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APPLICATION NUMBER	PATENT NUMBER	GROUP ART UNIT	REQUEST ID
14/849,981	9593066	1672	102656

PAIR Correspondence Address/Fee Address Change

The following fields have been changed to Customer Number 166905 on 01/03/2020 via Private PAIR in view of the certification copied below that authorized the change.

- Correspondence Address

The address for Customer Number 166905 is:
166905
Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

I certify, in accordance with 37 CFR 1.4(d)(4) that I am:

An attorney or Agent of Record registered to practice before the Patent and Trademark Office who has been given power of attorney in this application

Signature:	/Stephen B. Maebius/
Name:	Stephen B. Maebius
Registration Number:	35264



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Table with 5 columns: APPLICATION NO., ISSUE DATE, PATENT NO., ATTORNEY DOCKET NO., CONFIRMATION NO.
Row 1: 14/849,981, 03/14/2017, 9593066, 080618-1581, 6653
Row 2: 22428, 7590, 02/22/2017
Attorney: Foley & Lardner LLP, 3000 K STREET N.W., SUITE 600, WASHINGTON, DC 20007-5109

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

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

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

- Hitesh BATRA, Herndon, VA;
United Therapeutics Corporation, Silver Spring, MD;
Sudersan M. TULADHAR, Silver Spring, MD;
Raju PENMASTA, Herndon, VA;
David A. WALSH, Palmyra, VA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.



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NOTICE OF ALLOWANCE AND FEE(S) DUE

22428 7590 01/30/2017
Foley & Lardner LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

EXAMINER

VALENROD, YEVGENY

ART UNIT PAPER NUMBER

1672

DATE MAILED: 01/30/2017

Table with 5 columns: APPLICATION NO., FILING DATE, FIRST NAMED INVENTOR, ATTORNEY DOCKET NO., CONFIRMATION NO.
14/849,981 09/10/2015 Hitesh BATRA 080618-1581 6653

TITLE OF INVENTION: PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®

Table with 7 columns: APPLN. TYPE, ENTITY STATUS, ISSUE FEE DUE, PUBLICATION FEE DUE, PREV. PAID ISSUE FEE, TOTAL, FEE(S) DUE, DATE DUE
nonprovisional UNDISCOUNTED \$960 50 50 \$960 05/01/2017

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

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

HOW TO REPLY TO THIS NOTICE:

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

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

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

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

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

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

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

PART B - FEE(S) TRANSMITTAL

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

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

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

22428 7590 01/30/2017
Foley & Lardner LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

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

Certificate of Mailing or Transmission

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

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

APPLICATION NO: 14/849,981	FILING DATE 09/10/2015	FIRST NAMED INVENTOR Hitesh BATRA	ATTORNEY DOCKET NO: 080618-1581	CONFIRMATION NO: 6653
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TITLE OF INVENTION: PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®

APPLN. TYPE nonprovisional	ENTITY STATUS UNDISCOUNTED	ISSUE FEE DUE \$960	PUBLICATION FEE DUE \$0	PREV. PAID ISSUE FEE \$0	TOTAL FEE(S) DUE \$960	DATE DUE 05/01/2017
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EXAMINER VALENROD, YEVGENY	ART UNIT 1672	CLASS-SUBCLASS 562-466000
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1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

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

2. For printing on the patent front page, list

- (1) The names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____
- (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. 2 _____
- 3 _____

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

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

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

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

4a. The following fee(s) are submitted:

- Issue Fee
- Publication Fee (No small entity discount permitted)
- Advance Order - # of Copies _____

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- A check is enclosed.
- Payment by credit card. Form PTO-2038 is attached.
- The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

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

- Applicant certifying micro entity status. See 37 CFR 1.29
- Applicant asserting small entity status. See 37 CFR 1.27
- Applicant changing to regular undiscounted fee status.

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.

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.

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. _____



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3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

EXAMINER

VALENROD, YEVGENY

ART UNIT PAPER NUMBER

1672

DATE MAILED: 01/30/2017

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

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

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

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

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

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

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 14/849,981	Applicant(s) BATRA ET AL.	
	Examiner YEVGENY VALENROD	Art Unit 1672	AIA (First Inventor to File) Status No

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

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

1. This communication is responsive to RCE filed on 12/29/16.
 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 1,2 and 4-11. 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. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Examiner's Amendment/Comment |
| 2. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date <u>1/10/17; 12/29/16</u> | 6. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| 3. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 7. <input checked="" type="checkbox"/> Other <u>Continued Examination</u> . |
| 4. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____ | |

/YEVGENY VALENROD/
Primary Examiner, Art Unit 1672

The present application is being examined under the pre-AIA first to invent provisions.

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 12/29/16 has been entered.

Withdrawn rejections

Rejection of claims 1-2 and 4-11 over US patent 8,242,305 and application 14/754,932 is withdrawn in view of the terminal disclaimer filed on 12/29/16.

Conclusion

Claims 1-2 and 4-11 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to YEVGENY VALENROD whose telephone number is (571)272-9049. The examiner can normally be reached on mon-fri 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun G. Sajjadi can be reached on 571-572-3311. The fax phone

Application/Control Number: 14/849,981
Art Unit: 1672

Page 3

number for the organization where this application or proceeding is assigned is 571-273-8300.

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

/YEVGENY VALENROD/
Primary Examiner, Art Unit 1672

Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: <u>DEC 29 2016</u> (use as many sheets as necessary)		Application Number	14/849,981
		Filing Date	9/10/2015
Sheet 1 of 3		First Named Inventor	Hitesh BATRA
		Art Unit	1672
		Examiner Name	Yevgeny Valenrod
		Attorney Docket Number	080618-1581

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	D1	Redacted Petitioner's Reply to Patent Owner's Response to Petition filed on September 27, 2016 in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393, with Exhibits 1022-1028.	
	D2	Petitioner's Demonstratives filed November 28, 2016, in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393	
	D3	Patent Owner Response to Petition filed November 23, 2016, in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393, with Redacted Exhibits 2006, 2020, 2022, 2058 and 2059 filed November 23, 2016, 1151 pages.	
	D4	Patent Owner Demonstratives filed November 23, 2016, in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393, 62 pages.	
	D5	Decision Redacted Institute of <i>Inter Partes</i> Review dated November 23, 2016, in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393, 53 pages.	
	D6	Service copy of Third Party Submission dated October 16, 2016, filed but not entered in US 14/849,981 on October 16, 2016, with 6 indicated attachments, 822 pages.	
	D7	Redacted Defendant Sandoz Inc.'s Invalidity Contentions dated February 5, 2015, <i>United Therapeutics Corporation (Plaintiff) v. Sandoz Inc. (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:14-cv-5499(PGH)(LHG), 90 pages.	
	D8	Defendant Sandoz Inc.'s Invalidity Contention Chartss dated February 5, 2015, <i>United Therapeutics Corporation (Plaintiff) v. Sandoz Inc. (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:14-cv-5499(PGH)(LHG), 189 pages.	

Examiner Signature	Date Considered
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Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: <u>DEC 29 2016</u> (use as many sheets as necessary)		Application Number	14/849,981
		Filing Date	9/10/2015
Sheet 2 of 3		First Named Inventor	Hitesh BATRA
		Art Unit	1672
		Examiner Name	Yevgeny Valenrod
		Attorney Docket Number	080618-1581

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ^a
	D9	Defendant Actavis Laboratories FL, Inc. Preliminary Invalidation Contentions, dated August 30, 2016, <i>United Therapeutics Corporation, and Supernus Pharmaceuticals, Inc., (Plaintiff) v. Actavis Laboratories FL, Inc., (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:16-cv-01816-PGS-LHG, Civil Action No. 3:16-cv-03642-PGS-LHG, 330 pages, (see particularly pages 18-20, 42-62 and 269-280).	
	D10	Exhibit G, Invalidation Claim Chart for the '393 patent, January 12, 2015, 66 pages.	
	D11	Defendant Teva Pharmaceuticals USA, Inc.'s Amended Non-Infringement and Invalidation Contentions, dated April 24, 2015, <i>United Therapeutics Corporation (Plaintiff) v. Teva Pharmaceuticals USA, Inc. (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:14-cv-05498(PGS)(LHG), 94 pages, (see particularly pages 22-54).	
	D12	Arumugan et al., "A New Purification Process for Pharmaceutical and Chemical Industries," Organic Process Research & Development, 2005, 9:319-320.	
	D13	Burk et al., "An Enantioselective Synthesis of (S)-(+)-3-Aminomethyl-5-methylhexanoic Acid via Asymmetric Hydrogenation," J. Org. Chem., 2003, 68:5731-5734.	
	D14	Eliel et al., Stereochemistry of Organic Compounds, 1994, 322-325.	
	D15	Harwood et al., Experimental organic chemistry: Principles and Practice, 1989, 127-134.	
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	D19	Monson, Richard S., Advanced Organic Synthesis, Methods and Techniques, 1971, 178-188.	
	D20	Ohno et al., "Development of Dual-Acting Benzofurans for Thromboxane A2 Receptor Antagonist and Prostacyclin Receptor Agonist: Synthesis, Structure-Activity Relationship, and Evaluation of Benzofuran Derivatives," J. Med. Chem., 2005, 48:5279-5294.	
	D21	Olmsted III et al., Chemistry, The Molecular Science, Mosby-Year Book, Inc., Chapter 10 "Effects of Intermolecular Forces," 1994, 428-486.	
	D22	Pavia et al., Introduction to Organic Laboratory Techniques, First Edition, 1998, 648.	
	D23	Physicians' Desk Reference, 59 Edition, 2005, for Bicillin® L-A (penicillin G benzathine suspension), 5 pages.	
	D24	Priscinzano et al., "Piperidine Analogues of 1-[2-[Bis(4-fluorophenyl)methoxy]ethyl]-4-(3-phenylpropyl)piperazine (GBR 12909): High Affinity Ligands for the Dopamine Transporter," J. Med. Chem., 2002, 45:4371-4374.	

Examiner Signature	Date Considered
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Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: <u>DEC 29 2016</u> (use as many sheets as necessary)		Application Number	14/849,981
		Filing Date	9/10/2015
Sheet 3 of 3		First Named Inventor	Hitesh BATRA
		Art Unit	1672
		Examiner Name	Yevgeny Valenrod
		Attorney Docket Number	080618-1581

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	D25	REMODULIN® label, 2014, 17 pages.	
	D26	Schoffstall, et al., Microscale and Miniscale Organic Chemistry Laboratory Experiments, 2004, 2 nd Ed., 200-202.	
	D27	Sorrell, Thomas N., Organic Chemistry, 1999, 755-758.	
	D28	Wiberg, Laboratory Technique in Organic Chemistry, 1960, 112.	
	D29	Yu et al., "Novel Synthetic Route of a Pivotal Intermediate for the Synthesis of 1β-Methyl Carbapenem Antibiotics," Organic Process Research & Development, 2006,10:829-832.	

Examiner Signature	/YEVGENY VALENROD/	Date Considered	01/25/2017
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Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
		Filing Date	9/10/2015
Date Submitted: <u>JAN 10 2017</u>		First Named Inventor	Hitesh BATRA
(use as many sheets as necessary)		Art Unit	1672
		Examiner Name	Yevgeny Valenrod
Sheet	1	of	1
		Attorney Docket Number	080618-1581

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	E1	Redacted Defendant Watson Laboratories, Inc.'s Invalidation Contentions dated December 11, 2015, <i>United Therapeutics Corporation (Plaintiff) v. Watson Laboratories, Inc. (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:15-cv-05723-PGS-LHG, 35 pages.	

Examiner Signature	/YEVGENY VALENROD/	Date Considered	01/25/2017
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Search Notes 	Application/Control No. 14849981	Applicant(s)/Patent Under Reexamination BATRA ET AL.
	Examiner YEVEGENY VALENROD	Art Unit 1672

CPC- SEARCHED		
Symbol	Date	Examiner
C07C 59/72; 51/08; 51/41; 51/412; 213/08; 405/0075	1/25/2017	YV

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
562/466		1/25/2017	YV

SEARCH NOTES		
Search Notes	Date	Examiner
EAST	1/25/2017	YV
Inventor	1/25/2017	YV
C07C 59/72; 51/08; 51/41; 51/412; 213/08; 405/0075	1/25/2017	YV

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

	/YEVEGENY VALENROD/ Primary Examiner, Art Unit 1672
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EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("8497393").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2017/01/25 16:15
L2	1	("8242305").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2017/01/25 16:15
L3	1	("4683330").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2017/01/25 16:15
L4	1	("4306075").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2017/01/25 16:15
L5	32	((Hitesh) near2 (Batra)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:15
L6	24	((Sudersan) near2 (Tuladhar)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:15
L7	30	((Raju) near2 (Penmasta)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:15
L8	248	((David) near2 (Walsh)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:15
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L14	47	L13 and treprostinil	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:15

EAST Search History (Prior Art)


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L21	1	("9156786").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2017/01/25 16:15
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L25	1034	C07C213/08.cpc.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2017/01/25 16:16

EAST Search History (Prior Art)

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L29	576	L27 and alkylation	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:17
L30	29	L28 and alkylation	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:17
L31	52	L28 and hydrolysis	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:17
L32	21	I31 and I30	US-PGPUB; USPAT; USOCR	OR	ON	2017/01/25 16:17

EAST Search History (Interference)


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Issue Classification 	Application/Control No. 14849981	Applicant(s)/Patent Under Reexamination BATRA ET AL.
	Examiner YEVEGENY VALENROD	Art Unit 1672

CPC						
Symbol					Type	Version
C07C	59	/	72		F	2013-01-01
C07C	51	/	08		I	2013-01-01
C07C	51	/	412		I	2013-01-01
C07C	213	/	08		I	2013-01-01
C07C	51	/	41		I	2013-01-01
A01N	37	/	10		A	2013-01-01
C07C	39	/	12		A	2013-01-01
C07C	39	/	17		A	2013-01-01
C07C	59	/	60		A	2013-01-01
C07C	405	/	0075		I	2013-01-01
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CPC Combination Sets								
Symbol					Type	Set	Ranking	Version
C07C	51	/	08		I	1	1	2013-01-01
C07C	59	/	72		I	1	2	2013-01-01
C07C	51	/	412		I	2	1	2013-01-01
C07C	59	/	72		I	2	2	2013-01-01

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	10	
/YEVEGENY VALENROD/ Primary Examiner, Art Unit 1672	01/25/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

Issue Classification 	Application/Control No. 14849981	Applicant(s)/Patent Under Reexamination BATRA ET AL.
	Examiner YEVEGENY VALENROD	Art Unit 1672

US ORIGINAL CLASSIFICATION					INTERNATIONAL CLASSIFICATION								
CLASS		SUBCLASS			CLAIMED				NON-CLAIMED				
562		466			C	0	7	C	59 / 72 (2006.01.01)				
CROSS REFERENCE(S)					C	0	7	C	51 / 08 (2006.01.01)				
					C	0	7	C	51 / 41 (2006.01.01)				
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				C	0	7	C	213 / 08 (2006.01.01)				

NONE		Total Claims Allowed:	
(Assistant Examiner)		10	
(Date)			
/YEVEGENY VALENROD/ Primary Examiner, Art Unit 1672		O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)		1	none
(Date)			
01/25/2017			

Issue Classification 	Application/Control No. 14849981	Applicant(s)/Patent Under Reexamination BATRA ET AL.
	Examiner YEVEGENY VALENROD	Art Unit 1672

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant		<input type="checkbox"/> CPA		<input checked="" type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47									
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1														
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3	4														
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8	9														
9	10														
10	11														

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	10	
YEVEGENY VALENROD/ Primary Examiner, Art Unit 1672	01/25/2017	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: **Mail** Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

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22428 7590 01/30/2017
Foley & Lardner LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

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.

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

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

APPLICATION NO: 14/849,981	FILING DATE 09/10/2015	FIRST NAMED INVENTOR Hitesh BATRA	ATTORNEY DOCKET NO: 080618-1581	CONFIRMATION NO: 6653
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TITLE OF INVENTION: PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®

APPLN. TYPE nonprovisional	ENTITY STATUS UNDISCOUNTED	ISSUE FEE DUE \$960	PUBLICATION FEE DUE \$0	PREV. PAID ISSUE FEE \$0	TOTAL FEE(S) DUE \$960	DATE DUE 05/01/2017
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EXAMINER VALENROD, YEVGENY	ART UNIT 1672	CLASS-SUBCLASS 562-466000
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1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

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

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

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

United Therapeutics Corporation

Silver Spring, MD

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

4a. The following fee(s) are submitted:

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

- Applicant certifying micro entity status. See 37 CFR 1.29
- Applicant asserting small entity status. See 37 CFR 1.27
- Applicant changing to regular undiscounted fee status.

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.

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.

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 /Stephen B. Maebius/

Date Jan. 30, 2017

Typed or printed name Stephen B. Maebius

Registration No. 35,264

Electronic Patent Application Fee Transmittal

Application Number:	14849981			
Filing Date:	10-Sep-2015			
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®			
First Named Inventor/Applicant Name:	Hitesh BATRA			
Filer:	Stephen Bradford Maebius			
Attorney Docket Number:	080618-1581			
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:				
UTILITY APPL ISSUE FEE	1501	1	960	960

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				960

Electronic Acknowledgement Receipt

EFS ID:	28203111
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh BATRA
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1581
Receipt Date:	30-JAN-2017
Filing Date:	10-SEP-2015
Time Stamp:	14:05:14
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$960
RAM confirmation Number	013117INTEFSW14100600
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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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Information:

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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.

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	14/849,981	BATRA ET AL.	
Document Code - DISQ		Internal Document – DO NOT MAIL	

TERMINAL DISCLAIMER	<input checked="" type="checkbox"/> APPROVED	<input type="checkbox"/> DISAPPROVED
Date Filed : 12/29/16	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:
Lawana Hixon

U.S. Patent and Trademark Office

Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
		Filing Date	9/10/2015
Date Submitted: <u>JAN 10 2017</u>		First Named Inventor	Hitesh BATRA
(use as many sheets as necessary)		Art Unit	1672
Sheet 1 of 1		Examiner Name	Yevgeny Valenrod
		Attorney Docket Number	080618-1581

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	E1	Redacted Defendant Watson Laboratories, Inc.'s Invalidation Contentions dated December 11, 2015, <i>United Therapeutics Corporation (Plaintiff) v. Watson Laboratories, Inc. (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:15-cv-05723-PGS-LHG, 35 pages.	

Examiner Signature	Date Considered
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Electronic Acknowledgement Receipt

EFS ID:	28022515
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh BATRA
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1581
Receipt Date:	10-JAN-2017
Filing Date:	10-SEP-2015
Time Stamp:	14:34:10
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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Multipart Description/PDF files in .zip description					
Document Description			Start	End	
Transmittal Letter			1	2	
Information Disclosure Statement (IDS) Form (SB08)			3	3	
Warnings:					
Information:					
2	Other Reference-Patent/App/Search documents	WatsonInvContRedacted.pdf	352468	no	35
Warnings:					
Information:					
Total Files Size (in bytes):			503210		
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS TO PREPARE
TREPROSTINIL, THE ACTIVE INGREDIENT IN
REMODULIN®
Application No.: 14/849,981
Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation No.: 6653

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

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

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a

competent reference any document submitted herewith. However, in accordance with MPEP § 609.04(a)(I), Applicant hereby states that for items for which the date of publication supplied does not include the month of publication, the year of publication is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the particular month of publication is not in issue.

CONCISE EXPLANATION OF RELEVANCE

An invalidity contention filed against parent U.S. Patent 8,497,393 is filed with this submission. Certain information not related to the '393 patent is redacted.

TIMING OF THE DISCLOSURE

The listed document is being submitted in compliance with 37 CFR §1.97(b), before the mailing of a first Office action after the filing of a RCE.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account Number 19-0741.

Respectfully submitted,

Date Jan. 10, 2017

By /Stephen B. Maebius/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS TO PREPARE
TREPASTINIL, THE ACTIVE INGREDIENT
IN REMODULIN®
Appl. No.: 14/849,981
Appl. Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation Number: 6653

REQUEST FOR CONTINUED EXAMINATION (RCE)
TRANSMITTAL

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

Commissioner:

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application. This RCE and the enclosed items listed below are being filed prior to the earliest of: (1) payment of the issue fee (unless a petition under 37 C.F.R. § 1.313 is granted); (2) abandonment of the application; or (3) the filing of a notice of appeal to the U.S. Court of Appeals for the Federal Circuit under 35 U.S.C. §141, or the commencement of a civil action under 35 U.S.C. §145 or §146 (unless the appeal or civil action is terminated).

1. Submission required under 37 C.F.R. §1.114: (check items that apply)

a. Previously submitted:

- Please enter and consider the amendment and/or reply previously filed on __.
 - Please consider the Affidavit(s)/Declaration(s) previously filed on __ but not considered.
 - Please consider the arguments in the Appeal Brief or Reply previously filed on __.
 - Other Documents.
- b. Enclosed are:
- Amendment/Reply.
 - Terminal Disclaimer.
 - Information Disclosure Statement, Form PTO/SB/08

Miscellaneous:

- Suspension of action of the above-identified application is requested under 37 C.F.R. § 1.103(c) for a period of __ months.

The filing fee is calculated below at the large entity rate:

	Claims as Amended	Previously Paid For	Extra Claims Present	Rate	Fee Totals
RCE Fee 1.17(e):				\$1,200.00	= \$1,200.00
				0	
Total Claims:	9	-	20	= 0	x \$80.00 = \$0.00
Independents	2	-	3	= 0	x \$420.00 = \$0.00
First presentation of any Multiple Dependent Claims:				+ \$780.00	= \$0.00
CLAIMS FEE TOTAL:					= \$1,200.00

Applicant hereby petitions for an extension of time under 37 C.F.R. §1.136(a) for the total number of months checked below:

<input type="checkbox"/>	Extension for response filed within the first month:	\$200.00	0	\$0.00
<input type="checkbox"/>	Extension for response filed within the second month:	\$600.00		\$0.00
<input type="checkbox"/>	Extension for response filed within the third month:	\$1,400.00		\$0.00
<input type="checkbox"/>	Extension for response filed within the fourth month:	\$2,200.00		\$0.00
<input type="checkbox"/>	Extension for response filed within the fifth month:	\$3,000.00		\$0.00
	EXTENSION FEE SUBTOTAL:			\$0.00
	EXTENSION FEE ALREADY PAID: -			\$0.00
	EXTENSION FEE TOTAL			\$0.00
	CLAIMS AND EXTENSION FEE TOTAL:			\$1,200.00
	Prioritized Examination fee (Track I) under 37 C.F.R. § 1.17 (c)			\$0.00
	Processing Fee (Track I) under 37 C.F.R. § 1.17 (i)			\$0.00
	Publication Fee			\$0.00
<input type="checkbox"/>	Suspension of action requested under 37 C.F.R. § 1.103(c)			\$0.00
	TOTAL FEE:			\$1,200.00

The above-identified fees of \$1,200.00 are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date DEC 29 2016

By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS
TO PREPARE
TREPASTINIL, THE
ACTIVE INGREDIENT IN
REMODULIN®
Appl. No.: 14/849,981
Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation Number: 6653

REPLY UNDER 37 C.F.R. § 1.114

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

Commissioner:

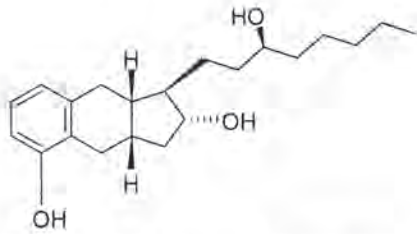
This paper responds to the outstanding Final Office Action mailed on November 30, 2016, and is accompanied by a Request for Continued Examination.

The listing of claims begins on page 2 of this document.

Remarks begin on page 4 of this document.

Listing of Claims:

1. (Previously Presented) A pharmaceutical composition comprising treprostnil or a pharmaceutically acceptable salt thereof, said composition prepared by a process comprising providing a starting batch of treprostnil having one or more impurities resulting from prior alkylation and hydrolysis steps, forming a salt of treprostnil by combining the starting batch and a base, isolating the treprostnil salt, and preparing a pharmaceutical composition comprising treprostnil or a pharmaceutically acceptable salt thereof from the isolated treprostnil salt, whereby a level of one or more impurities found in the starting batch of treprostnil is lower in the pharmaceutical composition, and wherein said alkylation is alkylation of benzindene triol.
2. (Previously Presented) The pharmaceutical composition of claim 1, wherein the salt is isolated in crystalline form.
3. (Canceled).
4. (Previously Presented) The pharmaceutical composition of claim 1, wherein the base is selected from the group consisting of sodium, ammonia, potassium, calcium, ethanolamine, diethanolamine, N-methylglucamine, and choline.
5. (Previously Presented) The pharmaceutical composition of claim 4, wherein the base is diethanolamine.
6. (Previously Presented) The pharmaceutical composition of claim 1, wherein the base is combined with treprostnil that has not been previously isolated.
7. (Previously Presented) The pharmaceutical composition of claim 1, wherein the isolated salt is stored at ambient temperature.
8. (Previously Presented) The pharmaceutical composition of claim 1, which is a pharmaceutical solution.
9. (Previously Presented) A process of preparing a pharmaceutical product comprising treprostnil or a pharmaceutically acceptable salt thereof, comprising alkylating a triol intermediate of the formula:



hydrolyzing the resulting compound to form treprostnil, forming a salt of treprostnil stable at ambient temperature, storing the treprostnil salt at ambient temperature, and preparing a pharmaceutical product from the treprostnil salt after storage, wherein the pharmaceutical product comprises treprostnil or a pharmaceutically acceptable salt thereof.

10. (Previously Presented) A pharmaceutical product prepared by the process of claim 9.

11. (Previously Presented) The process as claimed in claim 9, wherein forming the salt of treprostnil stable at ambient temperature is performed by adding diethanolamine to treprostnil.

REMARKS

Applicants respectfully request reconsideration and allowance of the present application.

Status of Claims

Claims 1, 2, and 4-11 are pending.

Double Patenting

Claims 1, 2, and 4-11 stand rejected as unpatentable on the ground of non-statutory double patenting over claims 24 and 26 of US Patent No. 8,242,305. Claims 1, 2, and 4-11 also stand provisionally rejected as unpatentable on the ground of non-statutory double patenting over claims 1-3 and 8-14 of co-pending Application No. 14/754,932, which was allowed on November 9, 2016. Without acquiescing in the correctness of the rejections, Applicants submit herewith a terminal disclaimer over the '305 patent and the '932 application to obviate the double patenting rejections.

Concluding Remarks

Applicants believe that the application is in condition for allowance. Favorable reconsideration is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance prosecution.

The Commissioner is hereby authorized to charge any additional fees that may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extension fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date DEC 29 2016

By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

TERMINAL DISCLAIMER

Docket Number (Optional)
080618-1581

In re Application of: United Therapeutics Corporation

Application No.: 14/849,981

Filed: 9/10/2015

For: AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®

The applicant, United Therapeutics Corporation, of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration dates of the full statutory term of prior patent No. 8,242,305 as the term of said prior patent is presently shortened by any terminal disclaimer. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent is commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the applicant does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later: expires for failure to pay a maintenance fee; is held unenforceable; is found invalid by a court of competent jurisdiction; is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321; has all claims canceled by a reexamination certificate; is reissued; or is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

And

The applicant, United Therapeutics Corporation, of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on co-pending U.S. Patent Application No. 14/754,932, filed June 30, 2015, as such term is defined in 35 U.S.C. 154 and 173, and as the term of any patent granted on said co-pending application may be shortened by any terminal disclaimer filed prior to the grant of any patent on said co-pending application. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent granted on said co-pending application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

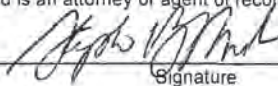
In making the above disclaimer, the applicant does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term as defined in 35 U.S.C. 154 and 173 of any patent granted on said co-pending application, as the term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

Check either box 1 or 2 below, if appropriate.

1. The undersigned is the applicant. If the applicant is an assignee, the undersigned is authorized to act on behalf of the assignee.

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

2. The undersigned is an attorney or agent of record, Reg. No. 35264



Signature

DEC 29 2016
Date

Stephen B. Maebius
Typed or printed name

(202) 672-5574
Telephone Number

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

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.321. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS TO PREPARE
TREPROSTINIL, THE ACTIVE INGREDIENT IN
REMODULIN®
Application No.: 14/849,981
Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation No.: 6653

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

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

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a

competent reference any document submitted herewith. However, in accordance with MPEP § 609.04(a)(I), Applicant hereby states that for items for which the date of publication supplied does not include the month of publication, the year of publication is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the particular month of publication is not in issue.

CONCISE EXPLANATION OF RELEVANCE

Invalidity contentions filed against parent U.S. Patent 8,497,393 (“the ‘393 parent patent”) and prior art mentioned therein are being filed in this submission. With respect to certain invalidity contentions that contain “confidential” designations, those documents were previously designated confidential at one time in the litigation, but they are no longer subject to confidentiality, except where certain information has been redacted.

Recent Patent Owner documents are also being cited herein from the related proceeding IPR2016-00006, *Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)*, Case IPR2016-00006, US Patent 8,497,393, which involves the same ‘393 parent patent of the above-captioned patent application. Although these documents were previously submitted, the versions filed with this Statement are new versions of certain documents filed recently in the IPR that have some information unredacted that was previously redacted in prior versions.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing of a first Office action after the filing of a RCE.

STATEMENT UNDER 37 CFR §1.97(e)

The undersigned hereby states in accordance with 37 CFR §1.97(e)(2) that no item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of the information disclosure statement.

FEE

Fees in the amount of \$180.00 to cover the fee associated with an information disclosure statement are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this submission under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account Number 19-0741.

Respectfully submitted,

Date DEC 29 2016

By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
		Filing Date	9/10/2015
Date Submitted: <u>DEC 29 2016</u>		First Named Inventor	Hitesh BATRA
(use as many sheets as necessary)		Art Unit	1672
		Examiner Name	Yevgeny Valenrod
Sheet	1	of	3
		Attorney Docket Number	080618-1581

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	D1	Redacted Petitioner's Reply to Patent Owner's Response to Petition filed on September 27, 2016 in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393, with Exhibits 1022-1028.	
	D2	Petitioner's Demonstratives filed November 28, 2016, in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393	
	D3	Patent Owner Response to Petition filed November 23, 2016, in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393, with Redacted Exhibits 2006, 2020, 2022, 2058 and 2059 filed November 23, 2016, 1151 pages.	
	D4	Patent Owner Demonstratives filed November 23, 2016, in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393, 62 pages.	
	D5	Decision Redacted Institute of <i>Inter Partes</i> Review dated November 23, 2016, in <i>Steadymed Ltd. (Petitioner), v. United Therapeutics Corporation (Patent Owner)</i> , Case IPR2016-00006, US Patent 8,497,393, 53 pages.	
	D6	Service copy of Third Party Submission dated October 16, 2016, filed but not entered in US 14/849,981 on October 16, 2016, with 6 indicated attachments, 822 pages.	
	D7	Redacted Defendant Sandoz Inc.'s Invalidity Contentions dated February 5, 2015, <i>United Therapeutics Corporation (Plaintiff) v. Sandoz Inc. (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:14-cv-5499(PGH)(LHG), 90 pages.	
	D8	Defendant Sandoz Inc.'s Invalidity Contention Chartss dated February 5, 2015, <i>United Therapeutics Corporation (Plaintiff) v. Sandoz Inc. (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:14-cv-5499(PGH)(LHG), 189 pages.	

Examiner Signature		Date Considered	
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Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
		Filing Date	9/10/2015
Date Submitted: <u>DEC 29 2016</u>		First Named Inventor	Hitesh BATRA
(use as many sheets as necessary)		Art Unit	1672
		Examiner Name	Yevgeny Valenrod
Sheet	2	of	3
		Attorney Docket Number	080618-1581

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ^a
	D9	Defendant Actavis Laboratories FL, Inc. Preliminary Invalidation Contentions, dated August 30, 2016, <i>United Therapeutics Corporation, and Supemus Pharmaceuticals, Inc., (Plaintiff) v. Actavis Laboratories FL, Inc., (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:16-cv-01816-PGS-LHG, Civil Action No. 3:16-cv-03642-PGS-LHG, 330 pages, (see particularly pages 18-20, 42-62 and 269-280).	
	D10	Exhibit G, Invalidation Claim Chart for the '393 patent, January 12, 2015, 66 pages.	
	D11	Defendant Teva Pharmaceuticals USA, Inc.'s Amended Non-Infringement and Invalidation Contentions, dated April 24, 2015, <i>United Therapeutics Corporation (Plaintiff) v. Teva Pharmaceuticals USA, Inc. (Defendant)</i> , In The United States District Court for the District of New Jersey, Civil Action No. 3:14-cv-05498(PGS)(LHG), 94 pages, (see particularly pages 22-54).	
	D12	Arumugan et al., "A New Purification Process for Pharmaceutical and Chemical Industries," Organic Process Research & Development, 2005, 9:319-320.	
	D13	Burk et al., "An Enantioselective Synthesis of (S)-(+)-3-Aminomethyl-5-methylhexanoic Acid via Asymmetric Hydrogenation," J. Org. Chem., 2003, 68:5731-5734.	
	D14	Eliel et al., Stereochemistry of Organic Compounds, 1994, 322-325.	
	D15	Harwood et al., Experimental organic chemistry: Principles and Practice, 1989, 127-134.	
	D16	Jones, Maitland Jr., Organic Chemistry, 2 nd Ed., 2000, 153-155.	
	D17	Lin et al., "Benzindene Prostaglandins. Synthesis of Optically Pure 15-Deoxy-U-68,215 and Its Enantiomer via a Modified Intramolecular Wadsworth-Emmons-Wittig Reaction," J. Org. Chem., 1987, 52:5594-5601.	
	D18	McManus et al., "Tetrazole Analogs of Plant Auxins," J. Org. Chem., 1959, 24:1464-1467.	
	D19	Monson, Richard S., Advanced Organic Synthesis, Methods and Techniques, 1971, 178-188.	
	D20	Ohno et al., "Development of Dual-Acting Benzofurans for Thromboxane A2 Receptor Antagonist and Prostacyclin Receptor Agonist: Synthesis, Structure-Activity Relationship, and Evaluation of Benzofuran Derivatives," J. Med. Chem., 2005, 48:5279-5294.	
	D21	Olmsted III et al., Chemistry, The Molecular Science, Mosby-Year Book, Inc., Chapter 10 "Effects of Intermolecular Forces," 1994, 428-486.	
	D22	Pavia et al., Introduction to Organic Laboratory Techniques, First Edition, 1998, 648.	
	D23	Physicians' Desk Reference, 59 Edition, 2005, for Bicillin® L-A (penicillin G benzathine suspension), 5 pages.	
	D24	Priscinzano et al., "Piperidine Analogues of 1-[2-[Bis(4-fluorophenyl)methoxy]ethyl]-4-(3-phenylpropyl)piperazine (GBR 12909): High Affinity Ligands for the Dopamine Transporter," J. Med. Chem., 2002, 45:4371-4374.	

Examiner Signature		Date Considered	
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Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
Date Submitted: <u>DEC 29 2016</u>		Filing Date	9/10/2015
<i>(use as many sheets as necessary)</i>		First Named Inventor	Hitesh BATRA
Sheet	3	Art Unit	1672
	of	Examiner Name	Yevgeny Valenrod
	3	Attorney Docket Number	080618-1581

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	D25	REMODULIN® label, 2014, 17 pages.	
	D26	Schoffstall, et al., Microscale and Miniscale Organic Chemistry Laboratory Experiments, 2004, 2 nd Ed., 200-202.	
	D27	Sorrell, Thomas N., Organic Chemistry, 1999, 755-758.	
	D28	Wiberg, Laboratory Technique in Organic Chemistry, 1960, 112.	
	D29	Yu et al., "Novel Synthetic Route of a Pivotal Intermediate for the Synthesis of 1 β -Methyl Carbapenem Antibiotics," Organic Process Research & Development, 2006,10:829-832.	

Examiner Signature	Date Considered
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Electronic Patent Application Fee Transmittal

Application Number:	14849981			
Filing Date:	10-Sep-2015			
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®			
First Named Inventor/Applicant Name:	Hitesh BATRA			
Filer:	Stephen Bradford Maebius/Karen Strawderman			
Attorney Docket Number:	080618-1581			
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:				
RCE- 1st Request	1801	1	1200	1200
STATUTORY OR TERMINAL DISCLAIMER	1814	1	160	160
Total in USD (\$)				1360

Electronic Acknowledgement Receipt

EFS ID:	27925600
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh BATRA
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1581
Receipt Date:	29-DEC-2016
Filing Date:	10-SEP-2015
Time Stamp:	12:04:25
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$1360
RAM confirmation Number	122916INTEFSW12062000
Deposit Account	
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

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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)	RCE.pdf	105762	no	4
			e71a0000001d460a1738a9d12bd37c951997		

Warnings:

This is not a USPTO supplied RCE SB30 form.

Information:

2		Amendment.pdf	132577	yes	5
			31676c271166596c5de6a6e832a072a11ccae8f		

Multipart Description/PDF files in .zip description

Document Description	Start	End
Amendment Submitted/Entered with Filing of CPA/RCE	1	1
Claims	2	3
Applicant Arguments/Remarks Made in an Amendment	4	5

Warnings:

Information:

3	Terminal Disclaimer Filed	TerminalDisclaimer.pdf	90939	no	1
			a300c0a896a5e8221f0b7c319d60014007925d		

Warnings:

Information:

4	Other Reference-Patent/App/Search documents	9-27-2016PetitionerReplytoPatentOwnerResponse.pdf	13659957	no	322
			007263441a6ca3c6e002b0705b9979ed57975d4		

Warnings:

Information:

5	Other Reference-Patent/App/Search documents	11-28-2016PetitionerDemonstratives.pdf	12565962	no	82
			714200935726c2f269caedc971e32152af519321		
Warnings:					
The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing					
Information:					
6	Other Reference-Patent/App/Search documents	11-23-2016PatentOwnerResponseandExhibits.pdf	5048622	no	1151
			85f049c2e11a99e2bc14f25f70b687aa6d9061e5		
Warnings:					
Information:					
7	Other Reference-Patent/App/Search documents	11-23-2016PatentOwnerDemonstratives.pdf	11944838	no	62
			039f9a327003270a209608858103141740c10e0e		
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8	Other Reference-Patent/App/Search documents	11-23-2016RedactedDecisiontoInstitute.pdf	2124535	no	53
			d17206c1100807978192430f114800d528e23e1		
Warnings:					
Information:					
9	Other Reference-Patent/App/Search documents	ThirdPtySubmPARTONE.pdf	12222250	no	400
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Warnings:					
Information:					
10	Other Reference-Patent/App/Search documents	ThirdPtySubmPARTTWO.pdf	12521559	no	422
			79f6e6e02329f1ca17c8c72e55d80db25e88a7f		
Warnings:					
Information:					
11	Other Reference-Patent/App/Search documents	SandozInvCont2-5-2015Redacted.pdf	603522	no	90
			e841455c0e110330791a154cc15e0d479c3010eb0		
Warnings:					
Information:					

12	Other Reference-Patent/App/Search documents	SandozInvContCharts2-5-2015.pdf	698449 u03f37ad11c3839e30470258a7507001231f49	no	189
Warnings:					
Information:					
13	Other Reference-Patent/App/Search documents	ActavisPreInvCont8-30-2016.pdf	1806962 f5699aa065c0ada08011c09f46c2f6d783d254	no	330
Warnings:					
Information:					
14	Other Reference-Patent/App/Search documents	Treprostinil_ Ex_G_invalidity_chart_for_the_393_patent_1-12-2015.pdf	304304 6ac080014897a84f5800f175e0d7085711b7ee92	no	66
Warnings:					
Information:					
15	Other Reference-Patent/App/Search documents	TevaInvCont4-24-2015.pdf	567620 955e02f52f11d3002c1a3892a1c070123a09c4	no	94
Warnings:					
Information:					
16	Non Patent Literature	Arumugam.pdf	510030 e37a3975900966a808334a109ba66ad67432170e	no	2
Warnings:					
Information:					
17	Non Patent Literature	Burk.pdf	704672 f808111ed05a39082a82c19d079b3d470b0a71	no	4
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Information:					
18	Non Patent Literature	Eliel.pdf	643300 9a821d0e720bd173fac80907adcae550ab0c0499	no	6
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Information:					

19	Non Patent Literature	Harwood.pdf	904588	no	11
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Information:					
20	Non Patent Literature	Jones.pdf	544757	no	5
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Warnings:					
Information:					
21	Non Patent Literature	Lin.pdf	1300793	no	8
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22	Non Patent Literature	McManus.pdf	745927	no	4
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23	Non Patent Literature	Monson.pdf	787507	no	13
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Information:					
25	Non Patent Literature	Olmsted.pdf	14163672	no	62
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Warnings:					
Information:					
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Information:					
29	Non Patent Literature	Remodulin.pdf	288112	no	17
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Warnings:					
Information:					
30	Non Patent Literature	Schoffstall.pdf	7105291	no	5
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Information:					
31	Non Patent Literature	Sorrell.pdf	560691	no	6
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Warnings:					
Information:					
32	Non Patent Literature	Wiberg.pdf	5760043	no	6
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Warnings:					
Information:					

33	Non Patent Literature	Yu.pdf	689895	no	4
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Warnings:					
Information:					
34		IDS.pdf	375470	yes	6
			d218b0e599f6815c7706326ae51796159629059		
Multipart Description/PDF files in .zip description					
Document Description		Start	End		
Transmittal Letter		1	3		
Information Disclosure Statement (IDS) Form (SB08)		4	6		
Warnings:					
Information:					
35	Fee Worksheet (SB06)	fee-info.pdf	32547	no	2
			80de9552d342020090c28b2a06106277401f5246		
Warnings:					
Information:					
Total Files Size (in bytes):			113982196		
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS TO PREPARE
TREPASTINIL, THE ACTIVE INGREDIENT IN
REMODULIN®
Appl. No.: 14/849,981
Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation Number: 6653

STATEMENT RE IDS CERTIFICATION

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

Commissioner:

In the Information Disclosure Statement Transmittal filed in the above application today, on page 3, a Statement Under 37 CFR 1.97(e)(2) is erroneously included. The documents cited in the IDS were not all recently discovered. However, in view of the RCE which accompanied the IDS, no certification or IDS fee needed to be included and the submission was properly filed in the absence of such certification and fee.

Respectfully submitted,

Date Dec. 29, 2016

By /Stephen B. Maebius/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

Electronic Acknowledgement Receipt

EFS ID:	27929099
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh BATRA
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1581
Receipt Date:	29-DEC-2016
Filing Date:	10-SEP-2015
Time Stamp:	14:32:17
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	StatementrelDSCert.pdf	93590 <small>9c97b0e0a1669f9c26e922641d66a00016631a57</small>	no	1

Warnings:

Information:	
Total Files Size (in bytes):	93590
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>	

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 14/849,981	Filing Date 09/10/2015	<input type="checkbox"/> To be Mailed.
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ENTITY: LARGE SMALL MICRO

APPLICATION AS FILED – PART I

FOR	NUMBER FILED	NUMBER EXTRA	RATE (\$)	FEE (\$)
<input type="checkbox"/> BASIC FEE <small>(37 CFR 1.16(a), (b), or (c))</small>	N/A	N/A	N/A	
<input type="checkbox"/> SEARCH FEE <small>(37 CFR 1.16(k), (l), or (m))</small>	N/A	N/A	N/A	
<input type="checkbox"/> EXAMINATION FEE <small>(37 CFR 1.16(o), (p), or (q))</small>	N/A	N/A	N/A	
TOTAL CLAIMS <small>(37 CFR 1.16(i))</small>	minus 20 =	*	X \$ =	
INDEPENDENT CLAIMS <small>(37 CFR 1.16(f))</small>	minus 3 =	*	X \$ =	
<input type="checkbox"/> APPLICATION SIZE FEE <small>(37 CFR 1.16(s))</small>	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).			
<input type="checkbox"/> MULTIPLE DEPENDENT CLAIM PRESENT <small>(37 CFR 1.16(j))</small>				
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL

APPLICATION AS AMENDED – PART II

	(Column 1)	(Column 2)	(Column 3)	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)
AMENDMENT	12/29/2016	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR			
	Total <small>(37 CFR 1.16(j))</small>	* 11	Minus ** 20	= 0	X \$80 =	0
	Independent <small>(37 CFR 1.16(h))</small>	* 2	Minus *** 3	= 0	X \$420 =	0
	<input type="checkbox"/> Application Size Fee <small>(37 CFR 1.16(s))</small>					
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM <small>(37 CFR 1.16(j))</small>					
					TOTAL ADD'L FEE	0

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

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

SLIE
HELENA PAYTON

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



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UNITED STATES DEPARTMENT OF COMMERCE
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/849,981	09/10/2015	Hitesh BATRA	080618-1581	6653

22428 7890 11/30/2016
Foley & Lardner LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

EXAMINER VALENROD, YEVGENY

ART UNIT 1672	PAPER NUMBER
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NOTIFICATION DATE 11/30/2016	DELIVERY MODE ELECTRONIC
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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):

ipdocketing@foley.com

Office Action Summary	Application No. 14/849,981	Applicant(s) BATRA ET AL.	
	Examiner YEVGENY VALENROD	Art Unit 1672	AIA (First Inventor to File) Status No

-- 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 8/24/16.
 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) 1,2 and 4-11 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) 1,2 and 4-11 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/inlt_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 2/29/16.
- 3) Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 4) Other: _____

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Withdrawn rejections / reasons for allowability

Rejection of claims 1-2, 4-10 under 35USC 103(a) as being unpatentable over Moriarty in view of Phares is withdrawn in view of applicants' arguments. Moriarty fails to teach formation of the salt prior to purification of treprostinil in the process described on page 1902. Moriarty also discloses that the sample of treprostinil obtained is in all respects identical to the authentic sample. In this respects the final product of Moriarty does not have the impurities from alkylation and hydrolysis because its a pure sample.

With respect to the sample prior to chromatography, Moriarty obtains crystals from the free acid of treprostinil. The crystals are also described as pure treprostinil and there is no basis to presume that the described impurities are present in the crystalized sample.

Furthermore, the declarations by Dr Williams and Dr. Ruffolo describe the product of Moriarty to have a different impurity profile from the product the instant claims where salt formation step is present.

Maintained Double Patenting Rejection

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 claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. 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 §§ 706.02(l)(1) - 706.02(l)(3) 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/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 <http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp>.

Claims 1-2 and 4-11 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 24 and 26 of U.S. Patent No. 8,242,305 ('305). Although the claims at issue are not identical, they are not patentably distinct from each other because:

Claim 24 of '305 is directed to a process for the preparation of compound IV (treprostinil). Said method comprises alkylation of benzindene triol to prepare compound (VI) followed by hydrolyzing compound (VI) and contacting the hydrolysis product with a base. In claim 26 the contacting base is diethanolamine.

Claims 1-2 and 4-11 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-3, 8-14, of copending Application No. 14/754,932 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because both the instant claims and claims of '932 are directed to a pharmaceutical product comprising treprostinil diethanolamine and a method of preparing said product via alkylation of benzindene triol, hydrolysis, contacting with a base to form a salt and isolation of the salt.

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

Conclusion

Claims 1-2 and 4-11 are pending

Claims 1-2 and 4-11 are rejected

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 YEVGENY VALENROD whose telephone number is (571)272-9049. The examiner can normally be reached on mon-fri 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun G. Sajjadi can be reached on 571-572-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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

/YEVGENY VALENROD/
Primary Examiner, Art Unit 1672

PTO/SB/08 (modified)

Substitute for form 1449/PTO		<i>Complete if Known</i>	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
Date Submitted: <u>FEB 29 2016</u>		Filing Date	9/10/2015
(use as many sheets as necessary)		First Named Inventor	Hitesh BATRA
Sheet	1	Art Unit	1672
	of	Examiner Name	Yevgeny Valenrod
	1	Attorney Docket Number	080618-1581

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
	C1	2001/0038855	A1	11/08/2001	Desjardin et al.	
	C2	2001/0056095	A1	12/27/2001	Mylari	
	C3	4,434,164	A	02/28/1984	Lombardino	
	C4	5,466,713	A	11/14/1995	Blitstein-Willinger et al.	
	C5	5,506,265	A	04/09/1996	Blitstein-Willinger	
	C6	6,706,283	B1	03/16/2004	Appel et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Country Code ³	Number ⁴ Kind Code ⁵ (if known)			
	C7	WO	98/18452 A1	05/07/1998	Shire Laboratories, Inc.	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	
	C8	BIGHLEY et al., "Salt Forms of Drugs and Absorption," Encyclopedia of Pharmaceutical Technology, Swarbrick et al., Eds., 1995, 13:453-499.	
	C9	SIMONNEAU et al., "Continuous Subcutaneous Infusion of Treprostinil, a Prostacyclin Analogue, in Patients with Pulmonary Arterial Hypertension," Am. J. Respir. Crit. Care Med., 2002, 165:800-804.	

Examiner Signature	/YEVGENY VALENROD/	Date Considered	11/23/2016
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4829-6306-5134.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /Y.V./

EAST Search History (Prior Art)


Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("8497393").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/11/23 18:45
L2	1	("8242305").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/11/23 18:45
L3	1	("4683330").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/11/23 18:45
L4	1	("4306075").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/11/23 18:45
L5	32	((Hitesh) near2 (Batra)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L6	24	((Sudersan) near2 (Tuladhar)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L7	30	((Raju) near2 (Penmasta)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L8	245	((David) near2 (Walsh)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L9	273	L5 or L6 or L7 or L8	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L10	24	L9 and treprostinil	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L11	534	c07c59/72.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L12	870	(562/466).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/11/23 18:45
L13	1277	L11 or L12	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2016/11/23 18:45
L14	44	L13 and treprostinil	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45

EAST Search History (Prior Art)

L15	40	L14 and purity	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L16	37	L15 and HPLC	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/23 18:45
L17	1	("6765117").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/11/23 18:45
L18	2	wo "2005007081"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2016/11/23 18:45
L19	2	"9242350"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2016/11/23 18:45
L20	1	("8242305").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/11/23 18:45
L21	1	("9156786").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/11/23 18:45


EAST Search History (Interference)

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Index of Claims 	Application/Control No. 14849981	Applicant(s)/Patent Under Reexamination BATRA ET AL.
	Examiner YEVEGENY VALENROD	Art Unit 1672

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant		<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47	
CLAIM		DATE					
Final	Original	02/22/2016	11/23/2016				
	1	✓	✓				
	2	✓	✓				
	3	✓	-				
	4	✓	✓				
	5	✓	✓				
	6	✓	✓				
	7	✓	✓				
	8	✓	✓				
	9	✓	✓				
	10	✓	✓				
	11		✓				

Search Notes 	Application/Control No. 14849981	Applicant(s)/Patent Under Reexamination BATRA ET AL.
	Examiner YEVEGENY VALENROD	Art Unit 1672

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES			
Search Notes	Date	Examiner	
EAST	11/23/2016	YV	
Inventor	11/23/2016	YV	

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

	/YEVEGENY VALENROD/ Primary Examiner, Art Unit 1672
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS
TO PREPARE
TREPASTINIL, THE
ACTIVE INGREDIENT IN
REMODULIN®
Appl. No.: 14/849,981
Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation Number: 6653

AMENDMENT AND REQUEST FOR RECONSIDERATION

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

Commissioner:

This amendment is submitted in response to the outstanding, non-final Office Action mailed on February 25, 2016.

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

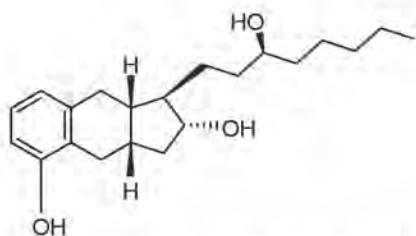
Remarks begin on page 4 of this document.

Amendments to the Claims:

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

Listing of Claims:

1. (Previously Presented) A pharmaceutical composition comprising treprostinil or a pharmaceutically acceptable salt thereof, said composition prepared by a process comprising providing a starting batch of treprostinil having one or more impurities resulting from prior alkylation and hydrolysis steps, forming a salt of treprostinil by combining the starting batch and a base, isolating the treprostinil salt, and preparing a pharmaceutical composition comprising treprostinil or a pharmaceutically acceptable salt thereof from the isolated treprostinil salt, whereby a level of one or more impurities found in the starting batch of treprostinil is lower in the pharmaceutical composition, and wherein said alkylation is alkylation of benzindene triol.
2. (Previously Presented) The pharmaceutical composition of claim 1, wherein the salt is isolated in crystalline form.
3. (Canceled).
4. (Previously Presented) The pharmaceutical composition of claim 1, wherein the base is selected from the group consisting of sodium, ammonia, potassium, calcium, ethanolamine, diethanolamine, N-methylglucamine, and choline.
5. (Previously Presented) The pharmaceutical composition of claim 4, wherein the base is diethanolamine.
6. (Previously Presented) The pharmaceutical composition of claim 1, wherein the base is combined with treprostinil that has not been previously isolated.
7. (Previously Presented) The pharmaceutical composition of claim 1, wherein the isolated salt is stored at ambient temperature.
8. (Previously Presented) The pharmaceutical composition of claim 1, which is a pharmaceutical solution.
9. (Previously Presented) A process of preparing a pharmaceutical product comprising treprostinil or a pharmaceutically acceptable salt thereof, comprising alkylating a triol intermediate of the formula:



hydrolyzing the resulting compound to form treprostinil, forming a salt of treprostinil stable at ambient temperature, storing the treprostinil salt at ambient temperature, and preparing a pharmaceutical product from the treprostinil salt after storage, wherein the pharmaceutical product comprises treprostinil or a pharmaceutically acceptable salt thereof.

10. (Previously Presented) A pharmaceutical product prepared by the process of claim 9.
11. (New) The process as claimed in claim 9, wherein forming the salt of treprostinil stable at ambient temperature is performed by adding diethanolamine to treprostinil.

REMARKS

Applicants respectfully request reconsideration and allowance of the present application.

Status of Claims

Applicants have canceled claim 3 and added claim 11 to depend from claim 9. Support for claim 11 can be found in examples 4-6. No new matter has been added.

After the amendment, claims 1, 2, and 4-11 are pending.

35 U.S.C. § 103

Claims 1-3, 6, 8, and 9 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Moriarty (2004) in view of Phares (WO 2005/007081 A2). Applicants respectfully request reconsideration of the rejection.

Applicants filed a notification of related proceedings to bring to the Examiner's attention documents from IPR2016-00006, which involves parent U.S. Patent No. 8,497,393. Certain information is redacted in those documents due to confidentiality. Documents provided in that notification include the Patent Owner's Response and expert declarations from Dr. Williams and Ruffolo. These documents address the subject matter of the '393 patent claims although certain information is relevant to the present claims as explained herein.

Claim 1 recites steps, including "forming a salt", which read on a commercial process used by the assignee of the present application. Prior to the current commercial process, the assignee used a process based on Moriarty 2004. Because the assignee used both processes, the assignee had the opportunity to analyze the resulting pharmaceutical products as reflected in certificates of analysis. In the IPR, Dr. Williams and Dr. Ruffolo used these certificates of analysis to explain that a pharmaceutical batch produced according to a salt formation process as covered by claim 1 is different from the product produced by the process described in Moriarty 2004. Williams Dec. at ¶¶94-99; Ruffolo Dec. at ¶¶66-72. Specifically, the processes result in products having different impurity profiles, and in fact, the pharmaceutical composition of claim 1 has higher average purity. Patent Owner's Response at Section III.C.

The differences are not merely academic, but critical to the successful manufacture of a clinical product. FDA uses both overall purity and levels of individual impurities (“purity specification”) as a basis to regulate the manufacturing of pharmaceuticals. Batches that fall outside of the purity specification cannot be sold or used to treat patients. As noted in the Patent Owner’s IPR Response, the differences between claim 1’s pharmaceutical composition and a product produced according to the process of Moriarty were significant enough to result in FDA’s acceptance of a new purity specification for the commercial product, thus proving that the products are not the same in the eyes of the FDA. Patent Owner’s Response at Section III.C. Furthermore, this change constitutes a “major” change according to the classification system for manufacturing changes used by FDA. Ruffolo Dec. at ¶¶70- 72.

The rejection further cites Phares for showing that it would have been obvious to form a diethanolamine salt using Moriarty’s treprostinil. However, the differences in the resulting products, as explained above, would not have been expected based on the prior art. In particular, it would not have been obvious to use the salt formation step of Phares to decrease amounts of stereoisomer impurities of treprostinil, which are acidic rather than neutral or basic. Williams Dec. at ¶102. When subject to salt-forming conditions, one of ordinary skill in the art would expect that any undesired stereoisomer of treprostinil would be included in the final salt product because the stereoisomer would also be converted to the corresponding salt under such salt-forming conditions. One of ordinary skill in the art would have had no reasonable expectation of success in removing any undesired treprostinil stereoisomer impurities by salt formation.

In addition, FDA’s decision to adopt a new purity specification for the resulting product further establishes unobviousness of the presently claimed invention. Indeed, as noted above, the specification change is classified as a “major” change according to the FDA’s classification system for manufacturing changes. *See Knoll Pharm. Co., Inc. v. Teva. Pharm. USA, Inc.*, 367 F.3d 1381, 1385 (Fed. Cir. 2004) (explaining that while FDA approval is not determinative of nonobviousness, it can be relevant in evaluating the objective indicia of nonobviousness). As noted in Dr. Ruffolo’s Declaration, even small changes in impurity are important to FDA: “Regulatory agencies have also sought to increase levels of purity, and consequently decrease levels of impurities, in order to provide to the maximum extent possible, the highest level of

safety to patients.” Ruffolo Dec. at ¶36. This is due to the fact that even trace amounts of impurities can sometime pose serious health concerns.

Accordingly, withdrawal of the rejection under 35 U.S.C. § 103(a) is requested.

Double Patenting

Claims 1-10 have been rejected for alleged non-statutory double patenting as unpatentable over claims 24 and 26 of US Patent No. 8,242,305. Applicants will address the rejection by filing a terminal disclaimer or other action if still necessary after the PTO’s consideration of the above arguments and confirmation that the present claims are otherwise in condition for allowance.

Concluding Remarks

Applicants believe that the application is in condition for allowance. Favorable reconsideration is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance prosecution.

The Commissioner is hereby authorized to charge any additional fees that may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extension fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Aug. 24, 2016

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

By /Stephen B. Maebius/

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS TO PREPARE
TREPASTINIL, THE ACTIVE INGREDIENT IN
REMODULIN®
Appl. No.: 14/849,981
Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation Number: 6653

PETITION FOR EXTENSION OF TIME

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

Commissioner:

Applicant hereby petitions the Commissioner under 37 C.F.R. §1.136(a) for a three-month extension of time for response in the above-identified application for the period required to make the attached response timely.

The extension fee for response within the third month is \$1,400.00.

The above-identified fees of \$1,400.00 are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Atty. Dkt. No 080618-1581

Respectfully submitted,

Date Aug. 24, 2016

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

By /Stephen B. Maebius/

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

Electronic Patent Application Fee Transmittal

Application Number:	14849981			
Filing Date:	10-Sep-2015			
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®			
First Named Inventor/Applicant Name:	Hitesh BATRA			
Filer:	Stephen Bradford Maebius/Mary Jo Boyce			
Attorney Docket Number:	080618-1581			
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(\$)
Extension - 3 months with \$0 paid	1253	1	1400	1400
Miscellaneous:				
Total in USD (\$)				1400

Electronic Acknowledgement Receipt

EFS ID:	26733306
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh BATRA
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Mary Jo Boyce
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1581
Receipt Date:	24-AUG-2016
Filing Date:	10-SEP-2015
Time Stamp:	13:14:09
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$ 1400
RAM confirmation Number	9977
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	134812 <small>1811174e959e880052830112c0c8d426e706770...</small>	yes	7
Multipart Description/PDF files in .zip description					
Document Description		Start	End		
Amendment/Req. Reconsideration-After Non-Final Reject		1	1		
Claims		2	3		
Applicant Arguments/Remarks Made in an Amendment		4	7		
Warnings:					
Information:					
2	Extension of Time	3EOT.pdf	97084 <small>0d1c21f80fca0e0c079a0e0e094a0e0d1c51760...</small>	no	2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	31318 <small>09ebc20b1c80f15a1409e0a33d49c0cc2d4490776...</small>	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			263214		

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.

Electronic Acknowledgement Receipt

EFS ID:	25046084
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh BATRA
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1581
Receipt Date:	29-FEB-2016
Filing Date:	10-SEP-2015
Time Stamp:	12:30:22
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	NotificationRltdProc.pdf	48752 <small>09791c50cd86430bb8dcd05e0f091a8ae78c92aa</small>	no	2

Warnings:

Information:

2	Miscellaneous Incoming Letter	POPrelRspandExhibits.pdf	21312387 <small>011b4814fe07ac5811115aa0066da702e65d6</small>	no	975
Warnings:					
Information:					
Total Files Size (in bytes):				21361139	
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

Substitute for form 1449/PTO		<i>Complete if Known</i>	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
Date Submitted: <u>FEB 29 2016</u>		Filing Date	9/10/2015
<i>(use as many sheets as necessary)</i>		First Named Inventor	Hitesh BATRA
Sheet	1	Art Unit	1672
	of	Examiner Name	Yevgeny Valenrod
	1	Attorney Docket Number	080618-1581

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	C1	2001/0038855 A1	11/08/2001	Desjardin et al.	
	C2	2001/0056095 A1	12/27/2001	Mylari	
	C3	4,434,164 A	02/28/1984	Lombardino	
	C4	5,466,713 A	11/14/1995	Blitstein-Willinger et al.	
	C5	5,506,265 A	04/09/1996	Blitstein-Willinger	
	C6	6,706,283 B1	03/16/2004	Appel et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				
	C7	WO 98/18452 A1	05/07/1998	Shire Laboratories, Inc.		

NON PATENT LITERATURE DOCUMENTS						
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.				T ⁶
			C8	BIGHLEY et al., "Salt Forms of Drugs and Absorption," Encyclopedia of Pharmaceutical Technology, Swarbrick et al., Eds., 1995, 13:453-499.		
	C9	SIMONNEAU et al., "Continuous Subcutaneous Infusion of Treprostinil, a Prostacyclin Analogue, in Patients with Pulmonary Arterial Hypertension," Am. J. Respir. Crit. Care Med., 2002, 165:800-804.				

Examiner Signature		Date Considered	
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Electronic Patent Application Fee Transmittal

Application Number:	14849981			
Filing Date:	10-Sep-2015			
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®			
First Named Inventor/Applicant Name:	Hitesh BATRA			
Filer:	Stephen Bradford Maebius/Karen Strawderman			
Attorney Docket Number:	080618-1581			
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:				
Submission-Information Disclosure Stmt	1806	1	180	180
Total in USD (\$)				180

Electronic Acknowledgement Receipt

EFS ID:	25050552
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh BATRA
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1581
Receipt Date:	29-FEB-2016
Filing Date:	10-SEP-2015
Time Stamp:	15:15:15
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$ 180
RAM confirmation Number	1953
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		IDS.pdf	173823 b9f041a9eb3762f8e0b3e1d3538b79887f662995	yes	3
Multipart Description/PDF files in .zip description					
	Document Description	Start	End		
	Transmittal Letter	1	2		
	Information Disclosure Statement (IDS) Form (SB08)	3	3		
Warnings:					
Information:					
2	Non Patent Literature	Bighley.pdf	2623108 a302f717f8f8f6211dc35e0a204mdac2ra97ce09	no	49
Warnings:					
Information:					
3	Non Patent Literature	Simonneau.pdf	87871 2515a0b30744603b7d0f5f17d1b13c94c58934171	no	5
Warnings:					
Information:					
4	Foreign Reference	WO9818452.pdf	1072536 610f0e0c01082978a03911d0a0d852c8a89707	no	32
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	31018 A40ee481a2960c6630166146643700521e040910	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			3988356		

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS TO PREPARE
TREPROSTINIL, THE ACTIVE INGREDIENT IN
REMODULIN®
Application No.: 14/849,981
Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation No.: 6653

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

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

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a

competent reference any document submitted herewith. However, in accordance with MPEP § 609.04(a)(1), Applicant hereby states that for items for which the date of publication supplied does not include the month of publication, the year of publication is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the particular month of publication is not in issue.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(c), before the mailing date of any of a final action under 37 CFR §1.113, a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application.

FEE

Fees in the amount of \$180.00 to cover the fee associated with an information disclosure statement are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this submission under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account Number 19-0741.

Respectfully submitted,

Date Feb. 29, 2016

By /Stephen B. Maebius/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264



UNITED STATES PATENT AND TRADEMARK OFFICE

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Table with 5 columns: APPLICATION NO., FILING DATE, FIRST NAMED INVENTOR, ATTORNEY DOCKET NO., CONFIRMATION NO. Includes fields for EXAMINER (VALENROD, YEVGENY), ART UNIT (1672), and DELIVERY MODE (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):

ipdocketing@foley.com

Office Action Summary	Application No. 14/849,981	Applicant(s) BATRA ET AL.	
	Examiner YEVGENY VALENROD	Art Unit 1672	AIA (First Inventor to File) Status No

-- 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 9/10/15.
 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) 1-10 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) 1-10 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/inft_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 9/10/15; 10/13/15
- 3) Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 4) Other: _____

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Claim Rejections - 35 USC § 103

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.

The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under pre-AIA 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of pre-AIA 35 U.S.C. 103(c) and potential pre-AIA 35 U.S.C. 102(e), (f) or (g) prior art under pre-AIA 35 U.S.C. 103(a).

Claims 1-10 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Moriarty et al (Journal of Organic Chemistry, 2004, 69, 1890-1902) in view of Phares et al (WO 2005/007081 A2).

Scope of prior art

Moriarty et al disclose a method for preparing treprostinil. Said method comprises the steps of: (a) alkylation of benzindene triol and (b) hydrolysis of the product of step (a) (page 1895, Scheme 4, compounds **34** to **35** to **7**; page 1902 preparation of compounds **35** and **7**). 441g of treprostinil (compound **7**) was prepared at 99.7% purity.

Ascertaining the difference

Moriarty fails to teach preparation of a diethanolamine salt of treprostinil.

Moriarty also fails to teach preparation of a pharmaceutical product comprising diethanolamine salt.

Secondary reference

Phares et al teach preparation of treprostinil diethanolamine by dissolving treprostinil acid and treating it with diethanolamine (page 22). Phares further discloses two polymorphs of treprostinil diethanolamine (page 85) and discloses stability via their moisture sorption/desorption data (figure 22).

Obviousness

One skilled in the art practicing the invention of Phares would have found it obvious to prepare a diethanolamine salt of treprostinil prepared by the method of Moriarty. Moriarty discloses a method for preparing a treprostinil acid which is a needed starting material for the process of Phares. The resulting salt would meet the limitations directed to pharmaceutical product because treprostinil diethanolamine is the sole claimed component of the claimed pharmaceutical product.

One skilled in the art would have found it obvious to prepare a pharmaceutical product from the treprostinil diethanolamine salt of Phares prepared from the treprostinil free acid that has been obtained by the process of Moriarty. One would also find it obvious to store the treprostinil diethanolamine salt prior to preparation of a pharmaceutical composition. On page 88 Phares describes minimal weight loss at 5%RH. One would simply store the product in an anhydrous environment to avoid loss of product.

Regarding the limitation directed to the level of impurities before and after formation of the diethanol amine salt from the starting batch of treprostinil: Phares meets the limitations directed to the method of preparing the diethanolamine salt of treprostinil. Phares teaches combining treprostinil with diethanol amine to form a salt and further obtains two different polymorphs of treprostinil via crystallization (page 85). Since the instantly claimed method is directed to the same sequence of steps the amount of impurities in the treprostinil diethanolamine is inherently lower than it was in the starting batch of treprostinil.

Regarding claim 8, directed to the claimed pharmaceutical composition being in solution. On page 58, Phares teaches a dosing solution comprising Treprostinil diethanolamine.

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 claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. 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 §§ 706.02(l)(1) - 706.02(l)(3) 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/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 <http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-l.jsp>.

Claims 1-10 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 24 and 26 of U.S. Patent No. 8,242,305 ('305). Although the claims at issue are not identical, they are not patentably distinct from each other because:

Claim 24 of '305 is directed to a process for the preparation of compound IV (treprostinil). Said method comprises alkylation of benzindene triol to prepare compound (VI) followed by hydrolyzing compound (VI) and contacting the hydrolysis product with a base. In claim 26 the contacting base is diethanolamine.

Claims 1-10 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-3, 8-14, of copending Application No. 14/754,932 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because both the instant claims and claims of '932 are directed to a pharmaceutical product comprising treprostinil diethanolamine and a method of preparing said product via alkylation of benzindene triol, hydrolysis, contacting with a base to form a salt and isolation of the salt.

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

Conclusion

Claims 1-10 are pending

Claims 1-10 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to YEVGENY VALENROD whose telephone number is (571)272-9049. The examiner can normally be reached on mon-fri 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun G. Sajjadi can be reached on 571-572-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number: 14/849,981
Art Unit: 1672

Page 8

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

/YEVGENY VALENROD/
Primary Examiner, Art Unit 1672

Notice of References Cited	Application/Control No. 14/849,981	Applicant(s)/Patent Under Reexamination BATRA ET AL.	
	Examiner YEVGENY VALENROD	Art Unit 1672	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-8,242,305 B2	08-2012	Batra; Hitesh	C07C51/08	562/466
	B	US-				
	C	US-				
	D	US-				
	E	US-				
	F	US-				
	G	US-				
	H	US-				
	I	US-				
	J	US-				
	K	US-				
	L	US-				
	M	US-				

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.

Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	Unassigned
		Filing Date	Herewith
		First Named Inventor	Hitesh BATRA
		Art Unit	Unassigned
		Examiner Name	Unassigned
		Attorney Docket Number	080618-1581
<i>(use as many sheets as necessary)</i>			
Sheet	1	of	4

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	A1	2002/0173672 A1	11/21/2002	Moriarty et al.	
	A2	2004/0176645 A1	09/09/2004	Moriarty et al.	
	A3	2005/0085540 A1	04/21/2005	Phares et al.	
	A4	2005/0101608 A1	05/12/2005	Santel, Donald J.	
	A5	2005/0165111 A1	07/28/2005	Wade et al.	
	A6	2005/0282903 A1	12/22/2005	Wade et al.	
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	A13	2009/0036465 A1	02/05/2009	Roscigno et al.	
	A14	2009/0163738 A1	06/25/2009	Batra et al.	
	A15	4,306,075 A	12/15/1981	Aristoff, Paul A.	
	A16	4,306,076	12/15/1981	Nelson	
	A17	4,424,376 A	01/03/1984	Moniot et al.	
	A18	4,463,183 A	07/31/1984	Haslanger, Martin F.	
	A19	4,486,598 A	12/04/1984	Aristoff, Paul A.	
	A20	4,544,764 A	10/01/1985	Aristoff, Paul A.	
	A21	4,668,814	05/26/1987	Aristoff	
	A22	4,668,814 A	05/26/1987	Aristoff, Paul A.	
	A23	4,683,330 A	07/28/1987	Aristoff, Paul A.	
	A24	5,153,222 A	10/06/1992	Tadepalli et al.	
	A25	6,054,486 A	04/25/2000	Crow et al.	
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		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
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	A38	CN 101891596 A	11/24/2010	Shanghai Techwell Biopharmaceutical Co. Ltd.		A ✓
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Examiner Signature	Date Considered
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Complete if Known	
				Application Number	Unassigned
<i>(use as many sheets as necessary)</i>				Filing Date	Herewith
				First Named Inventor	Hitesh BATRA
				Art Unit	Unassigned
				Examiner Name	Unassigned
Sheet	2	of	4	Attorney Docket Number	080618-1581

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ² Number ³ Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
	A42	EP 0 159 784 B1	06/07/1989	The Upjohn Company		
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	A53	WO 2009/117095 A1	09/24/2009	Arena Pharmaceuticals, Inc.		
	A54	WO 2012/009816 A1	01/26/2012	Alphora Research Inc.		

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
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Examiner Signature	Date Considered
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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /YV/

PTO/SB/08 (modified)

Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	Unassigned
		Filing Date	Herewith
		First Named Inventor	Hitesh BATRA
		Art Unit	Unassigned
		Examiner Name	Unassigned
		Attorney Docket Number	080618-1581
(use as many sheets as necessary)			
Sheet	3	of	4

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	A64	HARDINGER et al., "Triply-Convergent Syntheses of Two Homochiral Arene-Fused Prostacyclin Analogs Related to U68,215," Bioorganic & Medicinal Chemistry Letters, 1991, 1(1):79-82.	
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Examiner Signature	Date Considered
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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /YV/

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		Application Number	Unassigned
<i>(use as many sheets as necessary)</i>		Filing Date	Herewith
		First Named Inventor	Hitesh BATRA
		Art Unit	Unassigned
		Examiner Name	Unassigned
Sheet	4	of	4
		Attorney Docket Number	080618-1581

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
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Examiner Signature	/Yevgeny Valenrod/	Date Considered	02/22/2016
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Substitute for form 1449/PTO		<i>Complete if Known</i>	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
Date Submitted: <u>OCT 13 2015</u>		Filing Date	9/10/2015
(use as many sheets as necessary)		First Named Inventor	Hitesh BATRA
Sheet	1	Art Unit	1672
	of	Examiner Name	Yevgeny Valenrod
	1	Attorney Docket Number	080618-1581

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)				
	B1	3,703,544		11/21/1972	Morozowich	
	B2	3,888,916		06/10/1975	Sinkula	

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. ¹	Foreign Patent Document		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ^d
		Country Code ³	Number ⁴ Kind Code ⁵ (if known)				

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	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, page(s), volume-issue number(s), publisher, city and/or country where published.	T ^d
	B3	Steadymed Ltd., v. United Therapeutics Corporation, Petition for <i>Inter Partes</i> Review of U.S. Patent No. 8,497,393, under 37 CFR 42.100, dated October 1, 2015, with Exhibits 1009, 1010, 1017 and 1018.	
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Examiner Signature	/Yevgeny Valenrod/	Date Considered	02/22/2016
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Index of Claims 	Application/Control No. 14849981	Applicant(s)/Patent Under Reexamination BATRA ET AL.
	Examiner YEVEGENY VALENROD	Art Unit 1672

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

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

CLAIM		DATE							
Final	Original	02/22/2016							
	1	✓							
	2	✓							
	3	✓							
	4	✓							
	5	✓							
	6	✓							
	7	✓							
	8	✓							
	9	✓							
	10	✓							

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("8497393").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/22 13:03
L2	1	("8242305").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/22 13:03
L3	1	("4683330").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/22 13:03
L4	1	("4306075").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/22 13:03
L5	28	((Hitesh) near2 (Batra)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
L6	21	((Sudersan) near2 (Tuladhar)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
L7	29	((Raju) near2 (Penmasta)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
L8	235	((David) near2 (Walsh)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
L9	260	L5 or L6 or L7 or L8	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
L10	23	L9 and treprostinil	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
L11	516	c07c59/72.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
L12	867	(562/466).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/22 13:03
L13	1257	L11 or L12	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2016/02/22 13:03
L14	39	L13 and treprostinil	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03

EAST Search History (Prior Art)

L15	35	L14 and purity	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
L16	33	L15 and HPLC	US-PGPUB; USPAT; USOCR	OR	ON	2016/02/22 13:03
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L18	2	wo "2005007081"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2016/02/22 13:03
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L21	1	("9156786").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2016/02/22 13:03

EAST Search History (Interference)

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BIB DATA SHEET

CONFIRMATION NO. 6653

SERIAL NUMBER	FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.		
14/849,981	09/10/2015	562	1672	080618-1581		
RULE						
APPLICANTS United Therapeutics Corporation, Silver Spring, MD;						
INVENTORS Hitesh BATRA, Herndon, VA; Sudersan M. TULADHAR, Silver Spring, MD; Raju PENMASTA, Herndon, VA; David A. WALSH, Palmyra, VA;						
** CONTINUING DATA ***** This application is a DIV of 13/933,623 07/02/2013 PAT 9156786 which is a CON of 13/548,446 07/13/2012 PAT 8497393 which is a CON of 12/334,731 12/15/2008 PAT 8242305 which claims benefit of 61/014,292 12/17/2007						
** FOREIGN APPLICATIONS *****						
** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 09/23/2015						
Foreign Priority claimed 35 USC 119(a-d) conditions met Verified and Acknowledged	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No /YEVEGENY VALENROD/ Examiner's Signature	<input type="checkbox"/> Met after Allowance Initials	STATE OR COUNTRY VA	SHEETS DRAWINGS 0	TOTAL CLAIMS 10	INDEPENDENT CLAIMS 2
ADDRESS Foley & Lardner LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109 UNITED STATES						
TITLE PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®						
FILING FEE RECEIVED 1600	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:			<input type="checkbox"/> All Fees <input type="checkbox"/> 1.16 Fees (Filing) <input type="checkbox"/> 1.17 Fees (Processing Ext. of time) <input type="checkbox"/> 1.18 Fees (Issue) <input type="checkbox"/> Other _____ <input type="checkbox"/> Credit		

Search Notes 	Application/Control No. 14849981	Applicant(s)/Patent Under Reexamination BATRA ET AL.
	Examiner YEVEGENY VALENROD	Art Unit 1672

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES			
Search Notes	Date	Examiner	
EAST	2/22/2016	YV	
Inventor	2/22/2016	YV	

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

	/YEVEGENY VALENROD/ Primary Examiner, Art Unit 1672
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/849,981	09/10/2015	Hitesh BATRA	080618-1581

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PUBLICATION NOTICE



22428
Foley & Lardner LLP
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Title:PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN?

Publication No.US-2015-0376106-A1

Publication Date:12/31/2015

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/>.

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Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	14/849,981
Date Submitted: <u>OCT 13 2015</u>		Filing Date	9/10/2015
(use as many sheets as necessary)		First Named Inventor	Hitesh BATRA
Sheet	1	Art Unit	1672
	of	Examiner Name	Yevgeny Valenrod
	1	Attorney Docket Number	080618-1581

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	B6	Wiberg, Kenneth, <i>Laboratory Technique in Organic Chemistry</i> , 1960, 112.	

Examiner Signature	Date Considered
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Electronic Acknowledgement Receipt

EFS ID:	23765084
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh BATRA
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Walker
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1581
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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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Warnings:					
Information:					
5	Non Patent Literature	Exhibit-1012Wiberg1960.pdf	890716	no	6
			5019331169c7a05263d1f091883140997415c		
Warnings:					
Information:					
Total Files Size (in bytes):			8215567		

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS TO PREPARE
TREPASTINIL, THE ACTIVE INGREDIENT IN
REMODULIN®
Appl. No.: 14/849,981
Filing Date: 9/10/2015
Examiner: Yevgeny Valenrod
Art Unit: 1672
Confirmation Number: 6653

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

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

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any

rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

CONCISE EXPLANATION OF RELEVANCE

Document B3 is a Petition for *Inter Partes* Review filed against parent patent U.S. 8,497,393, dated October 1, 2015, including Exhibits 1009, 1010, 1017 and 1018. Documents B1-B2 and B4-B6 are exhibits from said IPR Petition which are prior art items not already of record in the present application.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date OCT 1 3 2015

By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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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.	TOF CLAIMS	IND CLAIMS
14/849,981	09/10/2015	1629	1600	080618-1581	10	2

CONFIRMATION NO. 6653

FILING RECEIPT



22428
Foley & Lardner LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

Date Mailed: 09/25/2015

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Hitesh BATRA, Herndon, VA;
Sudersan M. TULADHAR, Silver Spring, MD;
Raju PENMASTA, Herndon, VA;
David A. WALSH, Palmyra, VA;

Applicant(s)

United Therapeutics Corporation, Silver Spring, MD;

Assignment For Published Patent Application

United Therapeutics Corporation, Silver Spring, MD

Power of Attorney: The patent practitioners associated with Customer Number 22428

Domestic Priority data as claimed by applicant

This application is a DIV of 13/933,623 07/02/2013 PAT 9156786
which is a CON of 13/548,446 07/13/2012 PAT 8497393
which is a CON of 12/334,731 12/15/2008 PAT 8242305
which claims benefit of 61/014,232 12/17/2007

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 - A proper **Authorization to Permit Access to Application by Participating Offices** (PTO/SB/39 or its equivalent) has been received by the USPTO.

If Required, Foreign Filing License Granted: 09/23/2015

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 14/849,981**

Projected Publication Date: 12/31/2015

Non-Publication Request: No

Early Publication Request: No
Title

PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®

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 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 Assets Control, 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).

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PATENT APPLICATION FEE DETERMINATION RECORD						Application or Docket Number 14/849,981			
Substitute for Form PTO-875									
APPLICATION AS FILED - PART I									
(Column 1)		(Column 2)		SMALL ENTITY		OTHER THAN SMALL ENTITY			
FOR	NUMBER FILED	NUMBER EXTRA	RATE(\$)	FEE(\$)	RATE(\$)	FEE(\$)			
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A		N/A	280			
SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A		N/A	600			
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A		N/A	720			
TOTAL CLAIMS (37 CFR 1.16(i))	10	minus 20 =			x 80 =	0.00	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	2	minus 3 =			x 420 =	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))									
* If the difference in column 1 is less than zero, enter "0" in column 2.									
			TOTAL		TOTAL			1600	
APPLICATION AS AMENDED - PART II									
(Column 1)		(Column 2)		(Column 3)		SMALL ENTITY		OTHER THAN SMALL ENTITY	
AMENDMENT A	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)	RATE(\$)	ADDITIONAL FEE(\$)		
	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))								
			TOTAL ADD'L FEE		TOTAL ADD'L FEE				
AMENDMENT B	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)	RATE(\$)	ADDITIONAL FEE(\$)		
	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))								
			TOTAL ADD'L FEE		TOTAL ADD'L FEE				
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.									
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20"									
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".									
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.									

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Hitesh BATRA

Title: AN IMPROVED PROCESS TO PREPARE
TREPROSTINIL, THE ACTIVE INGREDIENT IN
REMODULIN®

Prior Appl. No.: 13/933623

Prior Appl. Filing
Date: 7/2/2013

Examiner: Unassigned

Art Unit: Unassigned

CONTINUING PATENT APPLICATION
TRANSMITTAL LETTER

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

Commissioner:

Transmitted herewith for filing under 37 C.F.R. § 1.53(b) is a:

Continuation Division Continuation-In-Part (CIP)

of the above-identified copending prior application in which no patenting, abandonment, or termination of proceedings has occurred. Priority to the above-identified prior application is hereby claimed under 35 U.S.C. § 120 for this continuing application. The entire disclosure of the above-identified prior application is considered as being part of the disclosure of the accompanying continuing application and is hereby incorporated by reference therein.

Applicant claims small entity status under 37 CFR 1.27.

Enclosed are:

- Description, Claim(s), and Abstract (24 pages).
- Executed Declarations (4 pages).
- Power of Attorney (1 pages).
- Information Disclosure Statement, Form PTO-SB08.
- Application Data Sheet (37 CFR 1.76).

The adjustment to the number of sheets for EFS-Web filing follows:

Number of Sheets		EFS-Web Adjustment	Number of Sheets for EFS-Web
24	x	75%	18

The filing fee is calculated below at the large entity rate:

	Number Filed	Included in Basic Fee	Extra	Rate	Fee Totals
Basic Filing Fee				\$280.00 =	\$280.00
Search Fee				\$600.00	\$600.00
Examination Fee				\$720.00	\$720.00
Size Fee	18	-	100 = 0	x \$400.00	\$0.00
Total	10	-	20 = 0	x \$80.00 =	\$0.00
Claims:					
Independent:	2	-	3 = 0	x \$420.00 =	\$0.00
If any Multiple Dependent Claim(s) present:				+ \$780.00 =	\$0.00
Surcharge under 37 CFR 1.16(e) for late filing of Executed Declaration or late payment of filing fee				+ \$140.00 =	\$0.00
Prioritized Examination fee (Track I) under 37 C.F.R. § 1.17 (c)					\$0.00
Processing Fee (Track I) under 37 C.F.R. § 1.17 (i)					\$0.00
TOTAL FILING FEE:				=	\$1600.00
Assignment Recordation Fee:				+ \$40.00 =	\$0.00
Processing Fee under 37 CFR 1.17(i) for Late Filing of English Translation of Application:				+ \$140.00 =	\$0.00
Publication Fee					\$0.00
TOTAL FEE				=	\$1600.00

The above-identified fees of \$1600.00 are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date SEP 10 2015

By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

Electronic Patent Application Fee Transmittal

Application Number:				
Filing Date:				
Title of Invention:	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®			
First Named Inventor/Applicant Name:	Hitesh Batra			
Filer:	Kristel Schorr/Karen Walker			
Attorney Docket Number:	080618-1581			
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	280	280
Utility Search Fee	1111	1	600	600
Utility Examination Fee	1311	1	720	720
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 (\$)	1600

Electronic Acknowledgement Receipt

EFS ID:	23450626
Application Number:	14849981
International Application Number:	
Confirmation Number:	6653
Title of Invention:	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
First Named Inventor/Applicant Name:	Hitesh Batra
Customer Number:	22428
Filer:	Kristel Schorr/Karen Walker
Filer Authorized By:	Kristel Schorr
Attorney Docket Number:	080618-1581
Receipt Date:	10-SEP-2015
Filing Date:	
Time Stamp:	14:04:28
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$ 1600
RAM confirmation Number	299
Deposit Account	
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		Specification.pdf	249682 94ff66c31d2d7b4923d738ef3bab61b5576bc	yes	24

Multipart Description/PDF files in .zip description					
Document Description		Start	End		
Specification		1	21		
Claims		22	23		
Abstract		24	24		

Warnings:

Information:

2	Application Data Sheet	ADS.pdf	632785 096ab66c3746216ed0737afe150109a819201dad	no	7
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Warnings:

Information:

This is not an USPTO supplied ADS fillable form

3	Oath or Declaration filed	Declaration.pdf	256572 674148c5014b01088201ea1e9875a4d88a85fad	no	4
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Warnings:

Information:

4	Power of Attorney	POA.pdf	116513 77f9cb126c009214309de44f03e2d309017a080	no	1
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Warnings:

Information:

5		IDS.pdf	489028 0819126048041887102e16509b2cc7c31687a069	yes	6
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Multipart Description/PDF files in .zip description					
Document Description		Start	End		

	Transmittal Letter		1		2
	Information Disclosure Statement (IDS) Form (SB08)		3		6
Warnings:					
Information:					
6	Transmittal of New Application	Transmittal.pdf	103067	no	4
			<small>641f0975e62187a0b122103a2642002e69</small>		
Warnings:					
Information:					
7	Fee Worksheet (SB06)	fee-info.pdf	35437	no	2
			<small>641f0975e62187a0b122103a2642002e69</small>		
Warnings:					
Information:					
Total Files Size (in bytes):				1883087	
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

**AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE
INGREDIENT IN REMODULIN[®]**

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a Divisional of U.S. Application No. 13/933,623, filed July 2, 2013, which is a Continuation of U.S. Application No. 13/548,446, filed July 13, 2012, which is a Continuation of U.S. Application No. 12/334,731, filed December 15, 2008, which claims priority from U.S. Provisional Patent Application 61/014,232, filed December 17, 2007, the entire contents of which are incorporated herein by reference.

BACKGROUND

[0002] The present invention relates to a process for producing prostacyclin derivatives and novel intermediate compounds useful in the process.

[0003] Prostacyclin derivatives are useful pharmaceutical compounds possessing activities such as platelet aggregation inhibition, gastric secretion reduction, lesion inhibition, and bronchodilation.

[0004] Treprostinil, the active ingredient in Remodulin[®], was first described in US patent 4,306,075. Treprostinil, and other prostacyclin derivatives have been prepared as described in Moriarty, et al in *J. Org. Chem.* 2004, 69, 1890-1902, *Drug of the Future*, 2001, 26(4), 364-374, U.S. Pat. Nos. 6,441,245, 6,528,688, 6,765,117 and 6,809,223. Their teachings are incorporated by reference to show how to practice the embodiments of the present invention.

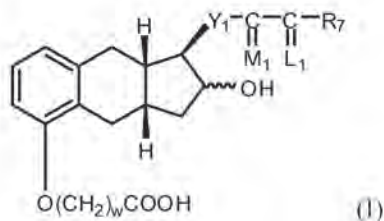
[0005] U.S. Patent No. 5,153,222 describes use of treprostinil for treatment of pulmonary hypertension. Treprostinil is approved for the intravenous as well as subcutaneous route, the latter avoiding septic events associated with continuous intravenous catheters. U.S. patents Nos. 6,521,212 and 6,756,033 describe administration of treprostinil by inhalation for treatment of pulmonary hypertension, peripheral vascular disease and other diseases and conditions. U.S. patent No. 6,803,386 discloses administration of treprostinil for treating cancer such as lung, liver, brain, pancreatic, kidney, prostate, breast, colon and head-neck cancer. U.S. patent application publication No. 2005/0165111 discloses treprostinil treatment of ischemic lesions. U.S. patent No. 7,199,157 discloses that treprostinil treatment improves kidney functions. U.S. patent application publication No. 2005/0282903 discloses treprostinil

treatment of neuropathic foot ulcers. U.S. application No. 12/028,471 filed February 8, 2008, discloses treprostinil treatment of pulmonary fibrosis. U.S. 6,054,486 discloses treatment of peripheral vascular disease with treprostinil. U.S. patent application 11/873,645 filed October 17, 2007 discloses combination therapies comprising treprostinil. U.S. publication No. 2008/0200449 discloses delivery of treprostinil using a metered dose inhaler. U.S. publication No. 2008/0280986 discloses treatment of interstitial lung disease with treprostinil. U.S. application No. 12/028,471 filed February 8, 2008 discloses treatment of asthma with treprostinil. U.S. 7,417,070, 7,384,978 and U.S. publication Nos. 2007/0078095, 2005/0282901, and 2008/0249167 describe oral formulations of treprostinil and other prostacyclin analogs.

[0006] Because Treprostinil, and other prostacyclin derivatives are of great importance from a medicinal point of view, a need exists for an efficient process to synthesize these compounds on a large scale suitable for commercial production.

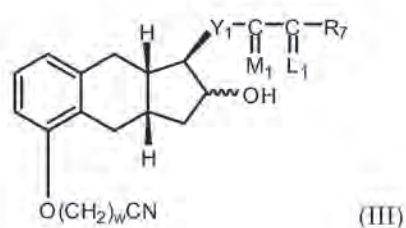
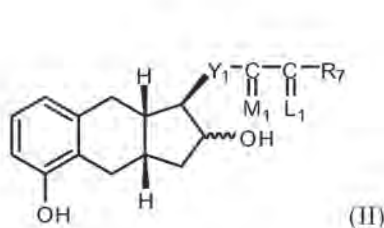
SUMMARY

[0007] The present invention provides in one embodiment a process for the preparation of a compound of formula I, hydrate, solvate, prodrug, or pharmaceutically acceptable salt thereof.



[0008] The process comprises the following steps:

- (a) alkylating a compound of structure II with an alkylating agent to produce a compound of formula III,



wherein

$w = 1, 2, \text{ or } 3$;

Y_1 is trans-CH=CH- , cis-CH=CH- , $-\text{CH}_2(\text{CH}_2)_m-$, or $-\text{C}\equiv\text{C-}$; m is 1, 2, or 3;

R_7 is

- (1) $-\text{C}_p\text{H}_{2p}-\text{CH}_3$, wherein p is an integer from 1 to 5, inclusive,
- (2) phenoxy optionally substituted by one, two or three chloro, fluoro, trifluoromethyl, (C_1-C_3) alkyl, or (C_1-C_3) alkoxy, with the proviso that not more than two substituents are other than alkyl, with the proviso that R_7 is phenoxy or substituted phenoxy, only when R_3 and R_4 are hydrogen or methyl, being the same or different,
- (3) phenyl, benzyl, phenylethyl, or phenylpropyl optionally substituted on the aromatic ring by one, two or three chloro, fluoro, trifluoromethyl, (C_1-C_3) alkyl, or (C_1-C_3) alkoxy, with the proviso that not more than two substituents are other than alkyl,

(4) $\text{cis-CH=CH-CH}_2-\text{CH}_3$,

(5) $-(\text{CH}_2)_2-\text{CH}(\text{OH})-\text{CH}_3$, or

(6) $-(\text{CH}_2)_3-\text{CH}=\text{C}(\text{CH}_3)_2$;

wherein $-\text{C}(\text{L}_1)-\text{R}_7$ taken together is

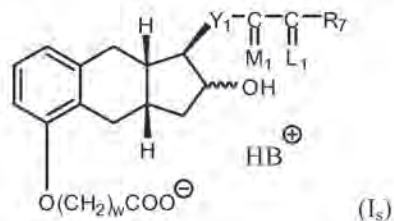
- (1) (C_4-C_7) cycloalkyl optionally substituted by 1 to 3 (C_1-C_5) alkyl;
- (2) 2-(2-furyl)ethyl,
- (3) 2-(3-thienyl)ethoxy, or
- (4) 3-thienyloxymethyl;

M_1 is $\alpha\text{-OH}:\beta\text{-R}_5$ or $\alpha\text{-R}_5:\beta\text{-OH}$ or $\alpha\text{-OR}_2:\beta\text{-R}_5$ or $\alpha\text{-R}_5:\beta\text{-OR}_2$, wherein R_5 is hydrogen or methyl, R_2 is an alcohol protecting group, and

L_1 is $\alpha\text{-R}_3:\beta\text{-R}_4$, $\alpha\text{-R}_4:\beta\text{-R}_3$, or a mixture of $\alpha\text{-R}_3:\beta\text{-R}_4$ and $\alpha\text{-R}_4:\beta\text{-R}_3$, wherein R_3 and R_4 are hydrogen, methyl, or fluoro, being the same or different, with the proviso that one of R_3 and R_4 is fluoro only when the other is hydrogen or fluoro.

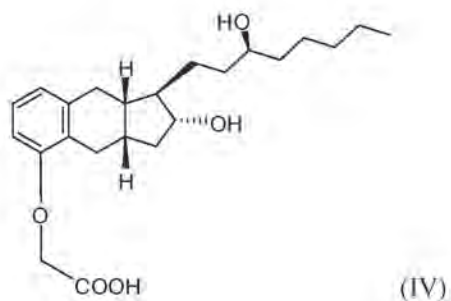
- (b) hydrolyzing the product of step (a) with a base,

- (c) contacting the product of step (b) with a base B to form a salt of formula I_s



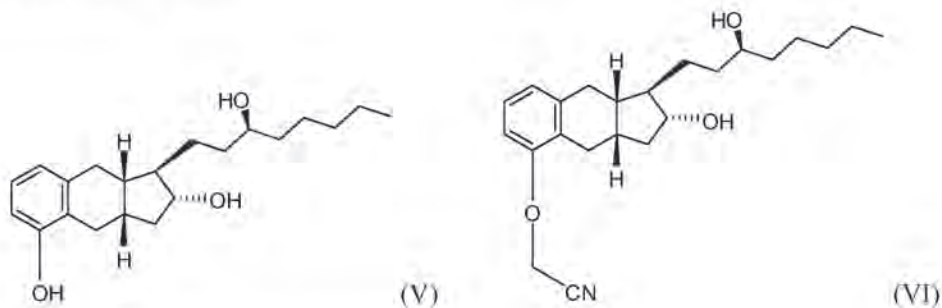
- (d) reacting the salt from step (c) with an acid to form the compound of formula I.

[0009] The present invention provides in another embodiment a process for the preparation of a compound of formula IV.



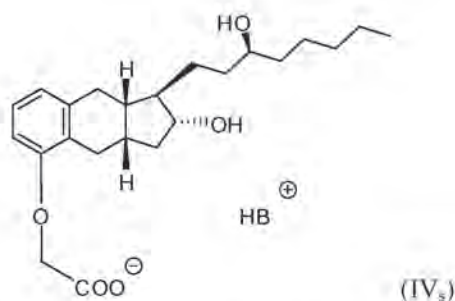
[0010] The process comprises the following steps:

- (a) alkylating a compound of structure V with an alkylating agent to produce a compound of formula VI,



- (b) hydrolyzing the product of step (a) with a base,
 (c) contacting the product of step (b) with a base B to form a salt of formula IV_s,

and



(d) reacting the salt from step (b) with an acid to form the compound of formula IV.

DETAILED DESCRIPTION

[0011] The various terms used, separately and in combinations, in the processes herein described are defined below.

[0012] The expression “comprising” means “including but not limited to.” Thus, other non-mentioned substances, additives, carriers, or steps may be present. Unless otherwise specified, “a” or “an” means one or more.

[0013] C₁₋₃-alkyl is a straight or branched alkyl group containing 1-3 carbon atoms. Exemplary alkyl groups include methyl, ethyl, n-propyl, and isopropyl.

[0014] C₁₋₃-alkoxy is a straight or branched alkoxy group containing 1-3 carbon atoms. Exemplary alkoxy groups include methoxy, ethoxy, propoxy, and isopropoxy.

[0015] C₄₋₇-cycloalkyl is an optionally substituted monocyclic, bicyclic or tricyclic alkyl group containing between 4-7 carbon atoms. Exemplary cycloalkyl groups include but not limited to cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[0016] Combinations of substituents and variables envisioned by this invention are only those that result in the formation of stable compounds. The term “stable”, as used herein, refers to compounds which possess stability sufficient to allow manufacture and which maintains the integrity of the compound for a sufficient period of time to be useful for the purposes detailed herein.

[0017] As used herein, the term “prodrug” means a derivative of a compound that can hydrolyze, oxidize, or otherwise react under biological conditions (*in vitro* or *in vivo*) to provide an active compound. Examples of prodrugs include, but are not limited to,

derivatives of a compound that include biohydrolyzable groups such as biohydrolyzable amides, biohydrolyzable esters, biohydrolyzable carbamates, biohydrolyzable carbonates, biohydrolyzable ureides, and biohydrolyzable phosphate analogues (*e.g.*, monophosphate, diphosphate or triphosphate).

[0018] As used herein, "hydrate" is a form of a compound wherein water molecules are combined in a certain ratio as an integral part of the structure complex of the compound.

[0019] As used herein, "solvate" is a form of a compound where solvent molecules are combined in a certain ratio as an integral part of the structure complex of the compound.

[0020] "Pharmaceutically acceptable" means in the present description being useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable and includes being useful for veterinary use as well as human pharmaceutical use.

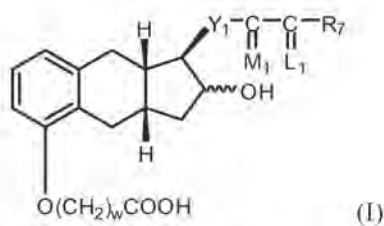
[0021] "Pharmaceutically acceptable salts" mean salts which are pharmaceutically acceptable, as defined above, and which possess the desired pharmacological activity. Such salts include acid addition salts formed with organic and inorganic acids, such as hydrogen chloride, hydrogen bromide, hydrogen iodide, sulfuric acid, phosphoric acid, acetic acid, glycolic acid, maleic acid, malonic acid, oxalic acid, methanesulfonic acid, trifluoroacetic acid, fumaric acid, succinic acid, tartaric acid, citric acid, benzoic acid, ascorbic acid and the like. Base addition salts may be formed with organic and inorganic bases, such as sodium, ammonia, potassium, calcium, ethanolamine, diethanolamine, N-methylglucamine, choline and the like. Included in the invention are pharmaceutically acceptable salts or compounds of any of the formulae herein.

[0022] Depending on its structure, the phrase "pharmaceutically acceptable salt," as used herein, refers to a pharmaceutically acceptable organic or inorganic acid or base salt of a compound. Representative pharmaceutically acceptable salts include, *e.g.*, alkali metal salts, alkali earth salts, ammonium salts, water-soluble and water-insoluble salts, such as the acetate, amsonate (4,4-diaminostilbene-2, 2'-disulfonate), benzenesulfonate, benzonate, bicarbonate, bisulfate, bitartrate, borate, bromide, butyrate, calcium, calcium edetate, camsylate, carbonate, chloride, citrate, clavulariate, dihydrochloride, edetate, edisylate, estolate, esylate, fumarate, gluceptate, gluconate, glutamate, glycolylarsanilate, hexafluorophosphate, hexylresorcinate, hydrabamine, hydrobromide, hydrochloride,

hydroxynaphthoate, iodide, isothionate, lactate, lactobionate, laurate, malate, maleate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, N-methylglucamine ammonium salt, 3-hydroxy-2-naphthoate, oleate, oxalate, palmitate, pamoate (1,1-methene-bis-2-hydroxy-3-naphthoate, einbonate), pantothenate, phosphate/diphosphate, picrate, polygalacturonate, propionate, p-toluenesulfonate, salicylate, stearate, subacetate, succinate, sulfate, sulfosalicylate, suramate, tannate, tartrate, teoclate, tosylate, trithiodide, and valerate salts.

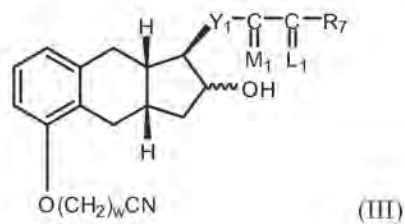
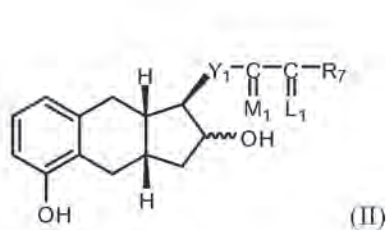
[0023] The present invention provides for a process for producing treprostinil and other prostacyclin derivatives and novel intermediate compounds useful in the process. The process according to the present invention provides advantages on large-scale synthesis over the existing method. For example, the purification by column chromatography is eliminated, thus the required amount of flammable solvents and waste generated are greatly reduced. Furthermore, the salt formation is a much easier operation than column chromatography. Moreover, it was found that the product of the process according to the present invention has higher purity. Therefore the present invention provides for a process that is more economical, safer, faster, greener, easier to operate, and provides higher purity.

[0024] One embodiment of the present invention is a process for the preparation of a compound of formula I, or a hydrate, solvate, prodrug, or pharmaceutically acceptable salt thereof.



[0025] The process comprises the following steps:

(a) alkylating a compound of formula II with an alkylating agent to produce a compound of formula III,



wherein

$w = 1, 2, \text{ or } 3$;

Y_1 is trans-CH=CH- , cis-CH=CH- , $-\text{CH}_2(\text{CH}_2)_m-$, or $-\text{C}\equiv\text{C-}$; m is 1, 2, or 3;

R_7 is

- (1) $-\text{C}_p\text{H}_{2p}-\text{CH}_3$, wherein p is an integer from 1 to 5, inclusive,
- (2) phenoxy optionally substituted by one, two or three chloro, fluoro, trifluoromethyl, $(\text{C}_1\text{-C}_3)$ alkyl, or $(\text{C}_1\text{-C}_3)$ alkoxy, with the proviso that not more than two substituents are other than alkyl, with the proviso that R_7 is phenoxy or substituted phenoxy, only when R_3 and R_4 are hydrogen or methyl, being the same or different,
- (3) phenyl, benzyl, phenylethyl, or phenylpropyl optionally substituted on the aromatic ring by one, two or three chloro, fluoro, trifluoromethyl, $(\text{C}_1\text{-C}_3)$ alkyl, or $(\text{C}_1\text{-C}_3)$ alkoxy, with the proviso that not more than two substituents are other than alkyl,

- (4) $\text{cis-CH=CH-CH}_2\text{-CH}_3$,
- (5) $-(\text{CH}_2)_2\text{-CH(OH)-CH}_3$, or
- (6) $-(\text{CH}_2)_3\text{-CH=C(CH}_3)_2$;

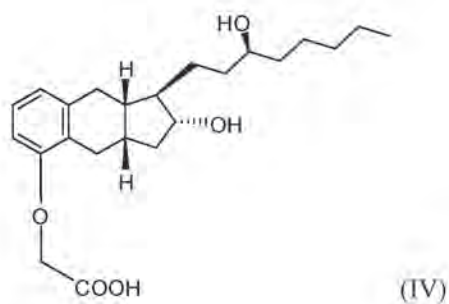
wherein $-\text{C}(\text{L}_1)\text{-R}_7$ taken together is

- (1) $(\text{C}_4\text{-C}_7)$ cycloalkyl optionally substituted by 1 to 3 $(\text{C}_1\text{-C}_5)$ alkyl;
- (2) 2-(2-furyl)ethyl,
- (3) 2-(3-thienyl)ethoxy, or
- (4) 3-thienyloxymethyl;

M_1 is $\alpha\text{-OH}:\beta\text{-R}_5$ or $\alpha\text{-R}_5:\beta\text{-OH}$ or $\alpha\text{-OR}_2:\beta\text{-R}_5$ or $\alpha\text{-R}_5:\beta\text{-OR}_2$, wherein R_5 is hydrogen or methyl, R_2 is an alcohol protecting group, and

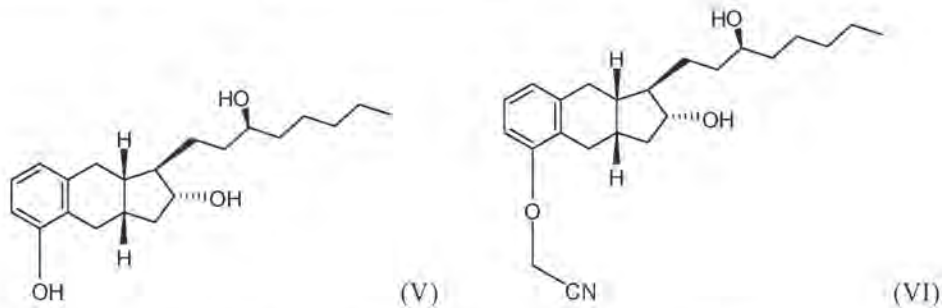
L_1 is $\alpha\text{-R}_3:\beta\text{-R}_4$, $\alpha\text{-R}_4:\beta\text{-R}_3$, or a mixture of $\alpha\text{-R}_3:\beta\text{-R}_4$ and $\alpha\text{-R}_4:\beta\text{-R}_3$, wherein R_3 and R_4 are hydrogen, methyl, or fluoro, being the same or different, with the proviso that one of R_3 and R_4 is fluoro only when the other is hydrogen or fluoro.

- (b) hydrolyzing the product of step (a) with a base,



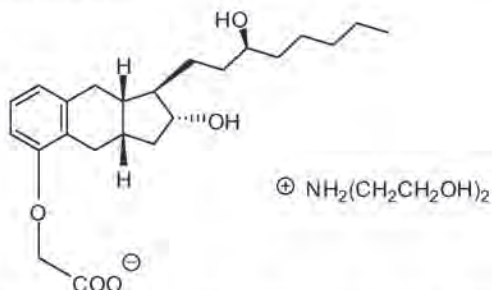
[0030] The process comprises

(a) alkylating a compound of structure V with an alkylating agent such as ClCH_2CN to produce a compound of formula VI,



(b) hydrolyzing the product of step (a) with a base such as KOH ,

(c) contacting the product of step (b) with a base B such as diethanolamine to form a salt of the following structure, and



(d) reacting the salt from step (b) with an acid such as HCl to form the compound of formula IV.

[0031] In one embodiment, the purity of compound of formula IV is at least 90.0%, 95.0%, 99.0%, 99.5%.

[0032] In one embodiment, the process further comprises a step of isolating the salt of formula IV_s.

[0033] In one embodiment, the base B in step (c) may be ammonia, N-methylglucamine, procaine, tromethamine, magnesium, L-lysine, L-arginine, or triethanolamine.

[0034] The following abbreviations are used in the description and/or appended claims, and they have the following meanings:

“MW” means molecular weight.

“Eq.” means equivalent.

“TLC” means thin layer chromatography.

“HPLC” means high performance liquid chromatography.

“PMA” means phosphomolybdic acid.

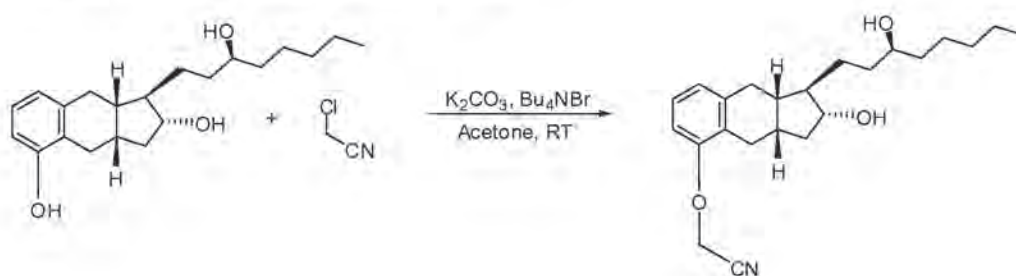
“AUC” means area under curve.

[0035] In view of the foregoing considerations, and specific examples below, those who are skilled in the art will appreciate that how to select necessary reagents and solvents in practicing the present invention.

[0036] The invention will now be described in reference to the following Examples. These examples are not to be regarded as limiting the scope of the present invention, but shall only serve in an illustrative manner.

EXAMPLES

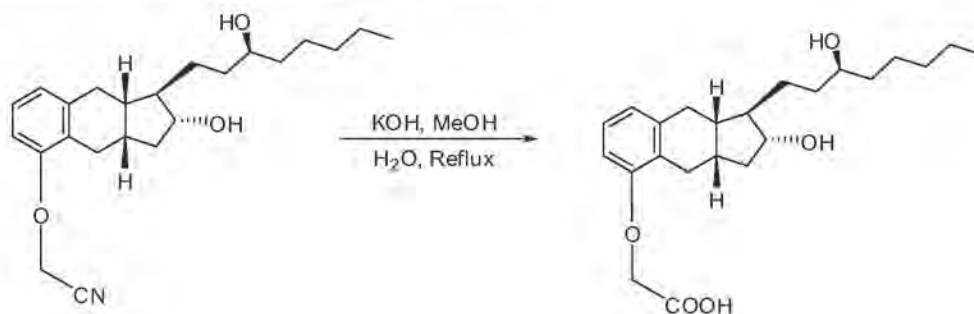
Example 1. Alkylation of Benzindene Triol



Name	MW	Amount	Mol.	Eq.
Benzindene Triol	332.48	1250 g	3.76	1.00
K ₂ CO ₃ (powder)	138.20	1296 g	9.38	2.50
ClCH ₂ CN	75.50	567 g	7.51	2.0
Bu ₄ NBr	322.37	36 g	0.11	0.03
Acetone	—	29 L	—	--
Celite [®] 545	—	115 g	—	--

[0037] A 50-L, three-neck, round-bottom flask equipped with a mechanical stirrer and a thermocouple was charged with benzindene triol (1250 g), acetone (19 L) and K₂CO₃ (powdered) (1296 g), chloroacetonitrile (567 g), tetrabutylammonium bromide (36 g). The reaction mixture was stirred vigorously at room temperature (23±2°C) for 16-72 h. The progress of the reaction was monitored by TLC. (methanol/CH₂Cl₂; 1:9 and developed by 10% ethanolic solution of PMA). After completion of reaction, the reaction mixture was filtered with/without Celite pad. The filter cake was washed with acetone (10L). The filtrate was concentrated *in vacuo* at 50-55°C to give a light-brown, viscous liquid benzindene nitrile. The crude benzindene nitrile was used as such in the next step without further purification.

Example 2. Hydrolysis of Benzindene Nitrile



Name	MW	Amount	Mol.	Eq.
Benzindene Nitrile	371.52	1397 g*	3.76	1.0
KOH	56.11	844 g	15.04	4.0
Methanol	--	12 L	--	--
Water	--	4.25 L	--	--

*Note: This weight is based on 100% yield from the previous step. This is not isolated yield.

[0038] A 50-L, cylindrical reactor equipped with a heating/cooling system, a mechanical stirrer, a condenser, and a thermocouple was charged with a solution of benzindene nitrile in methanol (12 L) and a solution of KOH (844 g of KOH dissolved in 4.25 L of water). The reaction mixture was stirred and heated to reflux (temperature 72.2°C). The progress of the reaction was monitored by TLC (for TLC purpose, 1-2 mL of reaction mixture was acidified with 3M HCl to pH 1-2 and extracted with ethyl acetate. The ethyl acetate extract was used for TLC; Eluent: methanol/CH₂Cl₂; 1:9, and developed by 10% ethanolic solution of PMA). After completion of the reaction (~5 h), the reaction mixture was cooled to -5 to 10°C and quenched with a solution of hydrochloric acid (3M, 3.1 L) while stirring. The reaction mixture was concentrated *in vacuo* at 50-55°C to obtain approximately 12-14 L of condensate. The condensate was discarded.

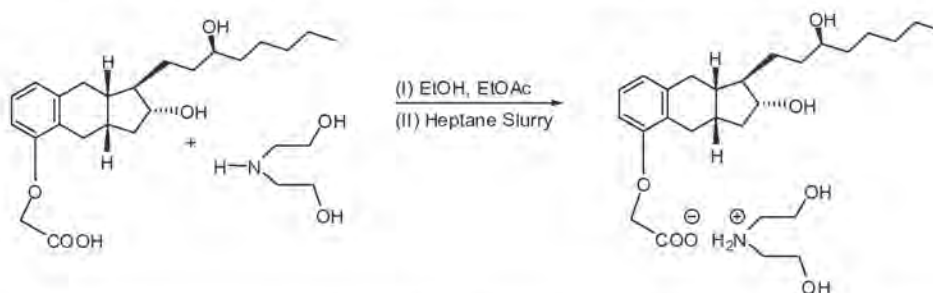
[0039] The aqueous layer was diluted with water (7-8 L) and extracted with ethyl acetate (2 × 6 L) to remove impurities soluble in ethyl acetate. To aqueous layer, ethyl acetate (22 L) was added and the pH of reaction mixture was adjusted to 1-2 by adding 3M HCl (1.7 L) with stirring. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 11 L). The combined organic layers were washed with water (3 × 10 L) and followed by washing with a solution of NaHCO₃ (30 g of NaHCO₃ dissolved in 12 L of water). The organic layer was further washed with saturated solution of NaCl (3372 g of NaCl dissolved in water (12 L)) and dried over anhydrous Na₂SO₄ (950-1000 g), once filtered.

[0040] The filtrate was transferred into a 72-L reactor equipped with mechanical stirrer, a condenser, and a thermocouple. To the solution of treprostinil in reactor was added activated carbon (110-130 g). The suspension was heated to reflux (temperature 68-70°C) for at least one hour. For filtration, a pad of Celite[®] 545 (300-600 g) was prepared in sintered glass

funnel using ethyl acetate. The hot suspension was filtered through the pad of Celite[®] 545. The Celite[®] 545 was washed with ethyl acetate until no compound was seen on TLC of the washings.

[0041] The filtrate (pale-yellow) was reduced to volume of 35-40 L by evaporation *in vacuo* at 50-55°C for direct use in next step.

Example 3. Conversion of Treprostinil to Treprostinil Diethanolamine Salt (1:1)



Name	MW	Amount	Mol	Eq
Treprostinil	390.52	1464 g*	3.75	1.0
Diethanolamine	105.14	435 g	4.14	1.1
Ethanol	--	5.1 L	--	--
Ethyl acetate	--	35L**	--	--
Treprostinil Diethanolamine Salt (seed)	--	12 g	--	--

*Note: This weight is based on 100% yield from benzindene triol. It is not isolated yield. The treprostinil was carried from previous step in ethyl acetate solution and used as such for this step.

**Note: The total volume of ethyl acetate should be in range of 35-36 L (it should be 7 times the volume of ethanol used). Approximately 35 L of ethyl acetate was carried over from previous step and additional 1.0 L of ethyl acetate was used for rinsing the flask.

[0042] A 50-L, cylindrical reactor equipped with a heating/cooling system, a mechanical stirrer, a condenser, and a thermocouple was charged with a solution of treprostinil in ethyl acetate (35-40 L from the previous step), anhydrous ethanol (5.1 L) and diethanolamine (435 g). While stirring, the reaction mixture was heated to 60-75°C, for 0.5-1.0 h to obtain a clear solution. The clear solution was cooled to 55±5°C. At this temperature, the seed of

polymorph B of treprostinil diethanolamine salt (~12 g) was added to the clear solution. The suspension of polymorph B was stirred at this temperature for 1 h. The suspension was cooled to 20±2°C overnight (over a period of 16-24 h). The treprostinil diethanolamine salt was collected by filtration using Aurora filter equipped with filter cloth, and the solid was washed with ethyl acetate (2 × 8 L). The treprostinil diethanolamine salt was transferred to a HDPE/glass container for air-drying in hood, followed by drying in a vacuum oven at 50±5°C under high vacuum.

[0043] At this stage, if melting point of the treprostinil diethanolamine salt is more than 104°C, it was considered polymorph B. There is no need of recrystallization. If it is less than 104°C, it is recrystallized in EtOH-EtOAc to increase the melting point.

Data on Treprostinil Diethanolamine Salt (1:1)

Batch No.	Wt. of Benzindene Triol (g)	Wt. of Treprostinil Diethanolamine Salt (1:1) (g)	Yield (%)	Melting point (°C)
1	1250	1640	88.00	104.3-106.3
2	1250	1528	82.00*	105.5-107.2
3	1250	1499	80.42**	104.7-106.6
4	1236	1572	85.34	105-108

*Note: In this batch, approximately 1200 mL of ethyl acetate solution of treprostinil before carbon treatment was removed for R&D carbon treatment experiments.

**Note: This batch was recrystallized, for this reason yield was lower.

Example 4. Heptane Slurry of Treprostinil Diethanolamine Salt (1:1)

Name	Batch No.	Amount	Ratio
Treprostinil Diethanolamine Salt	1	3168 g	1
Heptane	--	37,5 L	12

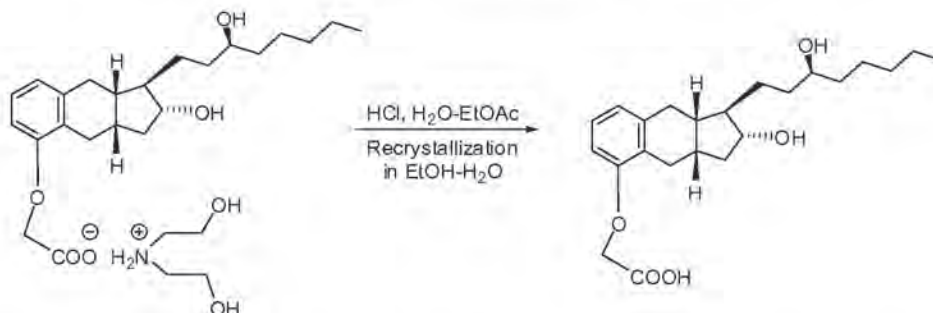
Name	Batch No.	Amount	Ratio
Treprostinil Diethanolamine Salt	2	3071 g	1
Heptane	--	36.0 L	12

[0044] A 50-L, cylindrical reactor equipped with a heating/cooling system, a mechanical stirrer, a condenser, and a thermocouple was charged with slurry of treprostinil diethanolamine salt in heptane (35-40 L). The suspension was heated to 70-80°C for 16-24 h. The suspension was cooled to 22±2°C over a period of 1-2 h. The salt was collected by filtration using Aurora filter. The cake was washed with heptane (15-30 L) and the material was dried in Aurora filter for 1 h. The salt was transferred to trays for air-drying overnight in hood until a constant weight of treprostinil diethanolamine salt was obtained. The material was dried in oven under high vacuum for 2-4 h at 50-55°C.

Analytical data on and Treprostinil Diethanolamine Salt (1:1)

Test	Batch 1	Batch 2
IR	Conforms	Conforms
Residue on Ignition (ROI)	<0.1% w/w	<0.1% w/w
Water content	0.1% w/w	0.0% w/w
Melting point	105.0-106.5°C	104.5-105.5°C
Specific rotation $[\alpha]_{589}^{25}$	+34.6°	+35°
Organic volatile impurities		
• Ethanol	• Not detected	• Not detected
• Ethyl acetate	• Not detected	• <0.05% w/w
• Heptane	• <0.05% w/w	• <0.05% w/w
HPLC (Assay)	100.4%	99.8%
Diethanolamine	Positive	Positive

Example 5. Conversion of Treprostinil Diethanolamine Salt (1:1) to Treprostinil



[0045] A 250-mL, round-bottom flask equipped with magnetic stirrer was charged with treprostinil diethanolamine salt (4 g) and water (40 mL). The mixture was stirred to obtain a clear solution. To the clear solution, ethyl acetate (100 mL) was added. While stirring, 3M HCl (3.2 mL) was added slowly until pH ~1 was attained. The mixture was stirred for 10 minutes and organic layer was separated. The aqueous layer was extracted with ethyl acetate (2 × 100 mL). The combined organic layers was washed with water (2 × 100 mL), brine (1 × 50 mL) and dried over anhydrous Na₂SO₄. The ethyl acetate solution of treprostinil was filtered and the filtrate was concentrated under vacuum at 50°C to give off-white solid. The crude treprostinil was recrystallized from 50% ethanol in water (70 mL). The pure treprostinil was collected in a Buchner funnel by filtration and cake was washed with cold 20% ethanolic solution in water. The cake of treprostinil was air-dried overnight and further dried in a vacuum oven at 50°C under high vacuum to afford 2.9 g of treprostinil (Yield 91.4%, purity (HPLC, AUC, 99.8%).

Analytical data on Treprostinil from Treprostinil Diethanolamine Salt (1:1) to Treprostinil

Batch No.	Yield	Purity (HPLC)
1	91.0%	99.8% (AUC)
2	92.0%	99.9% (AUC)
3	93.1%	99.7% (AUC)
4	93.3%	99.7% (AUC)
5	99.0 %	99.8% (AUC)
6	94.6%	99.8% (AUC)

Example 6. Comparison of the former process and a working example of the process according to the present invention

Step No.	Steps	Former Process (Batch size: 500g)	Working example of the Process according to the present invention (Batch size: 5 kg)
Nitrile			
1	Triol weight	500 g	5,000 g
2	Acetone	20 L (1:40 wt/wt)	75 L (1:15 wt/wt)
3	Potassium carbonate	1,300 g (6.4 eq)	5,200 g (2.5 eq)
4	Chloroacetonitrile	470 g (4.2 eq)	2,270 g (2 eq)
5	Tetrabutylammonium bromide	42 g (0.08 eq)	145 g (0.03 eq)
6	Reactor size	72-Liter	50- gallon
7	Reflux time	8 hours	No heating, Room temperature (r.t.) 45 h
8	Hexanes addition before filtration	Yes (10 L)	No
9	Filter	Celite	Celite
10	Washing	Ethyl acetate (10 L)	Acetone (50 L)
11	Evaporation	Yes	Yes
12	Purification	Silica gel column Dichloromethane:0.5 L Ethyl acetate: 45 L Hexane: 60 L	No column
13	Evaporation after column	Yes	No
14	Yield of nitrite	109-112 %	Not checked
Treprostnil (intermediate)			
15	Methanol	7,6 L (50-L reactor)	50 L (50-gal reactor)
16	Potassium hydroxide	650 g (8 eq)	3,375g (4 eq)
17	Water	2.2 L	17 L

18	% of KOH	30%	20%
19	Reflux time	3-3.5 h	4-5 h
20	Acid used	2.6 L (3 M)	12 L (3 M)
21	Removal of impurities	3 × 3 L Ethyl acetate	2 × 20 L Ethyl acetate
22	Acidification	0.7 L	6.5 L
23	Ethyl acetate extraction	5 × 17 L = 35 L	90+45+45 = 180 L
24	Water washing	2 × 8 L	3 × 40 L
25	Sodium bicarbonate washing	Not done	120 g in 30L water + 15 L brine
26	Brine washing	Not done	1 × 40 L
27	Sodium sulfate	1 kg	Not done
28	Sodium sulfate filtration	Before charcoal, 6 L ethyl acetate	N/A
29	Charcoal	170 g, reflux for 1.5 h, filter over Celite, 11 L ethyl acetate	Pass hot solution (75°C) through charcoal cartridge and clean filter, 70 L ethyl acetate
30	Evaporation	Yes, to get solid intermediate treprostinil	Yes, adjust to 150 L solution
Treprostinil Diethanolamine Salt			
31	Salt formation	Not done	1,744 g diethanolamine, 20 L ethanol at 60-75°C.
32	Cooling	N/A	To 20°C over weekend; add 40 L ethyl acetate; cooled to 10°C
33	Filtration	N/A	Wash with 70 L ethyl acetate
34	Drying	N/A	Air-dried to constant wt., 2 days
Treprostinil (from 1.5 kg Treprostinil diethanolamine salt)			
35	Hydrolysis	N/A	15 L water + 25 L ethyl acetate + HCl
36	Extraction	N/A	2 × 10 L ethyl acetate
37	Water wash	N/A	3 × 10 L

38	Brine wash	N/A	1 × 10 L
39	Sodium sulfate	N/A	1 kg, stir
40	Filter	N/A	Wash with 6 L ethyl acetate
41	Evaporation	N/A	To get solid, intermediate Treprostinil
42	Crude drying on tray	1 or 3 days	Same
43	Ethanol & water for cryst.	5.1 L + 5.1 L	10.2 L + 10.2 L (same %)
44	Crystallization in	20-L rotavap flask	50-L jacketed reactor
45	Temperature of crystallization	2 h r.t., fridge -0°C 24 h	50°C to 0°C ramp, 0°C overnight
46	Filtration	Buchner funnel	Aurora filter
47	Washing	20% (10 L) cooled ethanol-water	20% (20 L) cooled ethanol-water
48	Drying before oven	Buchner funnel (20 h) Tray (no)	Aurora filter (2.5 h) Tray (4 days)
49	Oven drying	15 hours, 55°C	6-15 hours, 55°C
50	Vacuum	<-0.095 mPA	< 5 Torr
51	UT-15 yield weight	~ 535 g	~ 1,100 g
52	% yield from triol)	~ 91%	~ 89%
53	Purity	~ 99.0%	99.9%

[0046] The quality of treprostinil produced according to this invention is excellent. The purification of benzindene nitrile by column chromatography is eliminated. The impurities carried over from intermediate steps (i.e. alkylation of triol and hydrolysis of benzindene nitrile) are removed during the carbon treatment and the salt formation step. Additional advantages of this process are: (a) crude treprostinil salts can be stored as raw material at ambient temperature and can be converted to treprostinil by simple acidification with diluted hydrochloric acid, and (b) the treprostinil salts can be synthesized from the solution of treprostinil without isolation. This process provides better quality of final product as well as saves significant amount of solvents and manpower in purification of intermediates.

[0047] Although the foregoing refers to particular preferred embodiments, it will be understood that the present invention is not so limited. It will occur to those of ordinary skill

in the art that various modifications may be made to the disclosed embodiments and that such modifications are intended to be within the scope of the present invention.

[0048] All of the publications, patent applications and patents cited in this specification are incorporated herein by reference in their entirety.

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising treprostinil or a pharmaceutically acceptable salt thereof, said composition prepared by a process comprising providing a starting batch of treprostinil having one or more impurities resulting from prior alkylation and hydrolysis steps, forming a salt of treprostinil by combining the starting batch and a base, isolating the treprostinil salt, and preparing a pharmaceutical composition comprising treprostinil or a pharmaceutically acceptable salt thereof from the isolated treprostinil salt, whereby a level of one or more impurities found in the starting batch of treprostinil is lower in the pharmaceutical composition, and wherein said alkylation is alkylation of benzindene triol.

2. The pharmaceutical composition of claim 1, wherein the salt is isolated in crystalline form.

3. The pharmaceutical composition of claim 2, wherein the isolated salt is at least 99.8% pure.

4. The pharmaceutical composition of claim 1, wherein the base is selected from the group consisting of sodium, ammonia, potassium, calcium, ethanolamine, diethanolamine, N-methylglucamine, and choline.

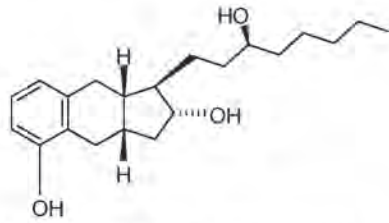
5. The pharmaceutical composition of claim 4, wherein the base is diethanolamine.

6. The pharmaceutical composition of claim 1, wherein the base is combined with treprostinil that has not been previously isolated.

7. The pharmaceutical composition of claim 1, wherein the isolated salt is stored at ambient temperature.

8. The pharmaceutical composition of claim 1, which is a pharmaceutical solution.

9. A process of preparing a pharmaceutical product comprising treprostinil or a pharmaceutically acceptable salt thereof, comprising alkylating a triol intermediate of the formula:



hydrolyzing the resulting compound to form treprostinil, forming a salt of treprostinil stable at ambient temperature, storing the treprostinil salt at ambient temperature, and preparing a pharmaceutical product from the treprostinil salt after storage, wherein the pharmaceutical product comprises treprostinil or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical product prepared by the process of claim 9.

ABSTRACT

This present invention relates to an improved process to prepare prostacyclin derivatives. One embodiment provides for an improved process to convert benzindene triol to treprostiniil via salts of treprostiniil and to purify treprostiniil.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	080618-1581
		Application Number	
Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®		
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					<input type="button" value="Remove"/>
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Hitesh		BATRA		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
City	Herndon	State/Province	VA	Country of Residence	US
Mailing Address of Inventor:					
Address 1	2461 Leyland Ridge Road				
Address 2					
City	Herndon	State/Province	VA		
Postal Code	20171	Country i	US		
Inventor 2					<input type="button" value="Remove"/>
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Sudersan	M.	TULADHAR		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
City	Silver Spring	State/Province	MD	Country of Residence	US
Mailing Address of Inventor:					
Address 1	1501 Haddon Manor Court				
Address 2					
City	Silver Spring	State/Province	MD		
Postal Code	20904	Country i	US		
Inventor 3					<input type="button" value="Remove"/>
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Raju		PENMASTA		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	080618-1581
		Application Number	
Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®		

City	Herndon	State/Province	VA	Country of Residence	US
------	---------	----------------	----	----------------------	----

Mailing Address of Inventor:

Address 1	12953 Centre Park Circle #115				
Address 2					
City	Herndon	State/Province	VA		
Postal Code	20171	Country	US		

Inventor 4	<input type="button" value="Remove"/>
------------	---------------------------------------

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	David	A.	WALSH	

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

City	Palmyra	State/Province	VA	Country of Residence	US
------	---------	----------------	----	----------------------	----

Mailing Address of Inventor:

Address 1	56 Wildwood Drive				
Address 2					
City	Palmyra	State/Province	VA		
Postal Code	22963	Country	US		

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

Customer Number	22428		
Email Address	IPDocketing@foley.com	<input type="button" value="Add Email"/>	<input type="button" value="Remove Email"/>

Application Information:

Title of the Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®		
Attorney Docket Number	080618-1581	Small Entity Status Claimed	<input type="checkbox"/>
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)		Suggested Figure for Publication (if any)	

Filing By Reference :

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1581
	Application Number	
Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®	

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: 22428

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 this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

When referring to the current application, please leave the application number blank.

Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
	Division of	13/933623	2013-07-02
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
13/933623	Continuation of	13/548446	2012-07-13
Prior Application Status			Remove

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	080618-1581
		Application Number	
Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®		
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
13/548446	Continuation of	12/334731	2008-12-15
Prior Application Status	<input type="button" value="Remove"/>		
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
12/334731	Claims benefit of provisional	61/014232	2007-12-17
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).

<input type="button" value="Remove"/>			
Application Number	Country ⁱ	Filing Date (YYYY-MM-DD)	Access Code ^j (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.

Authorization to Permit Access:

Authorization to Permit Access to the Instant Application by the Participating Offices

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1581
	Application Number	
Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®	

If 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 World Intellectual Property Office (WIPO), and any other intellectual property offices in which a foreign application claiming priority to the instant patent application is filed access to the instant patent application. See 37 CFR 1.14(c) and (h). This box should not be checked if the applicant does not wish the EPO, JPO, KIPO, WIPO, or other intellectual property office in which a foreign application claiming priority to the instant patent application is filed to have access to the instant patent application.

In accordance with 37 CFR 1.14(h)(3), access will be provided to a copy of the instant patent application with respect to: 1) the instant patent application-as-filed; 2) any foreign application to which the instant patent application claims priority under 35 U.S.C. 119(a)-(d) if a copy of the foreign application that satisfies the certified copy requirement of 37 CFR 1.55 has been filed in the instant patent application; and 3) any U.S. application-as-filed from which benefit is sought in the instant patent application.

In accordance with 37 CFR 1.14(c), access may be provided to information concerning the date of filing this Authorization.

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.

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 United Therapeutics Corporation

Mailing Address Information For Applicant:

Address 1	1040 Spring Street		
Address 2			
City	Silver Spring	State/Province	MD
Country	US	Postal Code	20910
Phone Number		Fax Number	

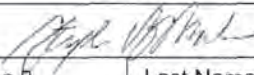
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	080618-1581
		Application Number	
Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®		
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.			
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. <input checked="" type="checkbox"/>			
Organization Name	United Therapeutics Corporation		
Mailing Address Information For Assignee including Non-Applicant Assignee:			
Address 1	1040 Spring Street		
Address 2			
City	Silver Spring	State/Province	MD
Country	US	Postal Code	20910
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 form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications.					
Signature			Date (YYYY-MM-DD)	SEP 10 2015	
First Name	Stephen B.	Last Name	Maebius	Registration Number	35264
Additional Signature may be generated within this form by selecting the Add button.					

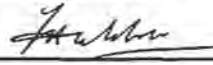
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1581
	Application Number	
Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®	

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.**

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

080618-1256

Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®	
As the below named inventor, I hereby declare that:		
This declaration is directed to:	<input checked="" type="checkbox"/>	The attached application, or
	<input type="checkbox"/>	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 (5) years, or both.		
WARNING:		
<p>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.</p>		
LEGAL NAME OF INVENTOR		
Inventor:	Sudersan M. TULADHAR	Date (Optional): <u>June 4, 2013</u>
Signature:		
<p>Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.</p>		

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

080618-1256

Title of Invention	AN IMPROVED PROCESS TO PREPARE TREPROSTINIL, THE ACTIVE INGREDIENT IN REMODULIN®
<p>As the below named inventor, I hereby declare that:</p> <p>This declaration is directed to: <input checked="" type="checkbox"/> The attached application, or <input type="checkbox"/> United States application or PCT international application number _____ filed on _____.</p> <p>The above-identified application was made or authorized to be made by me.</p> <p>I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.</p> <p>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 (5) years, or both.</p> <p style="text-align: center;">WARNING:</p> <p>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.</p>	
<p>LEGAL NAME OF INVENTOR</p> <p>Inventor: Raju PENMASTA Date (Optional): <u>Jun 04 2013</u></p> <p>Signature: <u>Raju Penmasta</u></p>	
<p>Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.</p>	

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POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

Practitioners associated with Customer Number: **22428**

OR

Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number	Name	Registration Number

As attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications a signed only to the undersigned according to the USPTO assignment records or assignments documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

The address associated with Customer Number: **22428**

OR

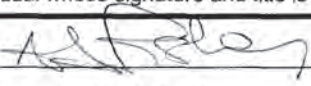
<input type="checkbox"/>	Firm or Individual Name			
	Address			
	City			
	Country			
	Telephone		Email	

Assignee Name and Address: **United Therapeutics Corporation
 1040 Spring Street
 Silver Spring, Maryland 20910**

A copy of this form, together with a statement under 37 CFR 3.73(c) (Form PTO/SB/96 or equivalent) is required to be Filed in each application in which this form is used. The statement under 37 CFR 3.73(c) may be completed by one of The practitioners appointed in this form, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature		Date	12/11/12
Name	Andrew J. Fisher	Telephone	202-742-1208
Title	Chief Strategic Officer & Deputy General Counsel		

This collection of information is required by 37 CFR 1.31, 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.**

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

First Inventor Name: Hitesh BATRA
Title: AN IMPROVED PROCESS TO PREPARE
TREPASTINIL, THE ACTIVE INGREDIENT IN
REMODULIN®
Appl. No.: Unassigned (DIV of 13/933,623)
Filing Date: Herewith
Examiner: Unassigned
Art Unit: Unassigned

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

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

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

Applicant requests that, in accordance with 37 CFR §1.98(d), the Examiner review all applications relied on for an earlier effective filing date under 35 U.S.C. 120, including application no. 12/334,731, filed 12/15/2008; application no. 13/548,446, filed 7/13/2012; application no. 13/933623, filed 7/2/2013, for copies of references of record therein that are not being provided here; although Applicant would be pleased to provide copies of any such documents at the Examiner's request.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date SEP 10 2015

By 

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Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

Substitute for form 1449/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	Unassigned
		Filing Date	Herewith
(use as many sheets as necessary)		First Named Inventor	Hitesh BATRA
		Art Unit	Unassigned
		Examiner Name	Unassigned
Sheet	1	of	4
		Attorney Docket Number	080618-1581

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Examiner Signature	Date Considered
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