deficiency of fees and credit any overpayments to Deposit Account Number 50-3478.

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.
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1	1772

52835 7590 02/02/2024

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
45 South Seventh Street
Suite 2700
Minneapolis, MN 55402-1683

EXAMINER
CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
02/02/2024	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOMail@hsml.com

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00359

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 17/226,671	**Applicant(s)** AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	**Art Unit** 1611	**AIA (FITF) Status** Yes

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

THE REPLY FILED 12 January 2024 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

NO NOTICE OF APPEAL FILED

1. ☑ The reply was filed after a final rejection. No Notice of Appeal has been filed. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114 if this is a utility or plant application. Note that RCEs are not permitted in design applications. The reply must be filed within one of the following time periods:
   a) ☑ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action; or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   c) ☐ A prior Advisory Action was mailed more than 3 months after the mailing date of the final rejection in response to a first after-final reply filed within 2 months of the mailing date of the final rejection. The current period for reply expires ____ months from the mailing date of *the prior Advisory Action* or SIX MONTHS from the mailing date of the final rejection, whichever is earlier.

   Examiner Note: If box 1 is checked, check either box (a), (b) or (c). ONLY CHECK BOX (b) WHEN THIS ADVISORY ACTION IS THE FIRST RESPONSE TO APPLICANTS FIRST AFTER-FINAL REPLY WHICH WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. ONLY CHECK BOX (c) IN THE LIMITED SITUATION SET FORTH UNDER BOX (c). See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) or (c) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37CFR 41.37(a).

AMENDMENTS

3. ☑ The proposed amendments filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   a) ☑ They raise new issues that would require further consideration and/or search (see NOTE below);
   b) ☐ They raise the issue of new matter (see NOTE below);
   c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: See Continuation Sheet (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☑ For purposes of appeal, the proposed amendment(s):(a) ☑ will not be entered, or (b) ☐ will be entered, and an explanation of how the new or amended claims would be rejected is provided below or appended.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____
9. ☐ The affidavit or other evidence filed after final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
10. ☐ The affidavit or other evidence filed after the date of filing the Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
11. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

12. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
13. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
14. ☑ Other: PTO-2323; PTO-413.

STATUS OF CLAIMS

15. The status of the claim(s) is (or will be) as follows:
    Claim(s) allowed: _____.
    Claim(s) objected to: _____.
    Claim(s) rejected: 1-5.
    Claim(s) withdrawn from consideration: _____.

/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00360

Continuation of 3. NOTE: the proposed amendment positively excludes a rescue medication from the claimed method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder and hence requires further consideration and/or search.

Examiner-Initiated Interview Summary	Application No. 17/226,671	Applicant(s) AHMAD et al.		
	Examiner LAKSHMI S CHANNAVAJJALA	Art Unit 1611	AIA (First Inventor to File) Status Yes	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
LAKSHMI S CHANNAVAJJALA	Primary Examiner	Telephonic
Yugho Maruta	Attorney of Record	

Date of Interview: 30 January 2024

Issues Discussed:

Other

Discussed the after-final amendment dated 1/12/24. Examiner informed that the proposed amendment positively excludes a rescue medication from the claimed method for maintaining a therapeutically effective concentration of endoxifen for the treatment of a patient with bipolar I disorder. Examiner informed that the newly added limitation requires further consideration and/or search, and will not be entered at this time. Examiner further informed that while the limitation may not render the rejection unobvious, the scope of the invention is different with the proposed amendment and hence requires further consideration.

	/LAKSHMI S CHANNAVAJJALA/ Primary Examiner, Art Unit 1611

Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04
Please further see:
MPEP 713.04
Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b)
37 CFR § 1.2 Business to be transacted in writing

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.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00362

AFCP 2.0 Decision

Application No.	Applicant(s)	
17/226,671	AHMAD et al.	
Examiner	**Art Unit**	**AIA (FITF) Status**
LAKSHMI S CHANNAVAJJALA	1611	Yes

This is in response to the After Final Consideration Pilot request filed 12 January 2024.

1. **Improper Request** – The AFCP 2.0 request is improper for the following reason(s) and the after final amendment submitted with the request will be treated under pre-pilot procedure.

   ☐ An AFCP 2.0 request form PTO/SB/434 (or equivalent document) was not submitted.

   ☐ A non-broadening amendment to at least one independent claim was not submitted.

   ☐ The request is not the first proper AFCP 2.0 request submitted in response to the most recent final rejection.

   ☐ Other: _____

2. **Proper Request**

   A. After final amendment submitted with the request will not be treated under AFCP 2.0.
   The after final amendment cannot be reviewed and a search conducted within the guidelines of the pilot program.

   ☐ The after final amendment will be treated under pre-pilot procedure.

   B. Updated search and/or completed additional consideration.
   The examiner performed an updated search and/or completed additional consideration of the after final amendment within the time authorized for the pilot program. The result(s) of the updated search and/or completed additional consideration are:

   ☐ 1. All of the rejections in the most recent final Office action are overcome and a Notice of Allowance is issued herewith.

   ☑ 2. The after final amendment would not overcome all of the rejections in the most recent final Office action . See attached interview summary for further details.

   ☑ 3. The after final amendment was reviewed, and it raises a new issue(s). See attached interview summary for further details.

   ☐ 4. The after final amendment raises new issues, but would overcome all of the rejections in the most recent final Office action. A decision on determining allowability could not be made within the guidelines of the pilot. See attached interview summary for further details, including any newly discovered prior art.

   ☐ 5. Other: _____

   Examiner Note: Please attach an interview summary when necessary as described above.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00363

DO NOT ENTER: /L.S.C/

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventorship:	AHMAD	Examiner:	CHANNAVAJJALA
Serial No.:	17/226,671	Group Art Unit:	1611
Filed:	April 9, 2021	Docket No.:	20110.0024USU1
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER		

CERTIFICATE OF TRANSMISSION.
I hereby certify that this paper is being transmitted by Patent Center to the United States Patent & Trademark Office on January 12, 2024.

By: /Maria K. Z. Wait/
Name: Maria K. Z. Wait

AMENDMENT AND RESPONSE AFTER FINAL

Mail Stop: AF
Commissioner for
Patents P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Commissioner:

In response to the final Office Action issued October 12, 2023, please amend the above- identified application as follows:

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

Remarks begin on page 3 of this paper.

After Final Consideration Pilot request is filed with this paper.

The Commissioner is hereby authorized to charge any deficiency of fees and credit any overpayments to Deposit Account Number 50-3478.

Doc code: RCEX
Doc description: Request for Continued Examination (RCE)

PTO/SB/30EFS (01-22)
Approved for use through 05/31/2024. 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	17/226,671	Filing Date	2021-04-09	Docket Number (if applicable)	20110.0024USU1	Art Unit	1611
First Named Inventor	AHMAD			Examiner Name	CHANNAVAJJALA		

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 orde 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 Amendment and Response filed January 12, 2024

☐ 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 one-month extension of time ($88 small entity)

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 503478

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00365

PTO/SB/30EFS (01-22)
Approved for use through 05/31/2024. 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	/Masako Yoshida/	Date (YYYY-MM-DD)	2024-02-05
Name	Masako Yoshida	Registration Number	70,057

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 t 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 estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Tim will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions fo 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 informatio 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 ma 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.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00367

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/226,671	**02/05/2024 04:34:13 PM Z ET**	**20110.0024USU1**

Title of Invention

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1772	FILED BY	Chad Vass
PATENT CENTER #	64213134	FILING DATE	04/09/2021
CUSTOMER #	52835	FIRST NAMED INVENTOR	Ateeq AHMAD
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Masako Yoshida

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
RCE.pdf	3	Request for Continued Examination (RCE)	1628 KB
Extension.pdf	2	Extension of Time	284 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
RCE.pdf	2F986F875152D080411A1B072E649AE925F91BABF5850AAB4E1833E7CF6621C22FA8F537361B5595EFADE17048659336BEE0F48F7978BF0A946824703179108A
Extension.pdf	B3BF2F5F7F910EF7549DEB7C375DCF65F469493858670A3CBEE3F030384587547D48AED549833B0359C43F1EB9543BC2D8

73BA36156C406EEDE01BE1EA0266F0

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 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/AIA/22 (11-23)
Approved for use through 05/31/2024. 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 displays a valid OMB control number.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional): 20110.0024USU1

Application Number: 17/226,671

Filed: April 9, 2021

For: ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Art Unit: 1611

Examiner: CHANNAVAJJALA

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))	$220	$88	$44	$ 88
☐	Two months (37 CFR 1.17(a)(2))	$640	$256	$128	$
☐	Three months (37 CFR 1.17(a)(3))	$1,480	$592	$296	$
☐	Four months (37 CFR 1.17(a)(4))	$2,320	$928	$464	$
☐	Five months (37 CFR 1.17(a)(5))	$3,160	$1,264	$632	$

☑ 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 503478.

☑ Payment made via USPTO patent electronic filing system.

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.

☑ attorney or agent of record. Registration number 70,057.

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____.

/Masako Yoshida/ — Signature

February 5, 2024 — Date

Masako Yoshida — Typed or printed name

(612) 455-3814 — 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.

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0031. Public burden for this form is estimated to average 6 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.** If filing this completed form by mail, 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.

Privacy Act Statement

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Routine uses of the information in this record may include disclosure to:

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2) a federal, state, local, or international agency, in response to its request;

3) a contractor of the USPTO having need for the information in order to perform a contract;

4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;

5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;

6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;

7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;

8) 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));

9) the Office of Personnel Management (OPM) for personnel research purposes; and

10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

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UNITED STATES
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ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/226,671	**02/05/2024 04:34:13 PM Z ET**	**20110.0024USU1**

Title of Invention

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1772	FILED BY	Chad Vass
PATENT CENTER #	64213134	AUTHORIZED BY	Masako Yoshida
CUSTOMER #	52835	FILING DATE	04/09/2021
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Ateeq AHMAD

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 1021	**E202425G34596553**	**Chad Vass**

PRE-AUTHORIZED ACCOUNT	PRE-AUTHORIZED CATEGORY
503478	**37 CFR 1.17 (Patent application and reexamination processing fees)**

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2251	EXTENSION FOR RESPONSE WITHIN FIRST MONTH	88.00	1	88.00
2820	REQUEST FOR CONTINUED EXAMINATION (RCE)- 2ND AND SUBSEQUENT REQUEST (SEE 37 CFR 1.114)	800.00	1	800.00
			TOTAL AMOUNT:	**$888.00**

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 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
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 17/226,671	Filing Date 04/09/2021	☐ 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), (l), 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 $50 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $240 =	
☐ 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	02/05/2024	(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))	* 5	Minus	** 20	= 0		x $40 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0		x $192 =	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 $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ 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.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/VICTOR BARLOW/
*** 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.	

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.**

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/226,671	**04/22/2024 04:05:05 PM Z ET**	**20110.0024USU1**

Title of Invention

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1772	FILED BY	Connie Cain
PATENT CENTER #	65193394	FILING DATE	04/09/2021
CUSTOMER #	52835	FIRST NAMED INVENTOR	Ateeq AHMAD
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Alejandro Menchaca

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
67908US01_POA_filed_22Apr2024.pdf	1	Power of Attorney	613 KB
67908US01_373c_Statement_filed_22Apr2024.pdf	3	Assignee showing of ownership per 37 CFR 3.73	230 KB
67908US01_Change_of_Correspondence_Address_22Apr2024.pdf	2	Change of Address	305 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)

67908US01_POA_filed_22Apr2024.pdf	A2FC238B78661F64CC1C36A0CC206AAE913A526137DD45A41B81C1BC548649F4ACF56AD3D9224E7670B0DD3372E0723A1659BAC8EA83CC5DF7E0EB7E1C053170
67908US01_373c_Statement_filed_22Apr2024.pdf	16B71FA874ACC177CFCA4D7DDF2E9A965EFC1A482981E87ED58DBF9F581B9FB2B31D3024ED9D4532976FCCE1AC50E964A06A1EE84FE6F6582457B85A91E68B57
67908US01_Change_of_Correspondence_Address_22Apr2024.pdf	7AC7F5B26F687B8709273E84C79D43E1931111DAF232A26431E8CDF6A7C46D3D2D7A1BDD526A88709576008995485D7DD099654AC5E1CC54E08FC03A2464B10B

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PTO/AIA/96 (11-23)
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STATEMENT UNDER 37 CFR 3.73(c)

First Named Inventor/Patent Owner: AHMAD, Ateeq, et al.

Application No./Patent No.: 17/226,671 Filed/Issue Date: April 9, 2021

Titled: Endoxifen for the Treatment of Bipolar I Disorders

Jina Pharmaceuticals, Inc., a Delaware Corporation

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☑ The assignee of the entire right, title, and interest.

2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):

   ☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

   ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. ☑ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 055880, Frame 0164, or for which a copy thereof is attached*.

B. ☐ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

   1. From: _____ To: _____

      The document was recorded in the United States Patent and Trademark Office at

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   2. From: _____ To: _____

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STATEMENT UNDER 37 CFR 3.73(c)

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☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☐ *As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Alejandro Menchaca/	April 22, 2024
Signature	Date
Alejandro Menchaca	34,389
Printed or Typed Name	Title or Registration Number

Privacy Act Statement

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If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Doc Code: PA..
Document Description: Power of Attorney

PTO/AIA/82B (07-13)
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POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date
17/226,671	4/09/2021

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

☑ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above: 23,446

OR

☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

Please recognize or change the correspondence address for the application identified in the attached transmittal letter or the boxes above to:

☑ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

☐ Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

Jina Pharmaceuticals, Inc., 28100 N. Ashley Circle, Suite 103 Libertyville, IL 60048

☐ Inventor or Joint Inventor (title not required below)

☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☑ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature		Date (Optional)	March 23, 2021
Name	Chad Shealy		
Title	Vice President		

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ Total of forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. 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 3 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.

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PTO/AIA/122 (05-23)
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CHANGE OF CORRESPONDENCE ADDRESS
Application

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

Application Number	17/226,671
Filing Date	April 9, 2021
First Named Inventor	AHMED, Ateeq et al.
Art Unit	1611
Examiner Name	LAKSHMI SARADA CHANNAVAJJALA
Attorney Docket Number	67908US01

Please change the Correspondence Address for the above-identified patent application to:

☑ The address associated with Customer Number: 23446

OR

☐ Firm or Individual Name

Address

City	State	Zip

Country

Telephone	Email

This form cannot be used to change the data associated with a Customer Number. To change the data associated with an existing Customer Number use "Request for Customer Number Data Change" (PTO/SB/124).

I am the:

☐ Applicant

☑ Attorney or agent of record. Registration Number 34,389

☐ Registered practitioner named in the application transmittal papers who acts in a representative capacity under 37 CFR 1.34. See 37 CFR 1.33(a)(1). Registration Number 34,389

Signature	/Alejandro Menchaca/
Typed or Printed Name	Alejandro Menchaca
Date April 22, 2024	Telephone 312-775-8000

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0035. Public burden for this form is estimated to average 3 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **If filing this completed form by mail, send to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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United States Patent and Trademark Office
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1

CONFIRMATION NO. 1772

POWER OF ATTORNEY NOTICE



52835
HSML P.C.
45 South Seventh Street
Suite 2700
MINNEAPOLIS, MN 55402-1683

Date Mailed: 04/24/2024

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/22/2024.

- The Power of Attorney to you in this application has been revoked by the applicant. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

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**.

/zretta/

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00383

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17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1

CONFIRMATION NO. 1772

POA ACCEPTANCE LETTER

OC000000071504547

23446
MCANDREWS HELD & MALLOY, LTD
500 WEST MADISON STREET
SUITE 3400
CHICAGO, IL 60661

Date Mailed: 04/24/2024

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/22/2024.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

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**.

/zretta/

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	20110.0024USU1	1772

23446 7590 05/22/2024
MCANDREWS HELD & MALLOY, LTD
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CHICAGO, IL 60661

EXAMINER
CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
05/22/2024	ELECTRONIC

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.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mhmpto@mcandrews-ip.com

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00385

Office Action Summary	Application No. 17/226,671	Applicant(s) AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	Art Unit 1611	AIA (FITF) Status Yes

-- 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 MONTHS 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 2/5/24.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

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

3)☐ 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.

4)☐ 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*

5) ☑ Claim(s) 1-5 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-5 is/are rejected.

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

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

* If any claims have been determined allowable, 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.**

Application Papers

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

11)☐ 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).

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).

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)).

** 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) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

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

4) ☐ Other: _____.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
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Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/5/24 has been entered.

Claims 1-5 are pending.

The previous rejection of record has been withdrawn and replaced by the following rejection:

Claim Rejections - 35 USC § 103

1.Claims 1-5 are rejected under 35 U.S.C. 103 as being unpatentable over Ahmad et al (2016, cited on IDS) in view of WO 2008/048194 to Yesilogluz (cited on IDS dated 8/1/21).

Instant claims are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days.

Claim 1 has been amended to recite "the method does not include a rescue medication for the treatment of bipolar I disorder".

Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BP) with current manic or mixed episode. Ahmad teaches that protein kinase C family of kinases play a vital role in cell signaling pathways including mood regulation; and PKC is a target for treating bipolar disorder (pa 252).

Ahmad describes that adherence to the treatment is affected by adverse effects such as sedation and weight gain, and that there is an urgent need to develop novel and more effective treatments for BP (p 252). Ahmad states that several drugs have been approved such as lithium, valproate, carbamazepine, and atypical antipsychotics for the treatment of acute bipolar mania, which while providing relief for many individuals with BP, significant issues with tolerability and efficacy still remain, whereas endoxifen shows 4-fold higher potency in inhibiting PKC activity.

Ahmad teaches enteric coated endoxifen citrate salt ("CgHgO7" is citric acid, see figure 1 and page 253, col. 2- Methodology) (claim 1). The results were expressed as Young Mania Rating Scale (YMRS) total score (≥50% decrease from baseline). Secondary end points were mean change from baseline to the end of treatment in the Montgomery–Åsberg Depression Rating Scale (MADRS) total score, Clinical Global Impressions–Severity of Illness Scale (CGI-S) score, and Columbia–Suicide Severity Rating Scale (C-SSRS) score, shown in Table 1. Ahmad teaches that a switch to depression remains a concern in all treatments of bipolar mania, depressive symptoms were assessed with the MADRS score throughout the trial. Ahmad teaches effectiveness of endoxifen 4 mg and 8 mg in alleviating depressive symptoms of mixed

episode of BPD similar to that of divalproex (p 256, col.1 & Table 2) (claim 1). Further, the administration of endoxifen (4 mg and 8 mg) provides a steady state plasma concentration of endoxifen for 14 and also 21 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect (which can be construed as without mixed episode) or mixed episodes patients of endoxifen (p 258). In a double-blind, active-controlled study, 84 subjects with BPD I were randomly assigned to receive endoxifen (4 mg/day or 8 mg/day) or divalproex in a 2:1 ratio. Patients orally administered 4 mg/day or 8 mg/day endoxifen showed significant improvement in mania assessed by the Young Mania Rating Scale as early as 4 days. The effect remained significant throughout the 21-day period. At study end point, response rates were 44.44% and 64.29% at 4 mg/day and 8 mg/day of endoxifen treatment, respectively (abstract). Thus, Ahmad teaches endoxifen has been shown as a promising novel antimanic or mood stabilizing agent, as seen by significantly improved YMRS scale at almost every treatment evaluation.

Ahmad teaches that the plasma concentration of endoxifen is maintained at 14 and 20 days, indicating steady state of the endoxifen (fig.4). Ahmad also teaches monotherapy trials of drugs for the treatment of bipolar disorder (table 3 and 4b). Further, with respect to maintaining the therapeutically effective concentration of endoxifen in the patient, Ahmad teaches that the concentration of endoxifen is maintained up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen).

Instant claim 1 has been amended to recite "the method does not include a rescue medication".

While Ahmad does not explicitly state "the method does not include a rescue medication", Ahmad also teaches that benzodiazepines are allowed as adjunctive medication as needed at the discretion of the investigator (p 254). Moreover, Ahmad does not require that additional rescue medication is evident from the study design (fig. 2), wherein the design does not include any benzodiazepines.

Thus, Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen.

In this regard, Ahmad also teaches that tamoxifen has a strong anti-manic property in both men and women, and that endoxifen has superior PKC inhibitory properties over tamoxifen (paragraphs bridging pages 252-253).

Moreover, Yesilogluz teaches the use of tamoxifen (PKC inhibitor) for the treatment of bipolar disorder, wherein tamoxifen treatment has been shown to have strong anti-manic properties (abstract). Yesilogluz describes the enrollment of patients and clinical study details on pages 8-11. Yesilogluz describes that tamoxifen alone provides 48% (14 out of 20) patients achieved a positive response, compared to only 1 out of 21 (page 12) and the measurement of improvement in YMRA scale, CGI-Mania scale and other parameters of mania in Table 1, and shows that tamoxifen proves an effective antimanic properties and an effective mood stabilizer in bipolar patients (p 13). It is to be noted that the tamoxifen treated group of patients in Yesilogluz does not require any additional antimanic or antidepressants compounds such as lithium or valproate, which are also implicated as standard treatments for bipolar disorder (see page 1- Field of Invention).

Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen citrate composition (the enteric coated composition of Ahmad) without any other medication such as benzodiazepines because, while Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2-pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Ahmad also recognizes that endoxifen is a metabolite of tamoxifen that is four-fold highly potent in inhibiting PKC, the latter being involved and highly implicated in involved in mood disorders (see Introduction section of Ahmad). In this regard, Yesilogluz shows that tamoxifen administration alone is effective for treating bipolar disorder, in particular, the clinical studies. Hence, one of an ordinary skill in the art would have been motivated to employ only endoxifen citrate of Ahmad, which has much higher potency than the parent compound (tamoxifen), with an expectation to provide an effective in treating bipolar disorder and also main therapeutically effective plasma concentration because Ahmad the same dosage regimen claimed for providing endoxifen concentration for up to 21 days.

Double Patenting

2.Claims 1-5 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 in view of Ahmad et al (2016, cited on IDS) and WO 2008/048194 to Yesilogluz (cited on IDS dated 8/1/21).

Instant claim 1 has been amended to recite "the method does not include a rescue medication".

Patented claims are directed to a method of delivering endoxifen to the plasma of a subject, comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver and the endoxifen is a synthetic endoxifen that is at least 80% z-endoxifen and in the form of a citrate salt.

Patented claims do not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patented claims also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5.

The teachings of Ahmad and Yesilogluz have been discussed above.

Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BP) with current manic or mixed episode. Ahmad teaches enteric coated endoxifen citrate, in the claimed amounts and for administering to patients with Bipolar I disorder for the claimed duration (21 days). Further, the administration of endoxifen (4 mg and 8 mg) provides a steady state plasma concentration of endoxifen for 14 and also 21 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect (which can be construed as without mixed episode) or mixed episodes patients of endoxifen (p 258). In a double-blind, active-controlled study, 84 subjects with BPD I were randomly assigned to receive endoxifen (4 mg/day or 8 mg/day) or divalproex in a 2:1 ratio. Patients orally

administered 4 mg/day or 8 mg/day endoxifen showed significant improvement in mania assessed by the Young Mania Rating Scale as early as 4 days. The effect remained significant throughout the 21-day period. At study end point, response rates were 44.44% and 64.29% at 4 mg/day and 8 mg/day of endoxifen treatment, respectively (abstract). Thus, Ahmad teaches endoxifen has been shown as a promising novel antimanic or mood stabilizing agent, as seen by significantly improved YMRS scale at almost every treatment evaluation.

Yesilogluz teaches the use of tamoxifen (PKC inhibitor) for the treatment of bipolar disorder, wherein tamoxifen treatment has been shown to have strong anti-manic properties (abstract). Yesilogluz describes the enrollment of patients and clinical study details on pages 8-11. Yesilogluz describes that tamoxifen alone provides 48% (14 out of 20) patients achieved a positive response, compared to only 1 out of 21 (page 12) and the measurement of improvement in YMRA scale, CGI-Mania scale and other parameters of mania in Table 1, and shows that tamoxifen proves an effective antimanic properties and an effective mood stabilizer in bipolar patients (p 13). It is to be noted that the tamoxifen treated group of patients in Yesilogluz does not require any additional antimanic or antidepressants compounds such as lithium or valproate, which are also implicated as standard treatments for bipolar disorder (see page 1- Field of Invention).

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions of patented claims comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts,

administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. While Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Yesilogluz shows that tamoxifen administration alone is effective for treating bipolar disorder. In this regard, Ahmad also recognizes that endoxifen is a metabolite of tamoxifen that is four-fold highly potent in inhibiting PKC, the latter being involved and highly implicated in involved in mood disorders (see Introduction section of Ahmad). Further, Yesilogluz shows that tamoxifen alone has been administered in the clinical studies, for treating bipolar disorder and therefore, one of an ordinary skill in the art would have been motivated to employ only endoxifen citrate of the patented claims, which has much higher potency than the parent compound (tamoxifen), with an expectation to provide an effective in treating bipolar disorder and also main therapeutically effective plasma concentration without any additional rescue medication because Ahmad the same dosage regimen claimed for providing endoxifen concentration for up to 21 days.

6. Claims 1-5 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over the claims 1-3 of US Patent 11672758 in view of Ahmad et al (2016, cited on IDS) and WO 2008/048194 to Yesilogluz (cited on IDS dated 8/1/21).

Instant claim 1 has been amended to recite "the method does not include a rescue medication".

Patent claims are directed to a method of inhibiting protein kinase C by administering an enteric coated tablet comprising endoxifen citrate. However, a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder. Patent claims lack the amounts of endoxifen citrate, for the duration of 21 days, and also lacks instant claims 4-5.

The teachings of Ahmad and Yesilogluz have been discussed above.

Ahmad teaches antimanic properties of endoxifen in patients with bipolar I disorder (BP) with current manic or mixed episode. Ahmad teaches enteric coated endoxifen citrate, in the claimed amounts and for administering to patients with Bipolar I disorder for the claimed duration (21 days). Further, the administration of endoxifen (4 mg and 8 mg) provides a steady state plasma concentration of endoxifen for 14 and also 21 days, and that doubling of the dose from 4 to 8 mg increases the plasma AUC by 2-fold (p 257), thus manifesting the anti-manic effect (which can be construed as without mixed episode) or mixed episodes patients of endoxifen (p 258). In a double-blind, active-controlled study, 84 subjects with BPD I were randomly assigned to receive endoxifen (4 mg/day or 8 mg/day) or divalproex in a 2:1 ratio. Patients orally administered 4 mg/day or 8 mg/day endoxifen showed significant improvement in mania assessed by the Young Mania Rating Scale as early as 4 days. The effect remained significant throughout the 21-day period. At study end point, response rates were 44.44% and 64.29% at 4 mg/day and 8 mg/day of endoxifen treatment, respectively (abstract). Thus, Ahmad teaches endoxifen has been shown as a promising novel

antimanic or mood stabilizing agent, as seen by significantly improved YMRS scale at almost every treatment evaluation.

Hence, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions (of the patent claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. While Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and that the concentration of endoxifen is maintained for up to 21 days (Fig.3 and p 256-col. 2- pharmacokinetics and pharmacokinetic-pharmacodynamic (PK-PD) relation of endoxifen), Yesilogluz shows that tamoxifen administration alone is effective for treating bipolar disorder. In this regard, Ahmad also recognizes that endoxifen is a metabolite of tamoxifen that is four-fold highly potent in inhibiting PKC, the latter being involved and highly implicated in involved in mood disorders (see Introduction section of Ahmad). Further, Yesilogluz shows that tamoxifen alone has been administered in the clinical studies, for treating bipolar disorder and therefore, one of an ordinary skill in the art would have been motivated to employ only endoxifen citrate of the patented claims, which has much higher potency than the parent compound (tamoxifen), with an expectation to provide an effective in treating bipolar disorder and also main therapeutically effective plasma

concentration without any additional rescue medication because Ahmad the same dosage regimen claimed for providing endoxifen concentration for up to 21 days.

Response to Arguments

Applicant's arguments filed 2/05/24 have been fully considered but they are not persuasive.

Rejections under 35 USC 103:

Applicants argue that instant claims now exclude the administration of rescue medication during the treatment of bipolar I disorder, because claims recite "that the method does not include a rescue medication". However, tin light of the amendment, the present rejection under 35 USC 103 does not rely on the combination of Ahmad et al in view of Ali et al. Further, the double patenting rejections do not rely on the combination of Ahmad et al in view of Ali et al. Accordingly, the arguments regarding the teachings of Ali are moot.

In light of the amendments, the present rejection under 35 USC 103 relies on Ahmad et al (2016, cited on IDS) and WO 2008/048194 to Yesilogluz (cited on IDS dated 8/1/21). While Ahmad et al teaches the administration of endoxifen citrate enteric coated tablet to treat bipolar I disorder, the reference also suggests that adjunct medication, benzodiazepine, is only administered as needed and further does not include benzodiazepine in the study design. The motivation to employ endoxifen citrate of Ahmad alone without any additional mood disorder or mania treating compounds

(such as benzodiazepine or lithium or valproate) comes not only from the teaching of Ahmad that adjunct medication is employed only as needed, but also from the teaching of Yesilogluz. Yesilogluz teaches administration of tamoxifen alone for treating bipolar I disorder, and in this regard, Ahmad teaches that endoxifen citrate is superior to and has a four-fold higher potency over tamoxifen in treating bipolar I disorder. Accordingly, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to choose to administer only endoxifen composition of Ahmad, without any other medication such as benzodiazepines, with an expectation to provide the therapeutically effective concentration of endoxifen even in the absence of a rescue medication and thus provide effective treatment of Bipolar I disorder.

Furthermore, while applicants argue that Ahmad requires adjunct medications along with endoxifen citrate treatment in order to treat BPD, applicants have not provided any data to show that the claimed endoxifen citrate alone provides a superior and unexpected effect in maintaining therapeutically effective concentration as well as provide an effective treatment of Bipolar I disorder. Whereas, one of an ordinary skill in the art would have reasonably expected that endoxifen citrate composition of Ahmad (in view of Yesilogluz), would provide the same or much higher efficacy than tamoxifen, without any rescue medications such as benzodiazepine.

Double Patenting rejections:

Applicants argue that Double patenting rejections over claims of US 10376479 in view of Ahmad et al., and Ali et al; and over the claims of US 11672758 in view of

Ahmad et al should be withdrawn because Ali and Ahmad do not teach the new limitation "that the method does not include a rescue medication". However, the present rejections do not rely on the teachings of Ali and instead both patented claim sets ('479 patent and '758 patent) are now rejected further in view of Ahmad et al and WO 2008/048194 to Yesilogluz. As explained in the rejections above, it would have been obvious for one of an ordinary skill in the art before the effective filing date of the instant invention to employ the oral enteric coated compositions ('479 patent claims or '758 patent claims) comprising enteric coated endoxifen-citrate, alone, in the claimed amounts and administer to treat bipolar disorder because Yesilogluz shows that tamoxifen administration alone is effective for treating bipolar disorder and Ahmad also recognizes that endoxifen is a metabolite of tamoxifen that is four-fold highly potent in inhibiting PKC, the latter being involved and highly implicated in involved in mood disorders (see Introduction section of Ahmad). Ahmad et al teaches the efficacy of enteric coated endoxifen-citrate in claimed amounts, administered for claimed amount of time, for treating manic depression in BPD patients and also shows that the administration when measured on YMRS scale is safe and tolerable suggesting mood stability of the patients. Ahmad suggests administering benzodiazepines only as needed during endoxifen treatment and do not include the same in the study design. Hence, one of an ordinary skill in the art would have been motivated to employ only endoxifen citrate of the patented claims, which has much higher potency than the parent compound (tamoxifen), with an expectation to provide an effective in treating bipolar disorder and also main therapeutically effective plasma concentration without any additional rescue medication because Ahmad the same dosage regimen claimed for

providing endoxifen concentration for up to 21 days. An "obvious to try" rationale may support a conclusion that a claim would have been obvious where one skilled in the art is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. " [A] person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was "obvious to try" might show that it was obvious under § 103." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ____, ____, 82 USPQ2d 1385, 1397 (2007).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKSHMI SARADA CHANNAVAJJALA whose telephone number is (571)272-0591. The examiner can normally be reached Generally M- F 9 AM to 6 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is

available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

CPC - Searched*		
Symbol	Date	Examiner
classification- attached	04/23/2022	LC
classification- attached	03/25/2023	
classification- attached	05/18/2024	

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00402

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

Search Notes		
Search Notes	**Date**	**Examiner**
PE2E search history- all data bases- inventor, classification, text- attached	04/23/2022	LC
google scholar	04/23/2022	LC
PE2E search history- all data bases- inventor, classification, text- attached	11/03/2022	LC
google scholar	11/03/2022	LC
google scholar	03/25/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	03/25/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	10/06/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	05/18/2024	LC
google; google scholar	05/18/2024	LC

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**

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PGR2026-00015
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Web Search History

date, time	web site	search string
5/18/2024 8:40:36 AM	Google Scholar	endoxifen enteric administration
5/18/2024 8:42:21 AM	Google	bipolar disorder
5/18/2024 8:48:16 AM	Google Scholar	endoxifen enteric administration (mania OR maniac OR psychiatric OR bipolar OR suicide OR depression OR suicidal OR mood disorder)
5/18/2024 8:50:58 AM	Google	Ahmad A, Sheikh S, Shah T, et al Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of Endoxifen. Clinical and Translational Science. 2016 01 Oct;9(5):252–9. doi: http://dx .doi.org/10.1111/cts.12407. PMID: 27346789 PMID/611114504 Embase. [PMC free article] [PubMed] [Reference list]
5/18/2024 9:40:53 AM	Google Scholar	Omar Troubles in the therapeutic relationship J. Clin psych 2000
5/18/2024 9:43:25 AM	Google Scholar	Omar J. Clin psych 2000
5/18/2024 9:51:19 AM	Google Scholar	endoxifen enteric administration (mania OR maniac OR psychiatric OR bipolar OR suicide OR depression OR suicidal OR mood)

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00404

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	26	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(US-PGPUB; USPAT)	OR	ON	ON	2024/05/18 08:20 AM
L2	139	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:20 AM
L3	20	(L1 OR L2) AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:22 AM
L4	15	(L1 OR L2) AND (A61K31/138).cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:23 AM
L5	1	17/226651	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:29 AM
L6	1	17/226703	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:29 AM
L7	78	endoxifen AND tablet AND enteric ADJ coat$5	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:40 AM
L8	3	"20190231687"	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 10:15 AM
L9	2	"20190231687" AND bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 10:15 AM
L10	0	17/226651 AND rescue	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:37 PM
L11	1	17/226671 AND rescue	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:37 PM
L12	7014	A61K31/138.cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:45 PM
L13	126	A61K31/138.cpc. AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:45 PM

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L14	27	A61K31/138.cpc. AND endoxifen AND (A61K9/06,08,20).cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:45 PM
L15	16	A61K31/138.cpc. AND endoxifen AND (A61K9/06,08,20,28,0053).cpc. AND (A61P25/18).cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:46 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

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TO: mhmpto@mcandrews-ip.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - e-Postcard Notification for Customer Number 23446

Wed May 29 10:06:40 EDT 2024

Dear Patent Center Customer:

Correspondence Address:

MCANDREWS HELD &MALLOY, LTD
500 WEST MADISON STREET
SUITE 3400
CHICAGO,ILLINOIS,60661
UNITED STATES

An email notification regarding the correspondence was sent to the following email address(es) associated with customer number 23446:

mhmpto@mcandrews-ip.com

This is a courtesy reminder that new correspondence is available for the application. If you have not done so already, please review the correspondence listed below. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

Application	Document	Mailroom Date	Attorney Docket No.
17226671	CTNF	05/22/2024	20110.0024USU1

To view your correspondence online, please sign in to Patent Center and then select Workbench/View correspondence. Or to update your email addresses, select Manage/Manage customer numbers.

If you have any questions, please contact the Patent Electronic Business Center (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team

UNITED STATES PATENT AND TRADEMARK OFFICE
Attorney Docket No. 67906US01

First Named Inventor:	Ateeq AHMAD
Application No.:	17/226,671
Filing Date:	April 9, 2021
Confirmation No.:	1772
Examiner Name:	LAKSHMI SARADA CHANNAVAJJALA
Group Art Unit:	1611
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

ELECTRONICALLY FILED:

August 22, 2024

RESPONSE TO NON-FINAL OFFICE ACTION OF MAY 22, 2024

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

Dear Examiner:

In response to the Non-Final Office Action mailed May 22, 2024, in the above-identified application, please enter the following amendments and consider the following remarks.

Amendments to the Claims begin on page 2 of this document.

Remarks begin on page 3 of this document.

CLAIMS

1. (Previously Presented) A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days,

wherein the method does not include a rescue medication for the treatment of the bipolar I disorder.

2. (Original) The method of claim 1, wherein the patient has manic episodes with mixed features.

3. (Original) The method of claim 1, wherein the patient has manic episodes without mixed features.

4. (Original) The method of claim 1, wherein the patient has depression.

5. (Previously Presented) The method of claim 1, wherein the patient has depressive episodes.

6. (New) A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days; and

monitoring the dose administered to the patient no sooner than 21 days after commencement of the administering to the patient;

wherein the method does not include a rescue medication for the treatment of the bipolar I disorder.

7. (New) The method of claim 6, wherein the patient has manic episodes with mixed features.

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8. (New) The method of claim 6, wherein the patient has manic episodes without mixed features.

9. (New) The method of claim 6, wherein the patient has depression.

10. (New) The method of claim 6, wherein the patient has depressive episodes.

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REMARKS

Claims 1-5 are pending in this application. The applicant has carefully considered the Office Action dated May 22, 2024. Claims 6-10 are newly added. No new matter has been added. Reconsideration and allowance of the subject application are respectfully requested.

THE REJECTIONS UNDER 35 U.S.C. §103

Claims 1-5 are rejected under 35 U.S.C. 103 as being unpatentable over Ahmad et al (2016, cited on IDS) in view of WO 2008/048194 to Yesilogluj[1] (cited on IDS dated 8/1/21). Applicant disagrees and traverses these rejections.

Claim 1 was previously amended to recite "[a] method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder...**wherein the method does not include a rescue medication** for the treatment of the bipolar I disorder." The Examiner asserts that "[t]he motivation to employ endoxifen citrate of Ahmad alone without any additional mood disorder or mania treating compounds (such as benzodiazepine or lithium or valproate) comes not only from the teaching of Ahmad that adjunct medication is employed only as needed, but also from the teaching of Yesilogluz." Office Action at 12. For the reasons set forth below, Applicant respectfully disagrees.

As an initial matter, the Application states that "[t]he term 'rescue medication' refers to an additional medication necessary to treat breakthrough or recurring symptoms." Application at [0020]. Thus, the term "rescue medication" is defined by the specification,

[1] The Examiner refers to WO 2008/048194 as "Yesilogluz." Applicant respectfully submits that the named inventor of WO 2008/048194 is "Yesilogluj." Applicant refers to this reference as Yesilogluj in this Response.

Atossa Therapeutics, Inc. Exhibit 1002
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and would be understood by a person of ordinary skill in the art, to be a medication that is not to be taken on a scheduled basis, but rather is administered as needed to treat breakthrough or recurring symptoms.

Ahmad does not provide any motivation to use endoxifen alone without a rescue medication. In describing the methods employed for its study, Ahmad includes a section titled "Concomitant medications" and states that "[a]ll psychotropic medications **except benzodiazepines** (lorazepam/diazepam only) were discontinued at least 2 days before randomization." Ahmad at 254. The Application explicitly defines benzodiazepines as rescue medications. *See* Application at [0020] ("For the present disclosure, the rescue medications are selected from the group of lithium, valproate, lamotrigine, benzodiazepines, anticholinergics and like thereof.") Thus, Ahmad does not teach a method that "does not include a rescue medication" as required by claim 1. To the contrary, Ahmad explicitly teaches that while certain medications were discontinued, benzodiazepines (i.e., rescue medications) were not discontinued.

The Examiner asserts that "Ahmad suggests one can include benzodiazepines only as needed and therefore it is not necessary to administer benzodiazepines during the administration of endoxifen." Office Action at 5. Applicant respectfully submits that an "as needed" medication is the very definition of a "rescue medication." As discussed above, the Application defines a "rescue medication" as a medication to be used on an as needed basis to treat breakthrough or recurring symptoms. *See* Application at [0020]. This is the exact same purpose that Ahmad teaches benzodiazepines should be employed. More specifically, Ahmad teaches that "[t]he usage of two benzodiazepines was permitted to reduce undue excitement by using these adjuvants in an appropriate

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manner." *Id.* Therefore, a person of ordinary skill in the art would be motivated by Ahmad to include a rescue medication as part of treatment as needed to treat breakthrough symptoms (e.g., undue excitement), not to exclude a rescue medication as required by claim 1.

Yesilogluj fails to cure these deficiencies of Ahmad. The Examiner states that "the tamoxifen treated group of patients in Yesilogluz does not require any additional antimanic or antidepressants compounds such as lithium or valproate, which are also implicated as standard treatments for bipolar disorder." Office Action at 6. However, like Ahmad, Yesilogluj specifically teaches the use of rescue medications (i.e., benzodiazepines) as a part of its treatment protocol. In particular, Yesilogluj states that "[a]ll psychotropic medication therapy (**except benzodiazepines**) are tapered during the screening period and 15 discontinued at least 1 day before randomization." Yesilogluj at 6:13-15. Thus, Yesilogluj teaches that while certain medications should be tapered, benzodiazepines (i.e., rescue medications) should not. Further, as the Examiner recognizes, Yesilogluj does not teach the use of endoxifen. Rather, Yesilogluj teaches the use of tamoxifen for treating bipolar disorder. As such, a POSA would not be motivated by Yesilogluj's teaching of employing tamoxifen with a rescue medication to employ endoxifen without a rescue medication.

For at least the reasons stated above, Applicant respectfully submits that the Ahmad/Yesilogluj combination does not render claim 1 obvious, nor any of the associated dependent claims. As such, Applicant requests withdrawal of the rejection under Section 103. Additionally, Applicant respectfully submits that newly added claim 6, and its associated dependent claims, are in condition for allowance.

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DOUBLE PATENTING

Claims 1-5 are rejected on the grounds of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 ("479 patent") in view of Ahmad et al (2016, cited on IDS) and WO 2008/048194 to Yesilogluj (cited on IDS dated 8/1/21). Applicant respectfully traverses this rejection. The sole claim of the 479 patent is directed to a method of delivering endoxifen. More specifically, claim 1 of the 479 patent recites "[a] method of delivering endoxifen to the plasma of a subject, comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver endoxifen to the plasma of the subject, wherein: i) said synthetic preparation of endoxifen is at least 80% Z-endoxifen; and ii) said synthetic preparation of endoxifen is in the form of a citrate salt." As the Examiner acknowledges, claim 1 of the 479 patent "[does] not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder" and "also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5." Office Action at 7. Further, claim 1 of the 479 patent does not include or suggest the requirement that "the method does not include a rescue medication for the treatment of the bipolar I disorder." As discussed above in response to the Examiner's rejection under 35 U.S.C. § 103, neither Ahmad nor Yesilogluj would render obvious the limitation that "the method does not include a rescue medication for the treatment of the bipolar I disorder." For at least these reasons, Applicant respectfully requests withdrawal of this rejection.

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Claims 1-5 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over the claims 1-3 of US Patent 11,672,758 ("758 patent") in view of Ahmad et al (2016, cited on IDS) and WO 2008/048194 to Yesilogluz (cited on IDS dated 8/1/21). Applicant respectfully traverses this rejection. Claim 1 of the 758 patent is directed to "[a] method of inhibiting protein kinase C (PKC) in a subject by delivering endoxifen to the plasma of the subject." As the Examiner recognizes, Claims 1-3 of the 758 patent "lack the amounts of endoxifen citrate, for the duration of 21 days, and also lacks instant claims 4-5." Office Action at 10. Additionally, the claims of the 758 patent do not include or suggest the requirement that "the method does not include a rescue medication for the treatment of the bipolar I disorder." *Id.* As discussed above in response to the Examiner's rejection under 35 U.S.C. § 103, neither Ahmad nor Yesilogluj would render obvious the limitation that "the method does not include a rescue medication for the treatment of the bipolar I disorder." For at least these reasons, Applicant respectfully requests withdrawal of this rejection.

CONCLUSION

Various statements made in the Office Action are not relevant and/or are rendered moot by way of this response. Accordingly, these statements are not addressed herein. However, should any of these statements become relevant, the applicant hereby reserves the right to address these statements as appropriate.

The Examiner is encouraged to contact the undersigned attorney to expedite prosecution of this application.

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The Commissioner is hereby authorized to charge any additional fees and/or to charge any fee deficiencies, or to credit any overpayments, to the deposit account of McAndrews, Held & Malloy, Account No. 13-0017.

Date: August 22, 2024

Respectfully submitted,

/Bradley P. Loren/

Bradley P. Loren, Ph.D.
Registration No. 82,885
Attorney for Applicant

McAndrews, Held & Malloy
500 West Madison Street
Suite 3400
Chicago, Illinois 60661
Telephone: (312) 775-8000
Facsimile: (312) 775-8100

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UNITED STATES PATENT AND TRADEMARK OFFICE
Attorney Docket No. 67906US01

First Named Inventor:	Ateeq AHMAD
Application No.:	17/226,671
Filing Date:	April 9, 2021
Confirmation No.:	1772
Examiner Name:	LAKSHMI SARADA CHANNAVAJJALA
Group Art Unit:	1611
Title:	ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

ELECTRONICALLY FILED:

August 22, 2024

RESPONSE TO NON-FINAL OFFICE ACTION OF MAY 22, 2024

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

Dear Examiner:

In response to the Non-Final Office Action mailed May 22, 2024, in the above-identified application, please enter the following amendments and consider the following remarks.

Amendments to the Claims begin on page 2 of this document.

Remarks begin on page 3 of this document.

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administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days,

wherein the method does not include a rescue medication for the treatment of the bipolar I disorder.

2. (Original) The method of claim 1, wherein the patient has manic episodes with mixed features.

3. (Original) The method of claim 1, wherein the patient has manic episodes without mixed features.

4. (Original) The method of claim 1, wherein the patient has depression.

5. (Previously Presented) The method of claim 1, wherein the patient has depressive episodes.

6. (New) A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

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monitoring the dose administered to the patient no sooner than 21 days after commencement of the administering to the patient;

wherein the method does not include a rescue medication for the treatment of the bipolar I disorder.

7. (New) The method of claim 6, wherein the patient has manic episodes with mixed features.

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8. (New) The method of claim 6, wherein the patient has manic episodes without mixed features.

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Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00419

REMARKS

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Atossa Therapeutics, Inc. Exhibit 1002
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and would be understood by a person of ordinary skill in the art, to be a medication that is not to be taken on a scheduled basis, but rather is administered as needed to treat breakthrough or recurring symptoms.

Ahmad does not provide any motivation to use endoxifen alone without a rescue medication. In describing the methods employed for its study, Ahmad includes a section titled "Concomitant medications" and states that "[a]ll psychotropic medications **except benzodiazepines** (lorazepam/diazepam only) were discontinued at least 2 days before randomization." Ahmad at 254. The Application explicitly defines benzodiazepines as rescue medications. *See* Application at [0020] ("For the present disclosure, the rescue medications are selected from the group of lithium, valproate, lamotrigine, benzodiazepines, anticholinergics and like thereof.") Thus, Ahmad does not teach a method that "does not include a rescue medication" as required by claim 1. To the contrary, Ahmad explicitly teaches that while certain medications were discontinued, benzodiazepines (i.e., rescue medications) were not discontinued.

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Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00421

manner." *Id.* Therefore, a person of ordinary skill in the art would be motivated by Ahmad to include a rescue medication as part of treatment as needed to treat breakthrough symptoms (e.g., undue excitement), not to exclude a rescue medication as required by claim 1.

Yesilogluj fails to cure these deficiencies of Ahmad. The Examiner states that "the tamoxifen treated group of patients in Yesilogluz does not require any additional antimanic or antidepressants compounds such as lithium or valproate, which are also implicated as standard treatments for bipolar disorder." Office Action at 6. However, like Ahmad, Yesilogluj specifically teaches the use of rescue medications (i.e., benzodiazepines) as a part of its treatment protocol. In particular, Yesilogluj states that "[a]ll psychotropic medication therapy (**except benzodiazepines**) are tapered during the screening period and 15 discontinued at least 1 day before randomization." Yesilogluj at 6:13-15. Thus, Yesilogluj teaches that while certain medications should be tapered, benzodiazepines (i.e., rescue medications) should not. Further, as the Examiner recognizes, Yesilogluj does not teach the use of endoxifen. Rather, Yesilogluj teaches the use of tamoxifen for treating bipolar disorder. As such, a POSA would not be motivated by Yesilogluj's teaching of employing tamoxifen with a rescue medication to employ endoxifen without a rescue medication.

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DOUBLE PATENTING

Claims 1-5 are rejected on the grounds of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 10,376,479 ("479 patent") in view of Ahmad et al (2016, cited on IDS) and WO 2008/048194 to Yesilogluj (cited on IDS dated 8/1/21). Applicant respectfully traverses this rejection. The sole claim of the 479 patent is directed to a method of delivering endoxifen. More specifically, claim 1 of the 479 patent recites "[a] method of delivering endoxifen to the plasma of a subject, comprising orally administering to the subject an enteric-coated tablet or enteric-coated capsule containing a pharmaceutical composition comprising an amount of a synthetic preparation of endoxifen effective to deliver endoxifen to the plasma of the subject, wherein: i) said synthetic preparation of endoxifen is at least 80% Z-endoxifen; and ii) said synthetic preparation of endoxifen is in the form of a citrate salt." As the Examiner acknowledges, claim 1 of the 479 patent "[does] not recite a method of maintaining a therapeutically effective concentration of endoxifen for treatment with a patient with bipolar I disorder" and "also lack the claimed amounts of endoxifen citrate and the period of administration, as well as claims 2-5." Office Action at 7. Further, claim 1 of the 479 patent does not include or suggest the requirement that "the method does not include a rescue medication for the treatment of the bipolar I disorder." As discussed above in response to the Examiner's rejection under 35 U.S.C. § 103, neither Ahmad nor Yesilogluj would render obvious the limitation that "the method does not include a rescue medication for the treatment of the bipolar I disorder." For at least these reasons, Applicant respectfully requests withdrawal of this rejection.

Atossa Therapeutics, Inc. Exhibit 1002
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Claims 1-5 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over the claims 1-3 of US Patent 11,672,758 ("758 patent") in view of Ahmad et al (2016, cited on IDS) and WO 2008/048194 to Yesilogluz (cited on IDS dated 8/1/21). Applicant respectfully traverses this rejection. Claim 1 of the 758 patent is directed to "[a] method of inhibiting protein kinase C (PKC) in a subject by delivering endoxifen to the plasma of the subject." As the Examiner recognizes, Claims 1-3 of the 758 patent "lack the amounts of endoxifen citrate, for the duration of 21 days, and also lacks instant claims 4-5." Office Action at 10. Additionally, the claims of the 758 patent do not include or suggest the requirement that "the method does not include a rescue medication for the treatment of the bipolar I disorder." *Id.* As discussed above in response to the Examiner's rejection under 35 U.S.C. § 103, neither Ahmad nor Yesilogluj would render obvious the limitation that "the method does not include a rescue medication for the treatment of the bipolar I disorder." For at least these reasons, Applicant respectfully requests withdrawal of this rejection.

CONCLUSION

Various statements made in the Office Action are not relevant and/or are rendered moot by way of this response. Accordingly, these statements are not addressed herein. However, should any of these statements become relevant, the applicant hereby reserves the right to address these statements as appropriate.

The Examiner is encouraged to contact the undersigned attorney to expedite prosecution of this application.

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The Commissioner is hereby authorized to charge any additional fees and/or to charge any fee deficiencies, or to credit any overpayments, to the deposit account of McAndrews, Held & Malloy, Account No. 13-0017.

Respectfully submitted,

Date: August 22, 2024

/Bradley P. Loren/

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Attorney for Applicant

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UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/226,671	08/22/2024 11:23:18 AM Z ET	20110.0024USU1

Title of Invention

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1772	FILED BY	Stacey Smalec
PATENT CENTER #	66883506	FILING DATE	04/09/2021
CUSTOMER #	23446	FIRST NAMED INVENTOR	Ateeq AHMAD
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Bradley Loren

Documents

TOTAL DOCUMENTS: 3

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
67908US01_Response.pdf		9	-	99 KB
67908US01_Response-A....pdf	(1-1)	1	Amendment/Request for Reconsideration-After Non-Final Rejection	69 KB
67908US01_Response-CLM.pdf	(2-3)	2	Claims	70 KB
67908US01_Response-REM.pdf	(4-9)	6	Applicant Arguments/Remarks Made in an Amendment	92 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)

67908US01_Response.pdf	0B0DC1B0EA8F66C2BB33EBC65A893B4130A5FE8479E8819B AE2ECB008E4F0869975E58E3F92CFDDECDEB23AAAF364FC A084F4ACA5A57821F8664BDC583916200
67908US01_Response-A....pdf	F2C8623C3369BFDC4EAABBB3DF7F7B1BCD5D9E028C6D457 99D06FDF4A8378C8C837105DB34998EF76988638948CBA1EE B805C6C667EF144491BE21A43214E543
67908US01_Response-CLM.pdf	D29C47D7B85C0FE11BA651412F2910C58A0E6C19973141682 0D820CCF0F77C88D89BB7F57963EBFA511363582AF70941C3 4F8A91A6D914CD262EDFDEA5A01F3C
67908US01_Response-REM.pdf	A84D5B794DDCDFFFD9769EA1A1E398F16AA151F6FDC947D2 8E9C2DD5D72B6F06D512D855747F888D05850985EDF77E730 6C9C9D28AE9334A71329799DD3B36B1

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 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 17/226,671	Filing Date 04/09/2021	☐ 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 $50 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $240 =	
☐ 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	08/22/2024	(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))	* 10	Minus	** 20	= 0		x $40 =	0
	Independent (37 CFR 1.16(h))	* 2	Minus	*** 3	= 0		x $192 =	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 $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ 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.	Examiner
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/Theresa OKON/
*** 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.	

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
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NOTICE OF ALLOWANCE AND FEE(S) DUE

23446 7590 11/27/2024

MCANDREWS HELD & MALLOY, LTD
500 WEST MADISON STREET
SUITE 3400
CHICAGO, IL 60661

EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1611	

DATE MAILED: 11/27/2024

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	67908US01	1772

TITLE OF INVENTION: ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	02/27/2025

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 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted 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. 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: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00429

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (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 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. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

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

23446 7590 11/27/2024
MCANDREWS HELD & MALLOY, LTD
500 WEST MADISON STREET
SUITE 3400
CHICAGO, IL 60661

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 transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	67908US01	1772

TITLE OF INVENTION: ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	02/27/2025

EXAMINER	ART UNIT	CLASS-SUBCLASS
CHANNAVAJJALA, LAKSHMI SARADA	1611	424-474000

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/AIA/122 or PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or 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 must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). 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. Fees submitted: ❑ Issue Fee ❑ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via the USPTO patent electronic filing system ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

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 (11/23) Approved for use through 03/31/2026 OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00430

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	67908US01	1772

23446 7590 11/27/2024

MCANDREWS HELD & MALLOY, LTD
500 WEST MADISON STREET
SUITE 3400
CHICAGO, IL 60661

EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1611	

DATE MAILED: 11/27/2024

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.

PTOL-85 (Rev. 11/23)

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00431

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 30 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. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/ owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).
https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf

Routine uses of the information in this record may include disclosure to:

1) law enforcement, in the event that the system of records indicates a violation or potential violation of law;

2) a federal, state, local, or international agency, in response to its request;

3) a contractor of the USPTO having need for the information in order to perform a contract;

4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;

5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;

6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;

7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;

8) 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));

9) the Office of Personnel Management (OPM) for personnel research purposes; and

10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Notice of Allowability	Application No. 17/226,671	Applicant(s) AHMAD et al.	
	Examiner LAKSHMI S CHANNAVAJJALA	Art Unit 1611	AIA (FITF) Status Yes

-- 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 8/22/24.
   ☐ 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 1-10 . 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 _____.

/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00433

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Allowable Subject Matter

Claims 1-10 are allowed.

The following is an examiner's statement of reasons for allowance: The closest prior art of record (Ahmad et al) does not teach the instant claimed method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days, "wherein the method does not include a rescue medication for the treatment of the bipolar I disorder". Ahmad et al teaches discontinuing all psychotropic medications, except benzodiazepines (lorazepam/diazepam only) were discontinued at least 2 days before randomization. The method of Ahmad requires administering up to 5 mg/day benzodiazepines as adjunct medication, thus teaching away from the limitation "wherein the method does not include a rescue medication for the treatment of the bipolar I disorder". Whereas, instant specification describes benzodiazepine as a rescue medication that is excluded from the instant method. In this regard, Yesilogluz et al (of record) also teaches that except benzodiazepine all the other psychotropic medications are tapered during the screening period. Related US Patent 11,291,640 ('640 Patent) claims a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising: administering to the patient, a dose in a range from 2 mg to 16 mg of

endoxifen citrate in an enteric coated tablet once per day for up to 21 days. Applicants have filed a terminal disclaimer over US Patent No.11,291,640 ('640 Patent), and further over US copending applications 17/226703 and 17/226651.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKSHMI SARADA CHANNAVAJJALA whose telephone number is (571)272-0591. The examiner can normally be reached Generally M- F 9 AM to 6 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bethany Barham can be reached on 571-272-6175. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-

center for more information about Patent Center and

https://www.uspto.gov/patents/docx for information about filing in DOCX format. For

additional questions, contact the Electronic Business Center (EBC) at 866-217-9197

(toll-free). If you would like assistance from a USPTO Customer Service

Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LAKSHMI S CHANNAVAJJALA/
Primary Examiner, Art Unit 1611

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	**Art Unit**
	LAKSHMI S CHANNAVAJJALA	1611

CPC								
Symbol							**Type**	**Version**
A61K	/	31	/	138			F	2013-01-01
A61P	/	25	/	18			I	2018-01-01
A61K	/	9	/	0053			I	2013-01-01
A61K	/	9	/	28			I	2013-01-01

CPC Combination Sets								
Symbol					**Type**	**Set**	**Ranking**	**Version**
	/		/					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	10	
/LAKSHMI S CHANNAVAJJALA/ Primary Examiner, Art Unit 1611	06 November 2024	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	--

U.S. Patent and Trademark Office

Part of Paper No.: 20241106

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00437

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	**Art Unit**
	LAKSHMI S CHANNAVAJJALA	1611

INTERNATIONAL CLASSIFICATION					
CLAIMED					
A61K	/	9	/	28	
A61K	/	31	/	138	
NON-CLAIMED					
	/		/		

US ORIGINAL CLASSIFICATION	
CLASS	**SUBCLASS**

CROSS REFERENCES(S)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**					

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	10	
/LAKSHMI S CHANNAVAJJALA/ Primary Examiner, Art Unit 1611	06 November 2024	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	--

U.S. Patent and Trademark Office

Part of Paper No.: 20241106

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00438

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	**Art Unit**
	LAKSHMI S CHANNAVAJJALA	1611

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

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	10	
/LAKSHMI S CHANNAVAJJALA/ Primary Examiner, Art Unit 1611	06 November 2024	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	--

U.S. Patent and Trademark Office

Part of Paper No.: 20241106

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

CPC - Searched*		
Symbol	Date	Examiner
classification- attached	04/23/2022	LC
classification- attached	03/25/2023	
classification- attached	05/18/2024	
classification- attached	11/06/2024	

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Atossa Therapeutics, Inc. Exhibit 1002
Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
PGR2026-00015
Page 00440

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/226,671	AHMAD et al.
	Examiner	Art Unit
	LAKSHMI S CHANNAVAJJALA	1611

Search Notes		
Search Notes	**Date**	**Examiner**
PE2E search history- all data bases- inventor, classification, text- attached	04/23/2022	LC
google scholar	04/23/2022	LC
PE2E search history- all data bases- inventor, classification, text- attached	11/03/2022	LC
google scholar	11/03/2022	LC
google scholar	03/25/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	03/25/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	10/06/2023	LC
PE2E search history- all data bases- inventor, classification, text- attached	05/18/2024	LC
google; google scholar	05/18/2024	LC
google; google scholar	11/06/2024	LC
PE2E search history- all data bases- inventor, classification, text- attached	11/06/2024	LC

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
	interference search history print out -attached	11/06/2024	LC

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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	26	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(US-PGPUB; USPAT)	OR	ON	ON	2024/05/18 08:20 AM
L2	139	((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:20 AM
L3	20	(L1 OR L2) AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:22 AM
L4	15	(L1 OR L2) AND (A61K31/138).cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:23 AM
L5	1	17/226651	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:29 AM
L6	1	17/226703	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:29 AM
L7	78	endoxifen AND tablet AND enteric ADJ coat$5	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 08:40 AM
L8	3	"20190231687"	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 10:15 AM
L9	2	"20190231687" AND bipolar	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 10:15 AM
L10	0	17/226651 AND rescue	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:37 PM
L11	1	17/226671 AND rescue	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:37 PM
L12	7014	A61K31/138.cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:45 PM
L13	126	A61K31/138.cpc. AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:45 PM

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Page 00442

L14	27	A61K31/138.cpc. AND endoxifen AND (A61K9/06,08,20).cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:45 PM
L15	16	A61K31/138.cpc. AND endoxifen AND (A61K9/06,08,20,28,0053).cpc. AND (A61P25/18).cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/05/18 02:46 PM
L17	0	("10376479").cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/11/04 11:44 PM
L18	2	("10376479").pn.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/11/04 11:45 PM
L19	19	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM. AND endoxifen	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/05 01:15 PM
L20	20	((((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin")))).INV.) AND endoxifen	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/11/05 01:19 PM
L21	20	(19 OR 20)	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/11/05 01:19 PM
L22	2	wo-2008048194-$.did.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2024/11/05 01:23 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N1	19	((((("AHMAD") near3 ("Ateeq")) OR (("AHMAD") near3 ("Imran")) OR (("AHMAD") near3 ("Moghisuddin")) OR (("ALI") near3 ("Shoukath") near3 ("M")) OR (("SHEIKH") near3 ("Saifuddin")))).INV.) AND endoxifen	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:18 AM

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Page 00443

N2	26	((("JINA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:18 AM
N3	11	A61K31/138.cpc. AND endoxifen AND (A61K9/06,08,20,28,0053).cpc. AND (A61P25/18).cpc.	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:19 AM
N4	91	A61K31/138.cpc. AND endoxifen	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:26 AM
N5	60	A61K31/138.cpc. AND endoxifen AND tablet	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:26 AM
N6	30	A61K31/138.cpc. AND endoxifen AND tablet SAME enteric	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:27 AM
N7	0	A61K31/138.cpc. AND endoxifen AND tablet SAME enteric adj5 coat	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:27 AM
N8	30	A61K31/138.cpc. AND endoxifen AND tablet SAME enteric	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:27 AM
N9	72	endoxifen AND tablet SAME enteric	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:29 AM
N10	72	endoxifen AND tablet SAME enteric SAME tablet	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:30 AM
N11	71	endoxifen AND tablet SAME enteric SAME coat$5	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:30 AM
N12	18	endoxifen AND tablet SAME enteric SAME coat$5 AND bipolar	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:31 AM
N13	18	endoxifen AND tablet SAME enteric SAME coat$5 AND bipolar AND (dose OR mg OR amount)	(US-PGPUB; USPAT)	OR	ON	ON	2024/11/06 08:31 AM

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Intas Pharms Ltd. v. Atossa Therapeutics, Inc.
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Web Search History

date, time	web site	search string
11/15/2024 4:34:31 PM	Google Scholar	endoxifen (valproate OR lithium OR rescue medication OR carbamazepine)
11/15/2024 4:38:31 PM	Google Scholar	endoxifen (atropine OR benztropine OR glycopyrrolate OR scopolamine OR trihexyphenidyl OR diphenhydramine OR clinidium OR flavoxate OR oxybutynin or phenadrinevalproate OR lithium OR rescue medication OR carbamazepine OR lamotrigine OR anticholinergic OR benzodiazepine)
11/15/2024 4:38:44 PM	Google Scholar	endoxifen exclusion (atropine OR benztropine OR glycopyrrolate OR scopolamine OR trihexyphenidyl OR diphenhydramine OR clinidium OR flavoxate OR oxybutynin or phenadrinevalproate OR lithium OR rescue medication OR carbamazepine OR lamotrigine OR anticholinergic OR benzodiazepine)
11/15/2024 4:39:01 PM	Google Scholar	endoxifen discontinue (atropine OR benztropine OR glycopyrrolate OR scopolamine OR trihexyphenidyl OR diphenhydramine OR clinidium OR flavoxate OR oxybutynin or phenadrinevalproate OR lithium OR rescue medication OR carbamazepine OR lamotrigine OR anticholinergic OR benzodiazepine)
11/15/2024 4:39:08 PM	Google Scholar	endoxifen discontinuation (atropine OR benztropine OR glycopyrrolate OR scopolamine OR trihexyphenidyl OR diphenhydramine OR clinidium OR flavoxate OR oxybutynin or phenadrinevalproate OR lithium OR rescue medication OR carbamazepine OR lamotrigine OR anticholinergic OR benzodiazepine)
11/15/2024 4:39:35 PM	Google Scholar	endoxifen discontinuation (atropine OR benztropine OR glycopyrrolate OR scopolamine OR trihexyphenidyl OR diphenhydramine OR clidinium OR flavoxate OR oxybutynin orphenadrine valproate OR lithium OR rescue medication OR carbamazepine OR lamotrigine OR anticholinergic OR benzodiazepine)
11/15/2024 4:39:40 PM	Google Scholar	bipolar endoxifen discontinuation (atropine OR benztropine OR glycopyrrolate OR scopolamine OR trihexyphenidyl OR diphenhydramine OR clidinium OR flavoxate OR oxybutynin orphenadrine valproate OR lithium OR rescue medication OR carbamazepine OR lamotrigine OR anticholinergic OR benzodiazepine)

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Page 00445

Bibliographic Data

Application No: 17/226,671

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☑ No ☐ Met After Allowance

Verified and Acknowledged: /LAKSHMI S CHANNAVAJJALA/ Examiner's Signature

Initials

Title: ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
04/09/2021	424	1611	20110.0024USU1
RULE			

APPLICANTS

Jina Pharmaceuticals, Inc., Libertyville, IL,

INVENTORS

Ateeq AHMAD, Wadsworth, IL, UNITED STATES

Imran AHMAD, Libertyville, IL, UNITED STATES

Moghisuddin AHMAD, Wadsworth, IL, UNITED STATES

Shoukath M ALI, Vernon Hills, IL, UNITED STATES

Saifuddin SHEIKH, Libertyville, IL, UNITED STATES

CONTINUING DATA

This application has PRO of 63008162 04/10/2020

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

04/15/2021

** **SMALL ENTITY** **

STATE OR COUNTRY

UNITED STATES

ADDRESS

MCANDREWS HELD & MALLOY, LTD
500 WEST MADISON STREET
SUITE 3400
CHICAGO, IL 60661
UNITED STATES

FILING FEE RECEIVED

$1,820

Web Search History

date, time	web site	search string
11/5/2024 1:57:09 PM	Google Scholar	endoxifen treatment benzodiazepine
11/6/2024 8:17:16 AM	Google Scholar	endoxifen treatment benzodiazepine (discontinuation OR discontinued OR dioscontinue)
11/6/2024 8:25:09 AM	Google Scholar	endoxifen rescue (discontinuation OR discontinued OR dioscontinue)
11/6/2024 2:32:13 PM	Google Scholar	endoxifen rescue (discontinuation OR discontinued OR discontinue)
11/6/2024 2:47:19 PM	Google Scholar	endoxifen tablet enteric coated

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UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/226,671	**02/07/2025 10:16:38 AM Z ET**	**67908US01**

Title of Invention

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1772	FILED BY	Stacey Smalec
PATENT CENTER #	69091740	AUTHORIZED BY	Bradley Loren
CUSTOMER #	23446	FILING DATE	04/09/2021
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Ateeq AHMAD

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 9661	**E202527A17026207**	**Stacey Smalec**

PRE-AUTHORIZED ACCOUNT

130017

PRE-AUTHORIZED CATEGORY

37 CFR 1.16 (National application filing, search, and examination fees); 37 CFR 1.17 (Patent application and reexamination processing fees); 37 CFR 1.19 (Document supply fees); 37 CFR 1.20 (Post Issuance fees); 37 CFR 1.21 (Miscellaneous fees and charges)

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2501	UTILITY ISSUE FEE	480.00	1	480.00
			TOTAL AMOUNT:	**$480.00**

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 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.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (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 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. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

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

23446 7590 11/27/2024
MCANDREWS HELD & MALLOY, LTD
500 WEST MADISON STREET
SUITE 3400
CHICAGO, IL 60661

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 transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

Bradley P. Loren	(Typed or printed name)
/Bradley P. Loren/	(Signature)
February 7, 2025	(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	67908US01	1772

TITLE OF INVENTION: ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	02/27/2025

EXAMINER	ART UNIT	CLASS-SUBCLASS
CHANNAVAJJALA, LAKSHMI SARADA	1611	424-474000

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/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or 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
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1 McAndrews, Held & Malloy, Ltd.
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3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

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(A) NAME OF ASSIGNEE: Jina Pharmaceuticals, Inc.

(B) RESIDENCE: (CITY and STATE OR COUNTRY): Libertyville, IL

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

4a. Fees submitted: ☒ Issue Fee ☐ Publication Fee (if required)

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

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☐ Applicant asserting small entity status. See 37 CFR 1.27

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☐ Applicant changing to regular undiscounted fee status.

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Authorized Signature /Bradley P. Loren/ Date February 6, 2025

Typed or printed name Bradley P. Loren Registration No. 82,885

PTOL-85 Part B (11/23) Approved for use through 03/31/2026 OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/226,671	**02/07/2025 10:16:38 AM Z ET**	**67908US01**

Title of Invention

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1772	FILED BY	Stacey Smalec
PATENT CENTER #	69091740	FILING DATE	04/09/2021
CUSTOMER #	23446	FIRST NAMED INVENTOR	Ateeq AHMAD
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Bradley Loren

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
67908US01_Issue Fee.pdf	1	Issue Fee Payment (PTO-85B)	98 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
67908US01_Issue Fee.pdf	F978ACFF1892253B22673E9F209E1D412F92A5E558120E4D52 94AC02A637F52D17A49BD2CA3F83D4FB845293F9C3A1006D5 701C2B9AD2FD4666DBA2ED8C76590

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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	03/11/2025	12245997	67908US01	1772

23446 7590 02/19/2025

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ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at https://patentcenter.uspto.gov/. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

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(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.

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INVENTOR(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional inventors):

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APPLICANT(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional applicants):

Jina Pharmaceuticals, Inc., Libertyville, IL;

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United States of America

To Promote the Progress of Science and Useful Arts

The Director

of the United States Patent and Trademark Office has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this United States

Patent

grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America, and if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States of America, products made by that process, for the term set forth in 35 U.S.C. 154(a)(2) or (c)(1), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b). See the Maintenance Fee Notice on the inside of the cover.

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Maintenance Fee Notice

If the application for this patent was filed on or after December 12, 1980, maintenance fees are due three years and six months, seven years and six months, and eleven years and six months after the date of this grant, or within a grace period of six months thereafter upon payment of a surcharge as provided by law. The amount, number and timing of the maintenance fees required may be changed by law or regulation. Unless payment of the applicable maintenance fee is received in the United States Patent and Trademark Office on or before the date the fee is due or within a grace period of six months thereafter, the patent will expire as of the end of such grace period.

Patent Term Notice

If the application for this patent was filed on or after June 8, 1995, the term of this patent begins on the date on which this patent issues and ends twenty years from the filing date of the application or, if the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121, 365(c), or 386(c), twenty years from the filing date of the earliest such application ("the twenty-year term"), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b), and any extension as provided by 35 U.S.C. 154(b) or 156 or any disclaimer under 35 U.S.C. 253.

If this application was filed prior to June 8, 1995, the term of this patent begins on the date on which this patent issues and ends on the later of seventeen years from the date of the grant of this patent or the twenty-year term set forth above for patents resulting from applications filed on or after June 8, 1995, subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b) and any extension as provided by 35 U.S.C. 156 or any disclaimer under 35 U.S.C. 253.

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US012245997B2

(12) **United States Patent**
Ahmad et al.

(10) **Patent No.: US 12,245,997 B2**
(45) **Date of Patent: *Mar. 11, 2025**

(54) **ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER**

(71) Applicant: **Jina Pharmaceuticals, Inc.**, Libertyville, IL (US)

(72) Inventors: **Ateeq Ahmad**, Wadsworth, IL (US); **Imran Ahmad**, Libertyville, IL (US); **Moghisuddin Ahmad**, Wadsworth, IL (US); **Shoukath M Ali**, Vernon Hills, IL (US); **Saifuddin Sheikh**, Libertyville, IL (US)

(73) Assignee: **Jina Pharmaceuticals, Inc.**, Libertyville, IL (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **17/226,671**

(22) Filed: **Apr. 9, 2021**

(65) **Prior Publication Data**

US 2021/0315845 A1 Oct. 14, 2021

Related U.S. Application Data

(60) Provisional application No. 63/008,162, filed on Apr. 10, 2020.

(51) **Int. Cl.**

A61K 9/28	(2006.01)
A61K 9/00	(2006.01)
A61K 31/138	(2006.01)
A61P 25/18	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/138*** (2013.01); ***A61K 9/0053*** (2013.01); ***A61K 9/28*** (2013.01); ***A61P 25/18*** (2018.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

9,333,190	B2	5/2016	Ahmad et al.	
10,376,479	B2 *	8/2019	Ahmad	A61K 9/48
11,291,640	B2 *	4/2022	Ahmad	A61K 9/28
2012/0201908	A1	8/2012	Miller	
2019/0231687	A1	8/2019	Ahmad et al.	

FOREIGN PATENT DOCUMENTS

WO	2008/048194	4/2008
WO	2009/152430	12/2009
WO	2014/141292	9/2014

OTHER PUBLICATIONS

Ahmad, et al., "Endoxifen, a New Treatment Option for Mania: A Double-Blind, Active-Controlled Trial Demonstrates the Antimanic Efficacy of Endoxifen", Clin Transl Sci (2016) 9, 252-259.

Ali, et al., "Endoxifen is a new potent inhibitor of PKC: A potential therapeutic agent for bipolar disorder", Bioorganic & Medicinal Chemistry Letters 20 (2010) 2665-2667.

International Search Report and Written Opinion issued in International Application No. PCT/IB2021/052972, Jul. 15, 2021, 9 pages.

* cited by examiner

Primary Examiner — Lakshmi S Channavajjala

(74) *Attorney, Agent, or Firm* — McAndrews, Held & Malloy, Ltd.

(57) **ABSTRACT**

A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder is provided. The said method includes administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Further, the patient is not required to be administered rescue medication during the administration of the endoxifen citrate.

10 Claims, No Drawings

ENDOXIFEN FOR THE TREATMENT OF BIPOLAR I DISORDER

FIELD OF THE INVENTION

The present disclosure relates to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, wherein the said method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Further, the patient is not required to be administered rescue medication during the administration of the endoxifen citrate.

BACKGROUND OF THE INVENTION

Bipolar disorder is currently a major health problem. Bipolar disorder is a chronic, debilitating illness that affects up to 3% of the US population. It causes significant morbidity and imposes a burden on the society. The causes of bipolar disorder are still unknown, and no agent has been specifically developed on the basis of an understanding of the pathophysiology of the illness or mechanism of action for effective treatments.

Several drugs have been approved for treatment of bipolar disorder, such as lithium, valproate or divalproex sodium, carbamazepine, and atypical antipsychotics for the treatment of acute bipolar mania. While these drugs have provided relief for many individuals with bipolar disorder, significant issues with tolerability, efficacy, and attempt suicide or have suicidal behaviour still remain. Further, there is also a need of rescue medications. Divalproex has a good tolerability but a high discontinuation rate. There is also a continuous need to observe the therapeutic dose monitoring in patients during the treatment. The clinicians, for example, may find themselves in situations in which better tolerated agents are less effective, and vice versa. Also, the adherence to the treatment is affected by adverse effects such as sedation, weight gain, thrombocytopenia, and thyroid disorders.

Available treatments help a substantial proportion of patients, but are not beneficial for an estimated 40-50% of the population.

SUMMARY OF THE INVENTION

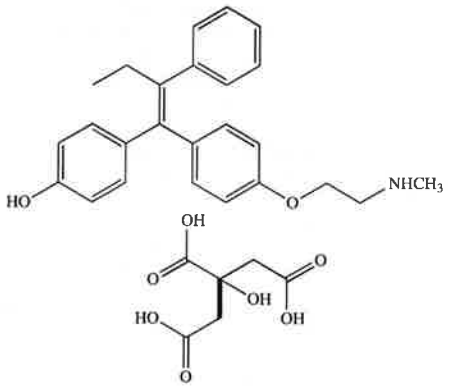
Protein kinase C (PKC) appears to have a role in bipolar disorder. PKC is involved in controlling the function of proteins through the phosphorylation of hydroxyl groups of serine and threonine amino acid residues on these proteins, which are known to play a vital role in cell signalling pathways. It regulates multiple neuronal processes implicated in mood regulation. In current clinical practice, mood stabilizers and antidepressants have been shown to modulate the PKC pathway. Disrupted PKC activity has been found both in post-mortem brains and platelet from patients with mood disorders. Accumulating evidence suggests an imbalance of the PKC signalling system in mood disorders. Thus, PKC is considered as a novel molecular target for the development of innovative medicine for bipolar disorder.

Targeting the PKC signalling pathway for bipolar disorder can improve the patient compliance, when therapeutic dose monitoring is not required in patient, and such treatment can provide significant improvement in mania and depression.

Endoxifen is a non-steroidal selective estrogen receptor modulator (SERM) of the triphenylethylene group. It is an active metabolite of tamoxifen and has been found to be effective in patients that have failed previous hormonal

therapies (tamoxifen, aromatase inhibitors, and fulvestrant). The prodrug tamoxifen is metabolized by the CYP2D6 enzyme to produce afimoxifene (4-hydroxytamoxifen) and endoxifen. The chemical name of endoxifen citrate is (Z)-1-(4-Hydroxyphenyl)-1-{4-[2-(monomethylamino) ethoxy] phenyl}-2-phenyl-1-butene citrate. The empirical formula of endoxifen citrate is $C_{25}H_{27}NO_2$—$C_6H_8O_7$, and has following chemical structure as given below (formula I):

(I)



The exact mechanism by which endoxifen exerts its therapeutic effects have not been established in bipolar disorder. However, the efficacy of endoxifen could be mediated through PKC. The PKC represents a family of enzymes highly enriched in brain, where it plays a major role in regulating both pre- and post-synaptic aspects of neurotransmission. Excessive activation of PKC results in symptoms related to bipolar disorder. The PKC signalling pathway is clearly a target for the actions of two structurally dissimilar antimanic agents—lithium and valproate. Tamoxifen, a widely used breast cancer drug is also known to inhibit PKC and demonstrate antimanic properties in human. Endoxifen exhibited four-fold higher potency compared to tamoxifen in inhibiting the PKC activity and is not dependent on the isozyme cytochrome P450 2D6 (CYP2D6) for action on the target tissues. Endxifen is a PKC inhibitor and is effective in the treatment of bipolar disorder. Further, endoxifen has a broad therapeutic index as compared to divalproex sodium.

An object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient, wherein the patient has manic episodes with or without mixed features.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient, wherein the patient has depression or associated with depressive episodes.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concen-

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tration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days.

Another object of the present disclosure is to provide a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days, wherein the patient does not require rescue medication.

The objects described herein are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Further, the said method as per the present disclosure, wherein the patient does not require rescue medication.

DETAILED DESCRIPTION OF THE INVENTION

All terms as used herein in this application, unless otherwise stated, shall be understood in their ordinary meaning as known in the art. Other more specific definitions for certain terms as used in the present application are as set forth below and are intended to apply uniformly throughout the specification and claims unless an otherwise expressly set out definition provides a broader definition.

For the purposes of the present application, any ranges given include both the lower and the upper end points of the range. Ranges given should be considered approximate, unless specifically stated.

The term "EOT" refers to end of treatment.

The term "therapeutically effective concentration" refers to a concentration of endoxifen in plasma which is sufficient to decrease or prevent or cure the symptoms associated with a medical condition or infirmity or to normalize body functions in disease or disorders that result in impairment of specific bodily functions.

The term "rescue medication" refers to an additional medication necessary to treat breakthrough or recurring symptoms. For present disclosure, the rescue medications are selected from the group of lithium, valproate, lamotrigine, benzodiazepines, anticholinergics and like thereof.

The term "enteric coating" refers to any pharmaceutically acceptable coating preventing the release of the active agent in the stomach and sufficiently disintegrating in the intestine tract (by contact with approximately neutral or alkaline intestine juices) to allow the resorption of the active agent through the walls of the intestinal tract. The enteric coating remains intact in the acidic environment of the stomach and then solubilize in the more alkaline environment of the small intestine. Generally speaking, enteric coating helps in preventing gastric mucosal irritation and can be used for acid labile drugs which gets denatured in acidic medium.

In one embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient, wherein the patient has manic episodes with or without mixed features.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for treatment of bipolar I disorder in a patient, wherein the patient has depression or associated with depressive episodes.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day.

In another embodiment the present application provides a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days.

In another embodiment of the present application is to provide a method for maintaining a therapeutically effective concentration of endoxifen for the treatment of patient with bipolar I disorder, wherein the method comprises administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days, wherein the patient does not require rescue medication.

The embodiments described herein are directed to a method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, wherein the method comprises an administering to the patient, a dose of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days. Further, the said method as per the present disclosure, wherein the patient does not require rescue medication.

The present application has been described by way of example only, and it is to be recognized that modifications thereto falling within the scope, and spirit of appended claims, and which would be obvious to a person skilled in the art based upon the disclosure herein, are also considered to be within the scope of this disclosure.

Clinical Study Data:

Clinical study of an enteric coated tablet comprising endoxifen citrate formulation was carried out by administering to the patient doses of 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for at least 21 days according to the present application.

Design of the Study:

The clinical study was a multicenter, randomized, double-blind, double-dummy, active controlled, parallel study to assess the efficacy and safety of endoxifen enteric coated tablet 8 mg and divalproex sodium extended release tablet 1000 mg in patients of bipolar I disorders.

Total 228 patients were enrolled in the study. All 228 patients were qualified for safety trial.

At the EOT, none of the patient required rescue medications, no rescue medications were administered to any of the patients, and none of the patient discontinue from the study.

The invention claimed is:

1. A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days,

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wherein the method does not include a rescue medication for the treatment of the bipolar I disorder.

2. The method of claim **1**, wherein the patient has manic episodes with mixed features.

3. The method of claim **1**, wherein the patient has manic episodes without mixed features.

4. The method of claim **1**, wherein the patient has depression.

5. The method of claim **1**, wherein the patient has depressive episodes.

6. A method for maintaining a therapeutically effective concentration of endoxifen for treatment of a patient with bipolar I disorder, said method comprising:

administering to the patient, a dose in a range from 2 mg to 16 mg of endoxifen citrate in an enteric coated tablet once per day for up to 21 days; and

monitoring the dose administered to the patient no sooner than 21 days after commencement of the administering to the patient;

wherein the method does not include a rescue medication for the treatment of the bipolar I disorder.

7. The method of claim **6**, wherein the patient has manic episodes with mixed features.

8. The method of claim **6**, wherein the patient has manic episodes without mixed features.

9. The method of claim **6**, wherein the patient has depression.

10. The method of claim **6**, wherein the patient has depressive episodes.

* * * * *

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/226,671	04/09/2021	Ateeq AHMAD	67908US01	1772

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APPLICATION NO.	ISSUE DATE	PATENT NO.
17/226,671	11-Mar-2025	12245997

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