UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/778,662	07/21/2020	10716793	080618-1916	4471

166905 7590 06/30/2020

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):

Horst OLSCHEWSKI, Graz, AUSTRIA;
United Therapeutics Corporation, Silver Spring, MD;
Robert ROSCIGNO, Chapel Hill, NC;
Lewis J. RUBIN, LaJolla, CA;
Thomas Schmehl, Giessen, GERMANY, Deceased;
Werner SEEGER, Giessen, GERMANY;
Carl STERRITT, Weybridge, UNITED KINGDOM;
Robert VOSWINCKEL, Giessen, GERMANY;

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
16/778,662	01/31/2020	1629	1720	080618-1916	8	1

CONFIRMATION NO. 4471

CORRECTED FILING RECEIPT

166905
Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

OC000000117826939

Date Mailed: 06/18/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Horst OLSCHEWSKI, Graz, AUSTRIA;
Robert ROSCIGNO, Chapel Hill, NC;
Lewis J. RUBIN, LaJolla, CA;
Thomas Schmehl, Giessen, GERMANY, Deceased;
Werner SEEGER, Giessen, GERMANY;
Carl STERRITT, Weybridge, UNITED KINGDOM;
Robert VOSWINCKEL, Giessen, GERMANY;

Applicant(s)

United Therapeutics Corporation, Siliver Spring, MD;

Assignment For Published Patent Application

United Therapeutics Corporation, Silver Spring, MD

Power of Attorney: The patent practitioners associated with Customer Number 166905

Domestic Priority data as claimed by applicant

This application is a CON of 16/536,954 08/09/2019
which is a CON of 15/011,999 02/01/2016 PAT 10376525
which is a DIV of 13/469,854 05/11/2012 PAT 9339507
which is a DIV of 12/591,200 11/12/2009 PAT 9358240
which is a CON of 11/748,205 05/14/2007 ABN
which claims benefit of 60/800,016 05/15/2006

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: No

Permission to Access Search Results: No

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

If Required, Foreign Filing License Granted: 06/17/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/778,662**

Projected Publication Date: Not Applicable

Non-Publication Request: No

Early Publication Request: No

Title

TREPROSTINIL ADMINISTRATION BY INHALATION

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 AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

166905 7590 06/12/2020

Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

EXAMINER
SCHMITT, MICHAEL J

ART UNIT	PAPER NUMBER
1629	

DATE MAILED: 06/12/2020

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916	4471

TITLE OF INVENTION: TREPROSTINIL ADMINISTRATION BY INHALATION

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1000	$0.00	$0.00	$1000	09/14/2020

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: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence 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)

166905 7590 06/12/2020

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 transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916	4471

TITLE OF INVENTION: TREPROSTINIL ADMINISTRATION BY INHALATION

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1000	$0.00	$0.00	$1000	09/14/2020

EXAMINER	ART UNIT	CLASS-SUBCLASS
SCHMITT, MICHAEL J	1629	514-569000

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 03-09 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

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

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

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

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

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

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

4a. Fees submitted: ❑ Issue Fee ❑ Publication Fee (if required) ❑ Advance Order - # of Copies _____

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via EFS-Web ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

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

❑ Applicant certifying micro entity status. See 37 CFR 1.29

❑ 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. _____

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916	4471

166905 7590 06/12/2020

Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

EXAMINER	
SCHMITT, MICHAEL J	
ART UNIT	PAPER NUMBER
1629	

DATE MAILED: 06/12/2020

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 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. 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, local, or foreign enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 16/778,662	Applicant(s) OLSCHEWSKI et al.	
	Examiner MICHAEL J SCHMITT	Art Unit 1629	AIA (FITF) 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 5/15/2020.
   ☐ 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 1-8 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

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

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

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

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

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

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

/MICHAEL J SCHMITT/ Examiner, Art Unit 1629	/JEFFREY S LUNDGREN/ Supervisory Patent Examiner, Art Unit 1629

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/778,662	OLSCHEWSKI et al.
	Examiner	Art Unit
	MICHAEL J SCHMITT	1629

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
EAST search	05/05/2020	MS
EAST search	06/04/2020	MS

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
514	183, 569	06/04/2020	MS

/MICHAEL J SCHMITT/ Examiner, Art Unit 1629	

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/778,662	OLSCHEWSKI et al.
	Examiner	**Art Unit**
	MICHAEL J SCHMITT	1629

CPC						
Symbol					**Type**	**Version**
A61K	/	31	/	557	F	2013-01-01
A61K	/	9	/	0078	I	2013-01-01
A61K	/	9	/	008	I	2013-01-01
A61K	/	31	/	192	I	2013-01-01

CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
	/		/					

/MICHAEL J SCHMITT/ Examiner, Art Unit 1629	04 June 2020	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/JEFFREY S LUNDGREN/ Supervisory Patent Examiner, Art Unit 1629	08 June 2020	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office

Part of Paper No.: 20200604

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/778,662	OLSCHEWSKI et al.
	Examiner	**Art Unit**
	MICHAEL J SCHMITT	1629

INTERNATIONAL CLASSIFICATION					
CLAIMED					
A61K31/557	/	31	/	557	
A61K9/00	/	9	/	00	
A61K31/192	/	31	/	192	

NON-CLAIMED				
	/		/	

US ORIGINAL CLASSIFICATION	
CLASS	**SUBCLASS**
514	183

CROSS REFERENCES(S)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**					
514	569					

/MICHAEL J SCHMITT/ Examiner, Art Unit 1629 (Assistant Examiner)	04 June 2020 (Date)	**Total Claims Allowed:** 8	
/JEFFREY S LUNDGREN/ Supervisory Patent Examiner, Art Unit 1629 (Primary Examiner)	08 June 2020 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure none

U.S. Patent and Trademark Office

Part of Paper No.: 20200604

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/778,662	OLSCHEWSKI et al.
	Examiner	**Art Unit**
	MICHAEL J SCHMITT	1629

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

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

/MICHAEL J SCHMITT/ Examiner, Art Unit 1629	04 June 2020	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	8	
/JEFFREY S LUNDGREN/ Supervisory Patent Examiner, Art Unit 1629	08 June 2020	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

Bibliographic Data

Application No: 16/778,662

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☐ No ☐ Met After Allowance

Verified and Acknowledged: /MICHAEL J SCHMITT/ Examiner's Signature | Initials

Title: TREPROSTINIL ADMINISTRATION BY INHALATION

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
01/31/2020	514	1629	080618-1916
RULE			

APPLICANTS

United Therapeutics Corporation, Siliver Spring, MD,

INVENTORS

Horst OLSCHEWSKI Graz, AUSTRIA

Robert ROSCIGNO Chapel Hill, NC, UNITED STATES

Lewis J. RUBIN LaJolla, CA, UNITED STATES

Thomas Schmehl Giessen, GERMANY

Werner SEEGER Giessen, GERMANY

Carl STERRITT Weybridge, UNITED KINGDOM

Robert VOSWINCKEL Giessen, GERMANY

CONTINUING DATA

This application is a CON of 16536954 08/09/2019

16536954 is a CON of 15011999 02/01/2016 PAT 10376525

15011999 is a DIV of 13469854 05/11/2012 PAT 9339507

13469854 is a DIV of 12591200 11/12/2009 PAT 9358240

12591200 is a CON of 11748205 05/14/2007ABN

11748205 has PRO of 60800016 05/15/2006

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

STATE OR COUNTRY

AUSTRIA

ADDRESS

Foley & Lardner LLP

3000 K Street N.W.

Suite 600
Washington, DC 20007-5109
UNITED STATES

FILING FEE RECEIVED

$5,860

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3	pulmonary.clm. and treprostinil.clm. and breath.clm. and microgram.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	ADJ	ON	2020/06/04 15:20
L2	10	pulmonary.clm. and treprostinil.clm. and breath.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	ADJ	ON	2020/06/04 15:20
L3	10	pulmonary.clm. and treprostinil.clm. and breaths.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	ADJ	ON	2020/06/04 15:20

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L4	3,337	514/183.ccls.	US-PGPUB; USPAT	ADJ	ON	2020/06/04 15:20
L5	1,502	514/569.ccls.	US-PGPUB; USPAT	ADJ	ON	2020/06/04 15:20

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence 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)

166905 7590 06/12/2020

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 transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916	4471

TITLE OF INVENTION: TREPROSTINIL ADMINISTRATION BY INHALATION

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1000	$0.00	$0.00	$1000	09/14/2020

EXAMINER	ART UNIT	CLASS-SUBCLASS
SCHMITT, MICHAEL J	1629	514-569000

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 03-09 or more recent) attached. **Use of a Customer Number is required.**

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

1 **Foley & Lardner LLP**
2
3

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

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: **United Therapeutics Corporation**

(B) RESIDENCE: (CITY and STATE OR COUNTRY): **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. Fees submitted: ☒ Issue Fee ❑ Publication Fee (if required) ❑ Advance Order - # of Copies _____

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

☒ Electronic Payment via EFS-Web ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. **19-0741**

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 **June 12, 2020**

Typed or printed name **Stephen B. Maebius** Registration No. **35,264**

Electronic Patent Application Fee Transmittal

Application Number:	16778662
Filing Date:	31-Jan-2020
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst OLSCHEWSKI
Filer:	Stephen Bradford Maebius/Karen Strawderman
Attorney Docket Number:	080618-1916

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	1000	1000

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**1000**

Electronic Acknowledgement Receipt

EFS ID:	39702767
Application Number:	16778662
International Application Number:	
Confirmation Number:	4471
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst OLSCHEWSKI
Customer Number:	166905
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1916
Receipt Date:	12-JUN-2020
Filing Date:	31-JAN-2020
Time Stamp:	12:10:29
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$1000
RAM confirmation Number	E20206BC10493521
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	Issue Fee Payment (PTO-85B)	IFTM.pdf	130851 b80826d8e49ec0aa628033a2111ab80e1f7cf7a2	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30715 077bfe3e585add3d7f03ff529feb34021e89daa4	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	161566		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916

CONFIRMATION NO. 4471

166905
Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

PUBLICATION NOTICE

OC00000017500744

Title:TREPROSTINIL ADMINISTRATION BY INHALATION

Publication No.US-2020-0171044-A1
Publication Date:06/04/2020

NOTICE OF PUBLICATION OF APPLICATION

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

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

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

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

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

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

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916	4471

166905 7590 05/15/2020

Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

EXAMINER
SCHMITT, MICHAEL J

ART UNIT	PAPER NUMBER
1629	

NOTIFICATION DATE	DELIVERY MODE
05/15/2020	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. 16/778,662	Applicant(s) OLSCHEWSKI et al.	
	Examiner MICHAEL J SCHMITT	Art Unit 1629	AIA (FITF) 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 1/31/2020.

☐ 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) 1-8 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) 1-8 is/are rejected.

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

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

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

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

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

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

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

Priority under 35 U.S.C. § 119

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

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

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

Attachment(s)

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

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

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

4) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending.

Notice of Pre-AIA or AIA Status

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

Priority

The instant application, filed 1/31/2020 is a continuation of 16/536,954, filed 8/9/2019. 16/536,954 is a continuation of 15/011,999, filed 2/1/2016, now U.S. Patent 10,376,525 and having 2 RCE-type filings therein. 15/011,999 is a division of 13/469,854, filed 5/11/2012, now U.S. Patent 9,339,507 and having 1 RCE-type filing therein. 13/469,854 is a division of 12/591,200, filed 11/12/2009, now U.S. Patent 9,358,240 and having 2 RCE-type filings therein. 12/591,200 is a continuation of 11/748,205, filed 5/14/2007, now abandoned and having 2 RCE-type filings therein. 11/748,205 claims Priority from Provisional Application 60/800,016, filed 5/15/2006.

Information Disclosure Statement

The Information Disclosure Statement (IDS) submitted on 1/31/2020, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the Information Disclosure Statement is being considered by the Examiner.

Double Patenting

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

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 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/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or

PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 1-8 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-9 of **U.S. Patent No. US 9,339,507**. Although the claims at issue are not identical, they are not patentably distinct from each other because '507 is a kit, a kit that would be used as directed in the instant method.

Claims 1-8 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-9 of **U.S. Patent No. US 9,358,240**. Although the claims at issue are not identical, they are not patentably distinct from each other because '240 is a directed towards treating the same disease with the same method as the instant, the two vary only in easily envisaged differences.

Claims 1-8 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-4 of **U.S. Patent No. US 10,376,525**. Although the claims at issue are not identical, they are not patentably distinct from each other because '525 is a directed towards treating the same disease with the same method as the instant, the two vary only in easily envisaged differences.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL J SCHMITT whose telephone number is (571)270-7047. The examiner can normally be reached on M-F 8-6 MidDay Flex.

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

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Lundgren can be reached on 571-272-5541. 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 https://ppair-my.uspto.gov/pair/PrivatePair. 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.

/MICHAEL J SCHMITT/
Examiner, Art Unit 1629

/JEFFREY S LUNDGREN/
Supervisory Patent Examiner, Art Unit 1629

Notice of References Cited	Application/Control No. 16/778,662	Applicant(s)/Patent Under Reexamination OLSCHEWSKI et al.	
	Examiner MICHAEL J SCHMITT	Art Unit 1629	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-9339507-B2	05-2016	Olschewski; Horst	A61P9/12	1/1
*	B	US-9358240-B2	06-2016	Olschewski; Horst	A61P43/00	1/1
*	C	US-10376525-B2	08-2019	Olschewski; Horst	A61P11/00	1/1
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

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

NON-PATENT DOCUMENTS

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

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	16/778,662	OLSCHEWSKI et al.
	Examiner	Art Unit
	MICHAEL J SCHMITT	1629

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
EAST search	05/05/2020	MS

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

/MICHAEL J SCHMITT/ Examiner, Art Unit 1629	

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	1	of	11	Attorney Docket Number	080618-1916

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	2003/0192532 A1	10/16/2003	Hopkins	
	A2	2004/0063912 A1	04/01/2004	Blumberg et al.	
	A3	2004/0105819 A1	06/03/2004	Hale et al.	
	A4	2004/0149282 A1	08/05/2004	Hickle	
	A5	2004/0265238 A1	12/30/2004	Chaudry, Imtiaz	
	A6	2005/0165111 A1	07/28/2005	Wade et al.	
	A7	2005/0166913 A1	08/04/2005	Sexton et al.	
	A8	2005/0183719 A1	08/25/2005	Wuttke et al.	
	A9	2005/0282901 A1	12/22/2005	Phares et al.	
	A10	2006/0147520 A1	07/06/2006	Ruegg, Curtis	
	A11	2006/0201500 A1	09/14/2006	Von Hollen et al.	
	A12	2008/0200449 A1	08/21/2008	Olschewski et al.	
	A13	2008/0280986A1	11/13/2008	Wade et al.	
	A14	2009/0036465 A1	02/05/2009	Roscigno et al.	
	A15	2010/0076083 A1	03/25/2010	Olschewski et al.	
	A16	2010/0236545 A1	09/23/2010	Kern	
	A17	2010/0282622 A1	11/11/2010	Phares, Kenneth R.	
	A18	2012/0177693 A1	07/12/2012	Cipolla et al.	
	A19	3,664,337	05/23/1972	Lindsey et al.	
	A20	4,001,650 A	01/04/1977	Romain	
	A21	4,281,113 A	07/28/1981	Axen et al.	
	A22	4,306,075	12/15/1981	Aristoff	
	A23	4,306,076 A	12/15/1981	Nelson, Norman A.	
	A24	4,349,689 A	09/14/1982	Aristoff, Paul A.	
	A25	4,473,296	09/25/1984	Shofner et al.	
	A26	4,486,598 A	12/04/1984	Aristoff, Paul A.	
	A27	4,495,944	01/29/1985	Brisson et al.	
	A28	4,635,647	01/13/1987	Choksi	
	A29	4,668,814 A	05/26/1987	Aristoff, Paul A.	
	A30	4,677,975	07/07/1987	Edgar et al.	
	A31	4,683,330 A	07/28/1987	Aristoff, Paul A.	
	A32	4,692,464 A	09/08/1987	Skuballa et al.	
	A33	4,708,963 A	11/24/1987	Skuballa et al.	
	A34	4,976,259	12/11/1990	Higson et al.	
	A35	4,984,158	01/08/1991	Hillsman	
	A36	5,063,922	11/12/1991	Hakkinen	
	A37	5,080,093 A	01/14/1992	Raabe et al.	
	A38	5,153,222	10/06/1992	Tadepalli et al.	
	A39	5,234,953 A	08/10/1993	Crow et al.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	2	of	11	Attorney Docket Number	080618-1916

U.S. PATENT DOCUMENTS

Examiner	Cite No.[1]	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant
	A40	5,322,057 A	06/21/1994	Raabe et al.	
	A41	5,361,989 A	11/08/1994	Merchat et al.	
	A42	5,363,842 A	11/15/1994	Mishelevich et al.	
	A43	5,497,763 A	03/12/1996	Lloyd et al.	
	A44	5,551,416 A	09/03/1996	Stimpson et al.	
	A45	5,727,542 A	03/17/1998	King	
	A46	5,865,171 A	02/02/1999	Cinquin	
	A47	5,881,715 A	03/16/1999	Shibasaki	
	A48	5,908,158 A	06/01/1999	Cheiman	
	A49	6,054,486 A	04/25/2000	Crow et al.	
	A50	6,123,068 A	09/26/2000	Lloyd et al.	
	A51	6,357,671	03/19/2002	Cewers, Goran	
	A52	6,521,212 B1	02/18/2003	GILLES et al.	
	A53	6,626,843 B2	09/30/2003	Hillsman	
	A54	6,756,033	06/29/2004	Cloutier et al.	
	A55	6,765,117 B2	07/20/2004	Moriarty et al.	
	A56	6,803,386 B2	10/12/2004	Shorr et al.	
	A57	6,809,223 B2	10/26/2004	Moriarty et al.	
	A58	7,172,557 B1	02/06/2007	Parker	
	A59	7,199,157 B2	04/03/2007	Wade et al.	
	A60	7,384,978 B2	06/10/2008	Phares et al.	
	A61	7,417,070 B2	08/26/2008	Phares et al.	
	A62	7,544,713 B2	06/09/2009	Phares et al.	
	A63	7,726,303 B2	07/01/2010	Tyvoll et al.	
	A64	4,007,238	02-08-1977	Glenn	
	A65	7,261,102	08-28-2007	Barney et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3]-Number[4]-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]
	A66	AU1999959533 B2	02/03/2000	Toray Industries, Inc.		
	A67	DE 19838711 C1	06/2000	Gessler		✓
	A68	DE 19934582 A1	01/2001	Buff		✓
	A69	FR 2783431 A1	03/24/2000	Systen Assistance Medical		A
	A70	JP 2003-522003 A	07/22/2003		=WO01/58514	✓
	A71	JP 2004-512101 A	04/22/2004	Glaxo Group Limited	=WO02/34318	✓
	A72	JP 2005-034341 A	02/10/2005	Teijin Ltd.		A
	A73	WO 93/00951 A1	01/21/1993	Inhale, Inc.		
	A74	WO 01/58514 A1	08/16/2001	Medic-Aid Limited		

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	3	of	11	Attorney Docket Number	080618-1916

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3]-Number[4]-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]
	A75	WO 01/85241 A1	11/15/2001	Pari GmbH		
	A76	WO 02/34318 A2	05/02/2002	Glaxo Group Limited		

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]
	A77	Abe et al., "Effects of inhaled prostacyclin analogue on chronic hypoxic pulmonary hypertension," J. Cardiovascular Pharmacology, 2001, 37, 239 251.	
	A78	Agnew JE, Bateman RM, Pavia D, Clarke SW. (1984) Radionuclide demonstration of ventilatory abnormalities in mild asthma. Clinical Science; 66: 525-531.	
	A79	Annals of the International Commission on Radiological Protection (ICRP) Vol 28, No. 3, 1998, Publication 80, Radiation Dose to Patients from Radiopharmaceuticals.	
	A80	Aradigm Corporation news release October 24, 2005, "Aradigm and United Therapeutics Sign Development and Commercialization Agreement Targeting Pulmonary Hypertension," Red Orbit News, http://www.redorbit.com/modules/news/tools.php?tool=print&id=281787, 2 pages.	
	A81	Aristoff et al., "Synthesis of benzopyran prostaglandins, potent stable prostacyclin analogs, via an intermolecular mitsunobu reaction," Tetrahedron Letters, 1984, 25(36):3955-3958.	
	A82	Badesch et al., "Prostanoid Therapy for Pulmonary Arterial Hypertension," Journal of the American College of Cardiology, 2004, 43(12:Suppl.S):56S-61S.	
	A83	Bein et al., "Cardiovascular and pulmonary effects of aerosolized prostacyclin administration in severe respiratory failure using a ventilator nebulization system," J. Cardiovascular Pharmacology, 1996, 27, 583-586.	
	A84	Benedict et al., "Evidence-based pharmacologic management of pulmonary arterial hypertension," Clinical Therapeutics, 2007, 29, 2134-2153.	
	A85	Bindl et al., "Aerosolised prostacyclin for pulmonary hypertension in neonates," Archives of disease in childhood, Fetal and neonatal edition, 1994, 71(3), F214-6.	
	A86	Blanchard, J.D., Cipolla, D., Liu, K., Morishige, R., Mudumba, S., Thipphawong, J., Taylor, G., Warren, S., Radhakrishnan, R., Van Vlasselaer, R., Visor , G. and Starko, K. (2003) Lung Deposition of Interferon Gamma-1b following Inhalation via AERx® System vs. Respirgard II™ Nebulizer Proc. ATS Annual Meeting (Abstract A373), Seattle.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	4	of	11	Attorney Docket Number	080618-1916

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]
	A87	Booke et al., "Prostaglandins in Patients with Pulmonary Hypertension: The Route of Administration," Anesth. Analg., 1998, 86:917, Letter to the Editor.	
	A88	Boyd, B., Noymer, P., Liu, K., Okikawa, J., Hasegawa, D., Warren, S., Taylor, G., Ferguson, E., Schuster, J., Farr, S., and Gonda, I. (2004) Effect of Gender and Device Mouthpiece Shape on Bolus Insulin Aerosol Delivery Using the AERx Pulmonary Delivery System. Pharmaceutical Research. 21 (10) 1776-1782.	
	A89	BYRON, Peter R., "Drug Delivery Devices, Issues in Drug Development," Proc. Am. Thorac. Soc., 2004, 1:321-328.	
	A90	Channick et al., "Safety and efficacy of inhaled treprostinil as add-on therapy to bosentan in pulmonary arterial hypertension," J. American College of Cardiology, 2006, 48, 1433-1437.	
	A91	Colthorpe P, Taylor G, Farr SJ. (1997) A comparison of two non-invasive methods for quantifying aerosol deposition in the lungs of rabbits. J. Aerosol Med.; 10:255	
	A92	Defendant Watson Laboratories, Inc.'s Invalidity Contentions for U.S. Patent Nos. 9,339,507 and 9,358,240, in The United States District Court for the District of New Jersey, Civil Action No. 3.15:cv-05723-PGS-LHG, August 5, 2016, 56 pages.	
	A93	Doyle et al., "Inhaled prostacyclin as a selective pulmonary vasodilator," Anaesthesia and Intensive Care, August 1996, 24(4):514-515.	
	A94	Dumas et al,. "Hypoxic pulmonary vasoconstriction," General Pharmacology, 1999, 33, 289-297.	
	A95	Dworetz et al., "Survival of infants with persistent pulmonary hypertension without extracorporeal membrane oxygenation," Pediatrics, 1989, 84, 1-6.	
	A96	EPA Integrated Risk Information System (IRIS): data sheet for 3-methylphenol (m-cresol). Accessed at http://www.epa.gov/iris/subst/0301/htm on 3/9/2014.	
	A97	EU Community Register, Annexes to Commission Decision C(2005)3436, September 5, 2005, http://ec.europa.eu/health/documents/communityregister/2005/2005090510259/anx_10259_en.pdf (Annex III –Ventavis® Labelling and Package Leaflet), 30 pages.	
	A98	Ewert et al., "Aerosolized iloprost for primary pulmonary hypertension," New England Journal of Medicine, 2000, 343, 1421-1422.	
	A99	Ewert et al., "Iloprost als inhalative bzw. Intravenose langzeitbehandlung von patienten mit primarer pulmonaler hypertonie," Z. Kardiol., 2000, 89, 987-999.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	5	of	11	Attorney Docket Number	080618-1916

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]
	A100	Farr et al., "Comparison of in vitro and in vivo efficiencies of a novel unit-dose liquid aerosol generator and a pressurized metered dose inhaler," International Journal of Pharmaceutics, 2000, 198:63-70.	
	A101	Final Office Action dated 10/10/2014 in US SN 12/591,200.	
	A102	Final Office Action dated 10/17/2012 in US SN 12/591,200.	
	A103	Final Office Action dated 11/4/2013 in US SN 12/303,877.	
	A104	Final Office Action dated 12/22/2011 in US SN 12/591,200.	
	A105	Final Office Action dated 7/2/2013 in US SN 13/120,015.	
	A106	Final Office Action dated 7/20/2015 in US SN 13/120,015.	
	A107	Final Office Action dated 8/1/2012 in US SN 12/303,877.	
	A108	Findlay et al., "Radioimmunoassay for the Chemical Stable Prostacyclin Analog, 15AU81: a Preliminary Pharmacokinetics Study in the Dog," Prostaglandins Leukot. Essent. Fatty Acids, February 1993, 48(2):167-174.	
	A109	Fink et al., "Use of Prostacyclin and its Analogues in the Treatment of Cardiovascular Disease," Heart Disease, 1999, 1:29-40.	
	A110	Gessler et al., "Ultrasonic versus jet nebulization of iloprost in severe pulmonary hypertension," Eur. Respir. J., 2001, 17, 14-19.	
	A111	GHOFRANI et al., "Hypoxia- and non-hypoxia-related pulmonary hypertension -- Established and new therapies," Cardiovascular Research, 2006, 72:30-40.	
	A112	Ghofrani et al., "New therapies in the treatment of pulmonary hypertension," Herz (Heart), 2005, 4:296-302, with English translation.	✓

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	6	of	11	Attorney Docket Number	080618-1916

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]
	A113	Hallioglu et al., "Comparison of Acute Hemodynamic Effects of Aerosolized and Intravenous *Iloprost* in Secondary Pulmonary Hypertension in Children With Congenital Heart Disease," Am. J. Cardiol., 2003, 92:1007-1009.	
	A114	Haraldsson et al., "Comparison of inhaled nitric oxide and inhaled aerosolized prostacyclin in the evaluation of heart transplant candidates with elevated pulmonary vascular resistance," Chest, 1998, 114, 780-786.	
	A115	Hoeper et al., "A comparison of the acute hemodynamic effects of inhaled nitric oxide and aerosolized iloprost in primary hypertension," J. American College of Cardiology, 2000, 35, 176-182.	
	A116	Hoeper et al., "Effects of inhaled nitric oxide and aerosolized iloprost in pulmonary veno-occlusive disease," Respiratory Medicine, 1999, 93, 62-70.	
	A117	Hoeper et al., "Long term treatment of primary pulmonary hypertension with aerosolized iloprost, a prostacyclin analogue," New England Journal of Medicine, 2000, 342, 1866-1870.	
	A118	Horn et al., "Treprostinil therapy for pulmonary artery hypertension," Expert Opinion on Investigational Drugs, 2002, 11(11):1615-1622.	
	A119	Howarth, P.H., "Why particle size should affect clinical response to inhaled therapy," Journal of Aerosol Medicine, 2001, 14 Supp. 1, S-27-S-34.	
	A120	Ichida et al., "Additive effects of beraprost on pulmonary vasodilation by inhaled nitric oxide in children with pulmonary hypertension," American Journal of Cardiology, 1997, 80, 662-664.	
	A121	Konorza et al., "Klinisch-pharmakologische Austestung bei pulmonaler Hypertonie zur Therapiefuehrung," Herz, 2005, 30:286-295, English abstract on first page.	A
	A122	Krause et al., "Pharmacokinetics and pharmacodynamics of the prostacyclin analogue iloprost in man," Eur. J. Clin. Pharmacol., 1986, 30, 61-68.	
	A123	Labiris et al., "Pulmonary drug delivery. Part II: The role of inhalant delivery devices and drug formulations in therapeutic effectiveness of aerosolized medications," Br. J. Clin. Pharmacol., 2003, 56(6):600-612.	
	A124	Lee et al., "Current strategies for pulmonary arterial hypertension," J. Internal Medicine, 2005, 258, 199-215.	
	A125	MARTIN, John C., "Inhaled Form of Remodulin in the Pipeline," http://www.phneighborhood.com/content/in_the_news/archive_2320.aspx, ph Neighborhood, October 28, 2005, 2 pages.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	7	of	11	Attorney Docket Number	080618-1916

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]
	A126	Max et al., "Inhaled prostacyclin in the treatment of pulmonary hypertension," Eur. J. Pediatr., 1999, 158 Suppl 1, S23-S26.	
	A127	McNulty et al., "The Pharmacokinetics and Pharmacodynamics of the Prostacyclin Analog 15AU81 in the Anesthetized Beagle Dog," Prostaglandins Leukot. Essent. Fatty Acids, February 1993, 48(2):159-166.	
	A128	Miller et al., "Standardisation of spirometry. Series ATS/ERS Task Force: Standardisation of Lung Function Testing" Eur Respir J 2005; 26: 319–338.	
	A129	Mueller et al., "Inhaled iloprost in the management of pulmonary hypertension in infants undergoing congenital heart surgery," European Journal of Anaesthesiology, June 2004, 21(Suppl.33):3, Abstract No. 084.	
	A130	National Radiological Protection Board. Doses to Patients from Medical Radiological Examinations in Great Britain. (1986) Radiological Protection Bulletin No. 77.	
	A131	Nebu-Tec med. Produkte Eike Kern GmbH, VENTA-NEB®-ir A-I-C-I® Operating Instrutions, Sep. 2005.	
	A132	Non-Final Office Action dated 1/29/2015 in US SN 13/120,015.	
	A133	Non-Final Office Action dated 10/11/2011 in US SN 12/303,877.	
	A134	Non-Final Office Action dated 10/31/2012 in US SN 13/120,015.	
	A135	Non-Final Office Action dated 12/30/2014 in US SN 12/303,877.	
	A136	Non-Final Office Action dated 3/15/2013 in US SN 12/303,877.	
	A137	Non-Final Office Action dated 3/9/2014 in US SN 12/591,200.	
	A138	Notes for Guidance on the Clinical Administration of Radiopharmaceuticals and Use of Sealed Radioactive Sources. Administration of Radioactive Substances Advisory Committee (ARSAC) (March 2006). ARSAC Secretariat, Chilton, Didcot, Oxon. OX11 0RQ.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: January 31, 2020

(use as many sheets as necessary)

Sheet 8 of 11

Complete if Known	
Application Number	Unassigned
Filing Date	Herewith
First Named Inventor	Horst OLSCHEWSKI
Art Unit	Unassigned
Examiner Name	Unassigned
Attorney Docket Number	080618-1916

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]
	A139	Notice of Allowance dated 6/11/2015 in US SN 12/303,877.	
	A140	Olschewski et al. for the German PPH Study Group, "Inhaled iloprost to treat severe pulmonary hypertension – An uncontrolled trial," Annals of Internal Medicine, 2000, 132, 435-443.	
	A141	Olschewski et al., "Aerosolized prostacyclin and iloprost in severe pulmonary hypertension,: Annals of Internal Medicine, 1996, 124, 820 824.	
	A142	Olschewski et al., "Inhaled Iloprost for Severe Pulmonary Hypertension," N. Eng. J. Med., August 1, 2002, 347(5):322-329.	
	A143	Olschewski et al., "Inhaled prostacyclin and iloprost in severe pulmonary hypertension secondary to lung fibrosis," Am. Respir. Crit. Care Med., 1999, 160, 600-607.	
	A144	Olschewski et al., "Pharmacodynamics and pharmacokinetics of inhaled iloprost, aerosolized by three different devices, in severe pulmonary hypertension," Chest, 2003, 124, 1294-1304.	
	A145	Olschewski et al., "Prostacyclin and its analogues in the treatment of pulmonary hypertension," Pharmacology and Therapeutics, 2004, 102, 139-153.	
	A146	Olschewski et al., "Recovery from circulatory shock in severe primary pulmonary hypertension (PPH) with aerosolization of iloprost," Intensive Care Med., 1998, 24, 631-634.	
	A147	Olschewski, Horst, "Therapie der pulmonalen Hypertonie," Pneumologe, 2004, 1:95-101.	
	A148	OPTINEB®-ir Operating Instructions, Unit Type ON-100/2-2.4 MHz, 2005, 33 pages, verified English translation.	
	A149	Pappert et al., "Aerosolized Prostacyclin Versus Inhaled Nitric Oxide in Children with Severe Acute Respiratory Distress Syndrome," Anesthesiology, June 1995, 82(6):1507-1511.	
	A150	Publications of the International Commission on Radiological Protection (ICRP) (1977) Recommendations of the International Commission on Radiological Protection 26.	
	A151	Pulmonary Delivery, ONdrugDelivery, 2006, 5 pages.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	9	of	11	Attorney Docket Number	080618-1916

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]
	A152	RIGBY, Jonathan, Aradigm Corporation, "Technological advances for success: Product pipeline in targeted pulmonary delivery," Pulmonary Delivery Innovative Technologies Breathing New Life into Inhalable Therapeutics, ONdrugDelivery, http://www.ondrugdelivery.com/publications/Pulmonary.pdf, 2006, 17-19.	
	A153	Rubin et al., "Pulmonary Arterial Hypertension: A Look to the Future," Journal of the American College of Cardiology, June 18, 2004, 43(12,Suppl.S):89S-90S.	
	A154	Saini et al., "Effect of Electrostatic Charge and Size Distributions on Respirable Aerosol Deposition in Lung Model," Industry Applications Conference, 2004, 39th IAS Annual Meeting, Conference Record of the 2004 IEEE Seattle, WA, October 3-7, 2004, 2:948-952.	
	A155	Sandifer et al., "Effects of Aerosol vs IV UT-15 on Prostaglandin H_2 Analog-Induced Pulmonary Hypertension in Sheep," Chest, 2005, 128:616S.	
	A156	SANDIFER et al., "Potent effects of aerosol compared with intravenous treprostinil on the pulmonary circulation," J. Appl. Physiol., 2005, 99:2363-2368.	
	A157	Santak et al., "Prostacyclin aerosol in an infant with pulmonary hypertension," Eur. J. Pediatr., 1995, 154, 233-235.	
	A158	Scientific discussion for the approval of Ventavis, European Medicines Agency (EMEA), October 20, 2004, 30 pages.	
	A159	Soditt et al., "Improvement of oxygenation induced by aerosolized prostacyclin in a preterm infant with persistent pulmonary hypertension of the newborn," Intensive Care Med., 1997, 23, 1275-1278.	
	A160	Steffen et al., "The Effects of 15AU81, a Chemically Stable Prostacyclin Analog, on the Cardiovascular and Renin-Angiotensis Systems of Anesthetized Dogs," Prostaglandins, Leukotrienes and Essential Fatty Acids," 1991, 43:277-286.	
	A161	Stricker et al., "Sustained improvement of performance and haemodynamics with long-term aerosolized prostacyclin therapy in severe pulmonary hypertension," Schweiz Med. Wochenschr., 1999, 129, 923-927.	
	A162	Van Heerden et al., "Inhaled aerosolized prostacyclin as a selective pulmonary vasodilator for the treatment of severe hypertension," Anaesthesia and Intensive Care, 1996, 24, 87-90.	
	A163	Van Heerden et al., "Re: Delivery of inhaled aerosolized prostacyclin (IAP)," Anaesthesia and Intensive Care, 1996, 24, 624-625.	
	A164	Voswinckel et al., "Acute effects of the combination of sildenafil and inhaled treprostinil on haemodynamics and gas exchange in pulmonary hypertension," Pulmonary Pharmacology & Therapeutics, 2008, 21, 824-832.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	10	of	11	Attorney Docket Number	080618-1916

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]
	A165	VOSWINCKEL et al., "Favorable Effects of Inhaled Treprostinil in Severe Pulmonary Hypertension," Journal of the American College of Cardiology, 2006, 48(8):1672-1681.	
	A166	VOSWINCKEL et al., "Inhaled Treprostinil for Treatment of Chronic Pulmonary Arterial Hypertension," Annals of Internal Medicine, January 17, 2006, 144(2):149-150.	
	A167	Voswinckel et al., "Inhaled treprostinil is a potent pulmonary vasodilator in severe pulmonary hypertension," European Heart Journal, Journal of the European Society of Cardiology, ESC Congress, August 28 - September 1, 2004, Munich, Germany, p. 22, abstract 218.	
	A168	Voswinckel et al., "Inhaled Treprostinil Sodium (TRE) for the Treatment of Pulmonary Hypertension," Circulation, October 2004, Abstract 1414, 110, 17 Supplement.	
	A169	Voswinckel et al., "Inhaled Treprostinil Sodium (TRE) for the Treatment of Pulmonary Hypertension," Circulation, October 26, 2004, Supplement, 110(17):295, abstract 1414.	
	A170	Walmrath et al., "Effects of inhaled versus intravenous vasodilators in experimental pulmonary hypertension," Eur. Respir. J., 1997, 10, 1084-1092.	
	A171	Wasserman et al., "Bronchodilator effects of prostacyclin (PGI2) in dogs and guinea pigs," European Journal of Pharmacology, 1980, 66, 53-63.	
	A172	*Watson Laboratories, Inc. (Petitioner) v. United Therapeutics Corp. (Patent Owner)*, Decision Granting Institute of *Inter Partes* Review 37 C.F.R. 42.108, IRP2017-01621, Patent No. 9,358,240, January 11, 2018.	
	A173	*Watson Laboratories, Inc. (Petitioner) v. United Therapeutics Corp. (Patent Owner)*, Decision Granting Institute of *Inter Partes* Review 37 C.F.R. 42.108, IRP2017-01622, Patent No. 9,339,507, January 11, 2018.	
	A174	*Watson Laboratories, Inc. (Petitioner) v. United Therapeutics, Inc. (Patent Owner)*, Petition for *Inter Partes* Review, IRP2017-01622, Patent No. 9,339,507, with all Exhibits on exhibit list.	
	A175	*Watson Laboratories, Inc. (Petitioner) v. United Therapeutics, Inc. (Patent Owner)*, Petition for *Inter Partes* Review, IRP2017-01621, Patent No. 9,358,240, with only Exhibits 1002, 1059, 1161 and 1164 and not including exhibits already provide with C2.	
	A176	Webb et al., "The use of inhaled aerosolized prostacyclin (IAP) in the treatment of pulmonary hypertension secondary to pulmonary embolism," Intensive Care Med., 1996, 22, 353-355.	
	A177	Wensel et al., "Effects of iloprost inhalation on exercise capacity and ventilator efficiency in patients with primary pulmonary hypertension," Circulation, 2000, 101, 2388-2392.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

PTO/SB/08 (09-06)
Approved for use through 03/31/2007. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	11	of	11	Attorney Docket Number	080618-1916

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]
	A178	Wetzel, R.C., "Aerosolized prostacyclin: in search of the ideal pulmonary vasodilator," Anesthesiology, 1995, 82, 1315-1317.	
	A179	Wittwer et al., "Inhalative Pre-Treatment of Donor Lungs Using the Aerosolized Prostacyclin Analog Iliprost Ameliorates Reperfusion Injury," J. Heart Lung Transplant, 2005, 24:1673-1679.	
	A180	Zanen et al., "Optimal particle size for beta 2 agonist and anticholinergic aerosols in patients with severe airflow obstruction," Thorax, 1996, 51, 977-980.	
	A181	Zanen et al., "The optimal particle size for β-adrenergic aerosols in mild asthmatics," International Journal of Pharmaceutics, 1994, 107, 211-217.	

Examiner Signature	/MICHAEL J SCHMITT/	Date Considered	05/05/2020

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.J.S/

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	2	pulmonary.clm. and treprostinil.clm. and breath.clm. and microgram.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	ADJ	ON	2020/05/05 15:36
S2	9	pulmonary.clm. and treprostinil.clm. and breath.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	ADJ	ON	2020/05/05 15:39
S3	9	pulmonary.clm. and treprostinil.clm. and breaths.clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	ADJ	ON	2020/05/05 15:39

EAST Search History (Interference)

		<This search history is empty>				

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:	Horst OLSCHEWSKI
Title:	TREPROSTINIL ADMINISTRATION BY INHALATION
Appl. No.:	16/778,662
Filing Date:	1/31/2020
Examiner:	Michael J. SCHMITT
Art Unit:	1629
Confirmation Number:	4471

RESPONSE

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

Commissioner:

This communication is responsive to the outstanding non-final Office Action mailed on May 15, 2020, concerning the above-referenced patent application.

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

Remarks begin on page 3 of this document.

Please amend the application as follows:

1. (Original) A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device, wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

2. (Original) The method of claim 1, wherein the inhalation device is a soft mist inhaler.

3. (Original) The method of claim 1, wherein the inhalation device is a pulsed ultrasonic nebulizer.

4. (Original) The method of claim 1, wherein the inhalation device is a dry powder inhaler.

5. (Original) The method of claim 1, wherein the inhalation device is a pressurized metered dose inhaler.

6. (Original) The method of claim 4, wherein the formulation is a powder.

7. (Original) The method of claim 6, wherein the powder comprises particles less than 5 micrometers in diameter.

8. (Original) The method of claim 1, wherein the formulation contains no metacresol.

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

Status of Claims

Claims 1-8 are pending. No claim is amended.

Obviousness-Type Double Patenting

Claims 1-8 are rejected under the judicially created doctrine of obviousness-type double patenting based upon claims of US Patent Nos. 9,339,507, 9,358,240, and 10,376,525. Without acquiescing in the rejection and solely to expedite prosecution, Applicant submits herewith a terminal disclaimer to obviate the rejections.

Applicant believes that the application is in condition for allowance. Favorable consideration 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 which may be required for this application to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extensions under 37 CFR § 1.136 and authorizes payment of any such extension fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date May 15, 2020

By /Stephen B. Maebius/

FOLEY & LARDNER LLP
Customer Number: 166905
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

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

Electronic Acknowledgement Receipt

EFS ID:	39451057
Application Number:	16778662
International Application Number:	
Confirmation Number:	4471
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst OLSCHEWSKI
Customer Number:	166905
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1916
Receipt Date:	15-MAY-2020
Filing Date:	31-JAN-2020
Time Stamp:	12:28:06
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		Response.pdf	122811 51bcde5197c516b8df7fca584d80f0839a0271ba	yes	3

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1
	Claims	2	2
	Applicant Arguments/Remarks Made in an Amendment	3	3
Warnings:			
Information:			
	Total Files Size (in bytes):	122811	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: DIST.E.FILE **Document Description: Electronic Terminal Disclaimer - Filed**	PTO/SB/26 U.S. Patent and Trademark Office Department of Commerce

Electronic Petition Request	**TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT**
Application Number	16778662
Filing Date	31-Jan-2020
First Named Inventor	Horst OLSCHEWSKI
Attorney Docket Number	080618-1916
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION

☒ Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action

☒ This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.

Owner	Percent Interest
United Therapeutics Corporation	100%

The owner(s) with percent interest listed above 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 prior patent number(s)

10376525

9358240

9339507

as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of 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.

◉ Terminal disclaimer fee under 37 CFR 1.20(d) is included with Electronic Terminal Disclaimer request.

○ I certify, in accordance with 37 CFR 1.4(d)(4), that the terminal disclaimer fee under 37 CFR 1.20(d) required for this terminal disclaimer has already been paid in the above-identified application.

Applicant claims the following fee status:

○ Small Entity

○ Micro Entity

◉ Regular Undiscounted

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

THIS PORTION MUST BE COMPLETED BY THE SIGNATORY OR SIGNATORIES

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

◉ An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application

Registration Number 35264

○ A sole inventor

○ A joint inventor; I certify that I am authorized to sign this submission on behalf of all of the inventors as evidenced by the power of attorney in the application

○ A joint inventor; all of whom are signing this request

Signature	/Stephen B. Maebius/
Name	Stephen B. Maebius

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

Electronic Patent Application Fee Transmittal

Application Number:	16778662
Filing Date:	31-Jan-2020
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst OLSCHEWSKI
Filer:	Stephen Bradford Maebius/Karen Strawderman
Attorney Docket Number:	080618-1916

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
STATUTORY OR TERMINAL DISCLAIMER	1814	1	160	160
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**160**

Doc Code: DISQ.E.FILE
Document Description: Electronic Terminal Disclaimer – Approved

Application No.: 16778662

Filing Date: 31-Jan-2020

Applicant/Patent under Reexamination: OLSCHEWSKI

Electronic Terminal Disclaimer filed on May 15, 2020

☒ APPROVED

This patent is subject to a terminal disclaimer

☐ DISAPPROVED

Approved/Disapproved by: Electronic Terminal Disclaimer automatically approved by EFS-Web

U.S. Patent and Trademark Office

Electronic Acknowledgement Receipt

EFS ID:	39451012
Application Number:	16778662
International Application Number:	
Confirmation Number:	4471
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst OLSCHEWSKI
Customer Number:	166905
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1916
Receipt Date:	15-MAY-2020
Filing Date:	31-JAN-2020
Time Stamp:	12:30:20
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$160
RAM confirmation Number	E20205EC30157071
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	Terminal Disclaimer-Filed (Electronic)	eTerminal-Disclaimer.pdf	33926 fcc82ab5224cb5995730caf4f14f924999efc24a	no	2
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30809 dc2b3b682521bf5062c3f9d5f4164fe0b0b0553d	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	64735		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 16/778,662	Filing Date 01/31/2020	☐ To be Mailed

ENTITY: ☑ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $100 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $460 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT	05/15/2020	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 8	Minus	** 20	= 0		x $100 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0		x $460 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

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

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

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

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

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916

CONFIRMATION NO. 4471

166905
Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

37 CFR 1.48 ACKNOWLEDGEMENT LETTER

OC000000115124715

Date Mailed: 03/04/2020

NOTICE OF ACCEPTANCE OF REQUEST UNDER 37 CFR 1.48(a)

This is in response to the applicant's request under 37 CFR 1.48(a) submitted on 02/24/2020.

The request under 37 CFR 1.48(a) to correct the inventorship, to correct or update the name of an inventor, or to correct the order of names of joint inventors is accepted.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/mmasfaw/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
16/778,662	01/31/2020	1629	1720	080618-1916	8	1

CONFIRMATION NO. 4471

UPDATED FILING RECEIPT

166905
Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

OC000000115124714

Date Mailed: 03/04/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Horst OLSCHEWSKI, Graz, AUSTRIA;
Robert ROSCIGNO, Chapel Hill, NC;
Lewis J. RUBIN, LaJolla, CA;
Thomas Schmehl, Giessen, GERMANY;
Werner SEEGER, Giessen, GERMANY;
Carl STERRITT, Weybridge, UNITED KINGDOM;
Robert VOSWINCKEL, Giessen, GERMANY;

Applicant(s)

United Therapeutics Corporation, Siliver Spring, MD;

Assignment For Published Patent Application

United Therapeutics Corporation, Silver Spring, MD

Power of Attorney: The patent practitioners associated with Customer Number 166905

Domestic Priority data as claimed by applicant

This application is a CON of 16/536,954 08/09/2019
which is a CON of 15/011,999 02/01/2016 PAT 10376525
which is a DIV of 13/469,854 05/11/2012 PAT 9339507
which is a DIV of 12/591,200 11/12/2009 PAT 9358240
which is a CON of 11/748,205 05/14/2007 ABN
which claims benefit of 60/800,016 05/15/2006

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: No

Permission to Access Search Results: No

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

Projected Publication Date: 06/04/2020

Non-Publication Request: No

Early Publication Request: No
Title

TREPROSTINIL ADMINISTRATION BY INHALATION

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 AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

United States Patent and Trademark Office

Office of the Chief Financial Officer

Document Code:WFEE

User :C46575

Sale Accounting Date:03/03/2020

Sale Item Reference Number	Effective Date
16778662	02/24/2020

Document Number	Fee Code	Fee Code Description	Amount Paid	Payment Method
I202033957539844	1830	PROCESSING FEE, EXCEPT PROV. APPLS.	$140.00	Deposit Account

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:	Horst OLSCHEWSKI
Title:	TREPROSTINIL ADMINISTRATION BY INHALATION
Appl. No.:	16/778,662
Filing Date:	1/31/2020
Examiner:	Unassigned
Art Unit:	Unassigned
Confirmation Number:	4471

REQUEST FOR CORRECTED FILING RECEIPT

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

Commissioner:

Attached is a copy of the updated Filing Receipt dated February 27, 2020, marked to request inclusion of the fourth inventor as follows:

The inventor names should read:

Horst OLSCHEWSKI, Graz, AUSTRIA;
Robert ROSCIGNO, Chapel Hill, NC;
Lewis J. RUBIN, LaJolla, CA;
Thomas SCHMEHL, Giessen, GERMANY;
Werner SEEGER, Giessen, GERMANY;
Carl STERRITT, Weybridge, UNITED KINGDOM;
Robert VOSWINCKEL, Giessen, GERMANY;

The correction is not due to any error by Applicant as the inventors appear correctly on the properly signed ADS filed on February 24, 2020. Accordingly, no fee is due.

Issuance of a corrected Filing Receipt is respectfully requested.

Respectfully submitted,

Date FEB 28 2020

By _____

FOLEY & LARDNER LLP
Customer Number: 166905
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
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL. FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
16/778,662	01/31/2020		1720	080618-1916	8	1

CONFIRMATION NO. 4471

UPDATED FILING RECEIPT

166905
Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

OC000000114984218

Date Mailed: 02/27/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Horst OLSCHEWSKI, Graz, AUSTRIA;
Robert ROSCIGNO, Chapel Hill, NC;
Lewis J. RUBIN, LaJolla, CA;
Werner SEEGER, Giessen, GERMANY;
Carl STERRITT, Weybridge, UNITED KINGDOM;
Robert VOSWINCKEL, Giessen, GERMANY;

Thomas SCHMEHL, Giessen, GERMANY >

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 166905

Domestic Priority data as claimed by applicant

This application is a CON of 16/536,954 08/09/2019
which is a CON of 15/011,999 02/01/2016 PAT 10376525
which is a DIV of 13/469,854 05/11/2012 PAT 9339507
which is a DIV of 12/591,200 11/12/2009 PAT 9358240
which is a CON of 11/748,205 05/14/2007 ABN
which claims benefit of 60/800,016 05/15/2006

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: No

Permission to Access Search Results: No

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

If Required, Foreign Filing License Granted: 02/19/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/778,662**

Projected Publication Date: 06/04/2020

Non-Publication Request: No

Early Publication Request: No
Title

TREPROSTINIL ADMINISTRATION BY INHALATION

Preliminary Class

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 AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

Electronic Acknowledgement Receipt

EFS ID:	38724626
Application Number:	16778662
International Application Number:	
Confirmation Number:	4471
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst OLSCHEWSKI
Customer Number:	166905
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1916
Receipt Date:	28-FEB-2020
Filing Date:	31-JAN-2020
Time Stamp:	14:08:04
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Corrected Filing Receipt	ReqCorrOFR.pdf	361191 913919266320bc2b4f049aaf1df7a9e30fa765ba	no	6

Warnings:

Information:	
Total Files Size (in bytes):	361191

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.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 16/778,662

APPLICATION AS FILED - PART I

	(Column 1)	(Column 2)	SMALL ENTITY		OR	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	300
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	660
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	760
TOTAL CLAIMS (37 CFR 1.16(i))	8 minus 20 =	*			OR	x 100 =	0.00
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*				x 460 =	0.00
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	1720

APPLICATION AS AMENDED - PART II

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

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

* 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.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
16/778,662	01/31/2020		1720	080618-1916	8	1

CONFIRMATION NO. 4471

UPDATED FILING RECEIPT

166905
Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

OC000000114984218

Date Mailed: 02/27/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Horst OLSCHEWSKI, Graz, AUSTRIA;
Robert ROSCIGNO, Chapel Hill, NC;
Lewis J. RUBIN, LaJolla, CA;
Werner SEEGER, Giessen, GERMANY;
Carl STERRITT, Weybridge, UNITED KINGDOM;
Robert VOSWINCKEL, Giessen, GERMANY;

Applicant(s)

United Therapeutics Corporation, Siliver Spring, MD;

Assignment For Published Patent Application

United Therapeutics Corporation, Silver Spring, MD

Power of Attorney: The patent practitioners associated with Customer Number 166905

Domestic Priority data as claimed by applicant

This application is a CON of 16/536,954 08/09/2019
which is a CON of 15/011,999 02/01/2016 PAT 10376525
which is a DIV of 13/469,854 05/11/2012 PAT 9339507
which is a DIV of 12/591,200 11/12/2009 PAT 9358240
which is a CON of 11/748,205 05/14/2007 ABN
which claims benefit of 60/800,016 05/15/2006

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: No

Permission to Access Search Results: No

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

If Required, Foreign Filing License Granted: 02/19/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/778,662**

Projected Publication Date: 06/04/2020

Non-Publication Request: No

Early Publication Request: No
Title

TREPROSTINIL ADMINISTRATION BY INHALATION

Preliminary Class

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 AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916

CONFIRMATION NO. 4471

166905
Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

POA ACCEPTANCE LETTER

OC000000114984184

Date Mailed: 02/27/2020

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 02/24/2020.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/agizaw/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/778,662	01/31/2020	Horst OLSCHEWSKI	080618-1916	4471

166905 7590 02/27/2020

Foley & Lardner LLP
3000 K Street N.W.
Suite 600
Washington, DC 20007-5109

EXAMINER	

ART UNIT	PAPER NUMBER
1629	

NOTIFICATION DATE	DELIVERY MODE
02/27/2020	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

Decision Granting Request for Prioritized Examination (Track I)	**Application No.** 16/778,662	**Applicant(s)** OLSCHEWSKI et al.	
	Examiner BRIAN W BROWN	**Art Unit** OPET	**AIA (FITF) Status** No

1. THE REQUEST FILED 31 January 2020 IS **GRANTED** .

The above-identified application has met the requirements for prioritized examination

A. ☑ for an original nonprovisional application (Track I).
B. ☐ for an application undergoing continued examination (RCE).

2. **The above-identified application will undergo prioritized examination**. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:

A. filing a **petition for extension of time** to extend the time period for filing a reply;

B. filing an **amendment to amend the application to contain more than four independent claims, more than thirty total claims** , or a multiple dependent claim;

C. filing a **request for continued examination** ;

D. filing a notice of appeal;

E. filing a request for suspension of action;

F. mailing of a notice of allowance;

G. mailing of a final Office action;

H. completion of examination as defined in 37 CFR 41.102; or

I. abandonment of the application.

Telephone inquiries with regard to this decision should be directed to BRIAN BROWN at (571)272-5338. In his/her absence, calls may be directed to Petition Help Desk at (571) 272-3282.

/BRIAN W BROWN/ Petitions Examiner, OPET	

PTO/AIA/80 (07-12)
Approved for use through 11/30/2014. OMB 0651-0035
U.S. Patent and Trademark Office; U.S DEPARTMENT OF COMMERCE

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: 166905

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 assigned 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: 166905

OR

☐

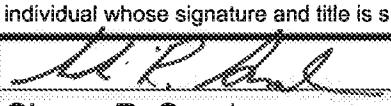
Firm or Individual Name			
Address			
City			
Country			
Telephone		Email	

Assignee Name and Address: United Therapeutics Corporation
1040 Spring Street
Silver Spring, MD 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	03 February 2020
Name	Shaun R. Snader	Telephone	202-304-1701
Title	Vice President, Associate General Counsel, IP		

Electronic Acknowledgement Receipt

EFS ID:	38673118
Application Number:	16778662
International Application Number:	
Confirmation Number:	4471
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst Olschewski
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1916
Receipt Date:	24-FEB-2020
Filing Date:	31-JAN-2020
Time Stamp:	16:18:43
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Applicant Response to Pre-Exam Formalities Notice	TMMP.pdf	112878 e72db3b71b8ee2f61ccdab9b642f66c5d689b9d3	no	2

Warnings:

Information:					
2	Application Data Sheet	MarkedADS.pdf	189949 460cb95ab7a0dd7dad86fddaabb8b5c865214061	no	11
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
3	Assignee showing of ownership per 37 CFR 3.73	373cStmt.pdf	1875981 11d871e8b63dbdea2eaee5f19d08a7271ab2fd38	no	3
Warnings:					
Information:					
4	Power of Attorney	UTC_USPOA_166905.pdf	135599 bddae766cf8b80d5ccae20f78254b4db6ac208ea	no	1
Warnings:					
Information:					
		Total Files Size (in bytes):	2314407		

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:	Horst OLSCHEWSKI
Title:	TREPROSTINIL ADMINISTRATION BY INHALATION
Application No.:	16/778,662
Filing Date:	1/31/2020
Examiner:	Unassigned
Art Unit:	Unassigned
Confirmation No.:	4471

TRANSMITTAL OF MISSING PARTS OF PATENT APPLICATION

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

Commissioner:

In response to the Notice to File Missing Parts of Application mailed February 21, 2020, in the above-identified patent application, transmitted herewith is a properly executed marked Application Data Sheet. Also submitted herewith are copies of the Statement Under 37 CFR 3.73(c) and Power of Attorney filed on February 5, 2020.

Favorable action is solicited.

It is believed no additional fees are required, however, authorization is given to charge any fees which may be required for this application to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date February 24, 2020

By /Stephen B. Maebius/

FOLEY & LARDNER LLP
Customer Number: 166905
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

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

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Horst		OLSCHEWSKI	

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

City	Graz	Country of Residence	AT

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation
Address 2	1040 Spring Street

City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Robert		ROSCIGNO	

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

City	Chapel Hill	State/Province	NC	Country of Residence	US

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation
Address 2	1040 Spring Street

City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 3 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Lewis	J.	RUBIN	

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

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

City	LaJolla	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 4 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Thomas		SCHMEHL	

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

City	Giessen	Country of Residence	DE

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 5 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Werner		SEEGER	

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

City	Giessen	Country of Residence	DE

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 6 Remove

Legal Name

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Prefix	Given Name	Middle Name	Family Name	Suffix
	Carl		STERRITT	

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

City	Weybridge	Country of Residence ⓘ	GB

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	**State/Province**	MD
Postal Code	20910	**Country** ⓘ	

Inventor 7 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Robert		VOSWINCKEL	

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

City	Giessen	Country of Residence ⓘ	DE

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	**State/Province**	MD
Postal Code	20910	**Country** ⓘ	

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

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

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

Customer Number	22428		
Email Address	IPDocketing@foley.com	Add Email	Remove Email

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Application Information:

Title of the Invention	TREPROSTINIL ADMINISTRATION BY INHALATION		
Attorney Docket Number	080618-1916	**Small Entity Status Claimed** ☐	
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	12	**Suggested Figure for Publication (if any)**	

Filing By Reference:

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

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

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

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	22428		

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	16/536954	2019-08-09
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
16/536954	Continuation of	15/011999	2016-02-01
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15/011999	Division of	13/469854	2012-05-11
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13/469854	Division of	12/591200	2009-11-12
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
12/591200	Continuation of	11/748205	2007-05-14
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
11/748205	Claims benefit of provisional	60/800016	2006-05-15

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

Foreign Priority Information:

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove

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

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

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

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

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Authorization or Opt-Out of Authorization to Permit Access:

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

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

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

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

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

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

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

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

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

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

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

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Applicant Information:

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

Applicant 1

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

Clear

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

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

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	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	
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.

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

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. ☒

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

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

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

Signature	~~/Stephen B. Maebius/~~ /Stephen B. Maebius/			Date (YYYY-MM-DD)	2020-01-31
First Name	Stephen B.	Last Name	Maebius	Registration Number	35264

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

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

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

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

1 The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3 A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent CooperationTreaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

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

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: United Therapeutics Corporation Atty. Dkt. No. 080618-1916

Application No./Patent No.: 16/778,662 Filed/Issue Date: 1/31/2020

Titled: TREPROSTINIL ADMINISTRATION BY INHALATION

United Therapeutics Corporation, a Corporation

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☑ The assignee of the entire right, title, and interest.

2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):

☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. ☑ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 023223, Frame 0716, or for which a copy thereof is attached.

B. ☐ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

2. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

4. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

5. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

6. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☐ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Stephen B. Maebius/	2/5/2020
Signature	Date
Stephen B. Maebius	35,264
Printed or Typed Name	Title or Registration 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.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
16/778,662	01/31/2020		1720	080618-1916	8	1

CONFIRMATION NO. 4471

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

FILING RECEIPT

OC000000114846828

Date Mailed: 02/21/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Horst Olschewski, Residence Not Provided;
Robert ROSCIGNO, Residence Not Provided;
Lewis J. RUBIN, Residence Not Provided;
Werner SEEGER, Residence Not Provided;

Applicant(s)

Horst Olschewski, Residence Not Provided;
Robert ROSCIGNO, Residence Not Provided;
Lewis J. RUBIN, Residence Not Provided;
Werner SEEGER, Residence Not Provided;

Assignment For Published Patent Application

United Therapeutics Corporation, Silver Spring, MD

Power of Attorney: None

Domestic Applications for which benefit is claimed - None.
A proper domestic benefit claim must be provided in an Application Data Sheet in order to constitute a claim for domestic benefit. See 37 CFR 1.76 and 1.78.

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: No

Permission to Access Search Results: No

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

If Required, Foreign Filing License Granted: 02/19/2020
The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/778,662**
Projected Publication Date: To Be Determined - pending completion of Missing Parts
Non-Publication Request: No
Early Publication Request: No
Title

TREPROSTINIL ADMINISTRATION BY INHALATION

Preliminary Class

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 AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop

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

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/778,662	01/31/2020	Horst Olschewski	080618-1916

CONFIRMATION NO. 4471

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

OC000000114846835

Date Mailed: 02/21/2020

Improper Submission of Authorization to Permit Access to Search Results under 37 CFR 1.14(h)(2)

The Authorization to Permit Access to the Search Results from the instant application under 37 CFR 1.14(h)(2) (authorization to permit access to search results) submitted on 01/31/2020 in the above-identified application is not accepted because:

- It was not properly signed. If applicant still wishes to provide authorization to permit access to the search results under 37 CFR 1.14(h)(2), applicant must submit a properly signed authorization (e.g., PTO/SB/69).

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/mhaile/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/778,662	01/31/2020	Horst Olschewski	080618-1916

CONFIRMATION NO. 4471

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

FORMALITIES LETTER

OC000000114846829

Date Mailed: 02/21/2020

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

Items Required To Avoid Abandonment:

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- Complete residence information, either city and state or city and country for **Horst Olschewski**, **Robert ROSCIGNO**, **Lewis J. RUBIN**, and **Werner SEEGER** has not been provided. Residence information is required, separately from the mailing address, if the inventor lives at a location which is different from where the inventor customarily receives mail. Also, a valid state code or a valid country code must be provided. For lists of valid state and valid country codes, see the Instructions for Application Data Sheet available at https://www.uspto.gov/patent/forms/forms-patent-applications-filed-or-after-september-16-2012. There is an indication on either the ADS or the inventor's oath or declaration that the mailing address and residence information is not the same for this inventor.
  Applicant must provide the residence information on either:
  - An inventor's oath or declaration in compliance with 37 CFR 1.63, or
  - A properly marked up application data sheet (ADS) in compliance with 37 CFR 1.76.
- A complete mailing address that includes either the city and state or city and country, for each inventor has not been submitted. Applicant must provide the mailing address on either:
  - An inventor's oath or declaration in compliance with 37 CFR 1.63, or
  - A properly marked up application data sheet (ADS) in compliance with 37 CFR 1.76.

  Note that an inventor's mailing address is required even if a correspondence address has been submitted. An inventor's mailing address may not necessarily be the same as the correspondence address for the application and must be separately submitted in the manner set forth above. If the inventor lives at a location which is different from the inventor's mailing address, the inventor's residence (either city and state or city and country) must also be separately submitted in the manner set forth above. For lists of valid state and valid country codes, see the Instructions for Application Data Sheet available at https://www.uspto.gov/patent/forms/forms-patent-applications-filed-or-after-september-16-2012.
  Mailing address information is needed for the following inventor(s): **Horst Olschewski**, **Robert ROSCIGNO**, **Lewis J. RUBIN**, and **Werner SEEGER**

Items Required To Avoid Processing Delays:

Applicant is notified that the above-identified application contains the deficiencies noted below. No period for reply is set forth in this notice for correction of these deficiencies. However, if a deficiency relates to the inventor's oath or declaration, the applicant must file an oath or declaration in compliance with 37 CFR 1.63, or a substitute statement in compliance with 37 CFR 1.64, executed by or with respect to each actual inventor no later than the expiration of the time period set in the "Notice of Allowability" to avoid abandonment. See 37 CFR 1.53(f).

- The ADS received on 01/31/2020 was not properly signed. Therefore, the Office will treat it only as a transmittal letter. See 37 CFR 1.76(e). Inventorship has not been set by this document and any foreign priority or domestic benefit claims contained therein are ineffective. See 37 CFR 1.55 or 37 CFR 1.78.
  If the applicant wishes to submit another ADS:
  - It must be properly signed by a party under 37 CFR 1.33(b), and be signed in compliance with 37 CFR 1.4(d).
  - Changes to the information of record must be properly marked up in compliance with 37 CFR 1.76(c), i.e., must identify the information that is being changed, with underlining for insertions, and strike-through or brackets for text removed. In general, the identification of the information being changed should be made relative to the most recent filing receipt.
  - Benefit and priority claims must be presented in an ADS in compliance with 37 CFR 1.76(c) and within the time periods specified in 37 CFR 1.55 and 1.78.

  If an ADS as set forth above is provided, the filing of the inventor's oath or declaration may be postponed until the application is otherwise in condition for allowance. See 37 CFR 1.53(f). Note that the inventor's oath or declaration must be filed no later than the date on which the issue fee has been paid.

In order to make changes to the information of record, an ADS must be properly signed and properly marked up relative to the current information of record.

Proper signature: The ADS must be signed with a handwritten signature or proper S-signature by:

- A patent practitioner, with the practitioner's registration number accompanying the signature (e.g., immediately below or adjacent to the signature), or
- The applicant, if the applicant is an individual other than the inventor(s) and no power of attorney has been appointed, or
- All of the inventors, if no other applicant has been established and no power of attorney has been appointed.

A proper S-signature consists of only letters and/or Arabic numerals, with appropriate spaces and commas, periods, apostrophes, or hyphens for punctuation contained between a first single forward slash mark before, and a second single forward slash mark after, the S-signature.

Proper markings: The ADS must identify the changes being made with underlining for insertions and strike-through or brackets for text removed. No other markings or indications are acceptable. Where an ADS providing corrected or updated information does not contain all of the sections of the ADS, the entire section in which changes are being made must be included in the ADS. Information of record can generally be found on the latest filing receipt.

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be mailed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web, including a copy of this Notice and selecting the document description "Applicant response to Pre-Exam Formalities Notice". https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at 1-866-217-9197 or visit our website at http://www.uspto.gov/ebc.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/mhaile/

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 16/778,662

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	300
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	660
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	760
TOTAL CLAIMS (37 CFR 1.16(i))	8 minus 20 =	*			OR	x 100 =	0.00
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*				x 460 =	0.00
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	1720

APPLICATION AS AMENDED - PART II

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

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

* 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.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/778,662	01/31/2020	Horst Olschewski	080618-1916

CONFIRMATION NO. 4471

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

OC000000114846832

Date Mailed: 02/21/2020

Improper Submission of Authorization to Permit Access to Application by Participating Offices under 37 CFR 1.14(h)(1) (Priority Document Exchange)

The Authorization to Permit Access to Application-As-Filed by Participating Offices under 37 CFR 1.14(h)(1) (authorization to permit access to application via priority document exchange) submitted on 01/31/2020 in the above-identified application is not accepted because:

- It was not properly signed. If applicant still wishes to provide authorization to permit access under 37 CFR 1.14(h)(1), applicant must submit a properly signed authorization (e.g., PTO/SB/39).

Any authorization should be submitted prior to filing a subsequent foreign application with a participating intellectual property office in which priority is claimed to the above-identified U.S. application to ensure that it is likely that the participating foreign intellectual property office will be successful in its attempt to retrieve a copy of the U.S. priority application from the Office.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/mhaile/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/778,662	01/31/2020	Horst Olschewski	080618-1916

CONFIRMATION NO. 4471

IMPROPER CPOA LETTER

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

OC000000114826321

Date Mailed: 02/21/2020

NOTICE REGARDING POWER OF ATTORNEY

This is in response to the power of attorney filed 01/31/2020. The power of attorney in this application is not accepted for the reason(s) listed below:

- The power of attorney has not been accepted because the party who is giving power has not been identified. Power of attorney may only be signed by the applicant for patent (37 CFR 1.42) or the patent owner. A party who is not the applicant must become the applicant in accordance with 37 CFR 1.46(c) and appoint any power of attorney in compliance with 37 CFR 3.71 and 3.73. For a reissue application, reexamination proceeding, or supplemental examination proceeding, a patent owner who was not the applicant under 37 CFR 1.46 must appoint any power of attorney in compliance with 37 CFR 3.71 and 3.73. See 37 CFR 1.32(b)(4).

/bnguyen/

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

PTO/AIA/80 (07-12)
Approved for use through 11/30/2014. OMB 0651-0035
U.S. Patent and Trademark Office; U.S DEPARTMENT OF COMMERCE

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: 166905

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 assigned 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: 166905

OR

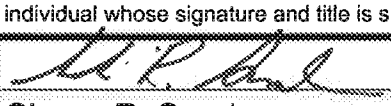
☐	Firm or Individual Name		
	Address		
	City		
	Country		
	Telephone		Email

Assignee Name and Address: United Therapeutics Corporation
1040 Spring Street
Silver Spring, MD 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	03 February 2020
Name	Shaun R. Snader	Telephone	202-304-1701
Title	Vice President, Associate General Counsel, IP		

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.

Electronic Acknowledgement Receipt

EFS ID:	38497965
Application Number:	16778662
International Application Number:	
Confirmation Number:	4471
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst Olschewski
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1916
Receipt Date:	05-FEB-2020
Filing Date:	
Time Stamp:	12:02:53
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Assignee showing of ownership per 37 CFR 3.73	373cStmt.pdf	1875981 11d871e8b63dbdea2eaee5f19d08a7271ab2fd38	no	3

Warnings:

Information:					
2	Power of Attorney	UTC_USPOA_166905.pdf	135599 bddae766cf8b80d5ccae20f78254b4db6ac208ea	no	1
Warnings:					
Information:					
			Total Files Size (in bytes):	2011580	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: United Therapeutics Corporation Atty. Dkt. No. 080618-1916

Application No./Patent No.: 16/778,662 Filed/Issue Date: 1/31/2020

Titled: TREPROSTINIL ADMINISTRATION BY INHALATION

United Therapeutics Corporation, a Corporation

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☑ The assignee of the entire right, title, and interest.

2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):

☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. ☑ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 023223, Frame 0716, or for which a copy thereof is attached.

B. ☐ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

2. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

4. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

5. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

6. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at

Reel _____, Frame _____, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☐ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/Stephen B. Maebius/	2/5/2020
Signature	Date
Stephen B. Maebius	35,264
Printed or Typed Name	Title or Registration 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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:	Horst OLSCHEWSKI
Title:	TREPROSTINIL ADMINISTRATION BY INHALATION
Prior Appl. No.:	16/536,954
Prior Appl. Filing Date:	8/9/2019
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:

[**X**] 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:

[**X**] Description, Claims, and Abstract (31 pages).

[**X**] Drawings (12 sheets, Figures 1-12).

[**X**] Executed Declarations/Substitute Statements from prior application (13 pages).

[**X**] Power of Attorney (1 pages).

[**X**] Information Disclosure Statement, Form PTO-SB08.

[**X**] Application Data Sheet (37 CFR 1.76).

[**X**] PTO/SB/424 - Request for Prioritized Examination.

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

Number of Sheets		**EFS-Web Adjustment**	**Number of Sheets for EFS-Web**
43	x	75%	33

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

	Number Filed		**Included in Basic Fee**		**Extra**		Rate		Fee Totals
Basic Filing Fee							$300.00	=	$300.00
Search Fee							$660.00		$660.00
Examination Fee							$760.00		$760.00
Sequence Listing fee									$0.00
Size Fee	33	-	100	=	0	x	$400.00		$0.00
Total Claims:	8	-	20	=	0	x	$100.00	=	$0.00
Independent:	1	-	3	=	0	x	$460.00	=	$0.00
If any Multiple Dependent Claim(s) present:						+	$820.00	=	$0.00
Surcharge under 37 CFR 1.16(e) for late filing of Executed Declaration or late payment of filing fee						+	$160.00	=	$0.00
Prioritized Examination fee (Track I) under 37 C.F.R. § 1.17 (c)									$4,000.00
Processing Fee (Track I) under 37 C.F.R. § 1.17 (i)									$140.00
TOTAL FILING FEE:								=	$5,860.00
Assignment Recordation Fee:						+	$50.00	=	$0.00
Processing Fee under 37 CFR 1.17(i) for Late Filing of English Translation of Application:						+	$140.00	=	$0.00
TOTAL FEE								=	$5,860.00

The above-identified fees of $5,860.00 are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any fees required to secure a filing date and maintain pendency of this application to Deposit Account No. 19-0741.

Respectfully submitted,

Date Jan. 31, 2020

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

TREPROSTINIL ADMINISTRATION BY INHALATION

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a Continuation of U.S. Application No. 16/536,954, filed August 9, 2019, which is a Continuation of U.S. Application No. 15/011,999, filed February 1, 2016, which is a Divisional of U.S. Application No. 13/469,854, filed May 11, 2012, Divisional of U.S. Application No. 12/591,200, filed November 12, 2009, which is a Continuation of U.S. Application No. 11/748,205, filed May 14, 2007, which claims priority to US provisional application No. 60/800,016 filed May 15, 2006, which are incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

[0002] The present application relates to methods and kits for therapeutic treatment and, more particularly, to therapeutic methods involving administering treprostinil using a metered dose inhaler and related kits.

BACKGROUND OF THE INVENTION

[0003] All blood is driven through the lungs via the pulmonary circulation in order, among other things, to replenish the oxygen which it dispenses in its passage around the rest of the body via the systemic circulation. The flow through both circulations is in normal circumstances equal, but the resistance offered to it in the pulmonary circulation is generally much less than that of the systemic circulation. When the resistance to pulmonary blood flow increases, the pressure in the circulation is greater for any particular flow. The above described condition is referred to as pulmonary hypertension (PH). Generally, pulmonary hypertension is defined through observations of pressures above the normal range pertaining in the majority of people residing at the same altitude and engaged in similar activities.

[0004] Pulmonary hypertension may occur due to various reasons and the different entities of pulmonary hypertension were classified based on clinical and pathological

grounds in 5 categories according to the latest WHO convention, see e.g. Simonneau G., et al. J. Am. Coll. Cardiol. 2004; 43(12 Suppl S):5S-12S. Pulmonary hypertension can be a manifestation of an obvious or explicable increase in resistance, such as obstruction to blood flow by pulmonary emboli, malfunction of the heart's valves or muscle in handling blood after its passage through the lungs, diminution in pulmonary vessel caliber as a reflex response to alveolar hypoxia due to lung diseases or high altitude, or a mismatch of vascular capacity and essential blood flow, such as shunting of blood in congenital abnormalities or surgical removal of lung tissue. In addition, certain infectious diseases, such as HIV and liver diseases with portal hypertension may cause pulmonary hypertension. Autoimmune disorders, such as collagen vascular diseases, also often lead to pulmonary vascular narrowing and contribute to a significant number of pulmonary hypertension patients. The cases of pulmonary hypertension remain where the cause of the increased resistance is as yet inexplicable are defined as idiopathic (primary) pulmonary hypertension (iPAH) and are diagnosed by and after exclusion of the causes of secondary pulmonary hypertension and are in the majority of cases related to a genetic mutation in the bone morphogenetic protein receptor-2 gene. The cases of idiopathic pulmonary arterial hypertension tend to comprise a recognizable entity of about 40% of patients cared for in large specialized pulmonary hypertension centers. Approximately 65% of the most commonly afflicted are female and young adults, though it has occurred in children and patients over 50. Life expectancy from the time of diagnosis is short without specific treatment, about 3 to 5 years, though occasional reports of spontaneous remission and longer survival are to be expected given the nature of the diagnostic process. Generally, however, disease progress is inexorable via syncope and right heart failure and death is quite often sudden.

[0005] Pulmonary hypertension refers to a condition associated with an elevation of pulmonary arterial pressure (PAP) over normal levels. In humans, a typical mean PAP is approximately 12-15 mm Hg. Pulmonary hypertension, on the other hand, can be defined as mean PAP above 25mmHg, assessed by right heart catheter measurement. Pulmonary arterial pressure may reach systemic pressure levels or even exceed these in severe forms of pulmonary hypertension. When the PAP

markedly increases due to pulmonary venous congestion, i.e. in left heart failure or valve dysfunction, plasma can escape from the capillaries into the lung interstitium and alveoli. Fluid buildup in the lung (pulmonary edema) can result, with an associated decrease in lung function that can in some cases be fatal. Pulmonary edema, however, is not a feature of even severe pulmonary hypertension due to pulmonary vascular changes in all other entities of this disease.

[0006] Pulmonary hypertension may either be acute or chronic. Acute pulmonary hypertension is often a potentially reversible phenomenon generally attributable to constriction of the smooth muscle of the pulmonary blood vessels, which may be triggered by such conditions as hypoxia (as in high-altitude sickness), acidosis, inflammation, or pulmonary embolism. Chronic pulmonary hypertension is characterized by major structural changes in the pulmonary vasculature, which result in a decreased cross-sectional area of the pulmonary blood vessels. This may be caused by, for example, chronic hypoxia, thromboembolism, collagen vascular diseases, pulmonary hypercirculation due to left-to-right shunt, HIV infection, portal hypertension or a combination of genetic mutation and unknown causes as in idiopathic pulmonary arterial hypertension.

[0007] Pulmonary hypertension has been implicated in several life-threatening clinical conditions, such as adult respiratory distress syndrome ("ARDS") and persistent pulmonary hypertension of the newborn ("PPHN"). Zapol et al., Acute Respiratory Failure, p. 241-273, Marcel Dekker, New York (1985); Peckham, J. Ped. 93:1005 (1978). PPHN, a disorder that primarily affects full-term infants, is characterized by elevated pulmonary vascular resistance, pulmonary arterial hypertension, and right-to-left shunting of blood through the patent ductus arteriosus and foramen ovale of the newborn's heart. Mortality rates range from 12-50%. Fox, Pediatrics 59:205 (1977); Dworetz, Pediatrics 84:1 (1989). Pulmonary hypertension may also ultimately result in a potentially fatal heart condition known as "cor pulmonale," or pulmonary heart disease. Fishman, "Pulmonary Diseases and Disorders" 2nd Ed., McGraw-Hill, New York (1988).

[0008] Currently, there is no treatment for pulmonary hypertension that can be administered using a compact inhalation device, such as a metered dose inhaler.

SUMMARY OF THE INVENTION

[0009] One embodiment is a method of delivering to a subject in need thereof a therapeutically effective amount of treprostinil, or treprostinil derivative or a pharmaceutically acceptable salt thereof comprising administering to the subject a therapeutically effective amount of the treprostinil or treprostinil derivative or a pharmaceutically acceptable salt thereof using a metered dose inhaler.

[0010] Another embodiment is a method for treating pulmonary hypertension comprising administering to a subject in need thereof treprostinil or its derivative, or a pharmaceutically acceptable salt thereof using a metered dose inhaler.

[0011] Yet another embodiment is a kit comprising a metered dose inhaler containing a pharmaceutical formulation comprising treprostinil or treprostinil derivative, or a pharmaceutically acceptable salt thereof.

[0012] And yet another embodiment is a kit for treating pulmonary hypertension in a subject, comprising (i) an effective amount of treprostinil or its derivative, or a pharmaceutically acceptable salt thereof; (ii) a metered dose inhaler; (iii) instructions for use in treating pulmonary hypertension.

[0013] Administration of treprostinil using a metered dose inhaler can provide patients, such as pulmonary hypertension patients, with a high degree of autonomy.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] FIGURE 1 pulmonary and systemic changes in hemodynamics following the inhalation of placebo (open circles), 30μg treprostinil (triangles), 45μg treprostinil (squares) or 60μg TREprostinil (black circles) applied by a Metered Dose Inhaler (MDI-TRE). A single short inhalation of treprostinil induced sustained reduction of PAP and PVR that outlasted the observation period of 120 minutes at doses of 45 and 60μg MDI-TRE. Systemic arterial pressure and resistance were not significantly

affected. PAP = mean pulmonary artery pressure; PVR = pulmonary vascular resistance; SAP = mean systemic arterial pressure; SVR = systemic vascular resistance. Data are given as mean value ± standard error of the mean (SEM).

[0015] FIG. 2 presents hemodynamic changes induced by the inhalation of placebo (open circles), 30µg treprostinil (triangles), 45µg treprostinil (squares) or 60µg treprostinil (black circles) applied by a metered dose inhaler. Treprostinil induced sustained elevation of cardiac output. Heart rate was rather unchanged as a sign for low spillover of MDI-TRE to the systemic circulation. Gas exchange was not negatively affected. CO = cardiac output; HR = heart rate; SaO2 = arterial oxygen saturation; SvO2 = central venous oxygen saturation. Data are given as mean value ± SEM.

[0016] FIG. 3 shows areas under the curve for changes in pulmonary vascular resistance (PVR) calculated for an observation period of 120 minutes after inhalation treprostinil using a metered dose inhaler. PVR was markedly lowered by treprostinil inhalation. The increased pulmonary vasodilation over time with the two highest doses mainly relies on the more sustained effect over time. Data are shown as mean value ± 95% confidence intervals.

[0017] FIG. 4 demonstrates Ventilation-perfusion matching measured with the multiple inert gas elimination technique. Five patients (30µg TRE, n=2; 45µg TRE, n=1; 60µg TRE, n=2) with pre-existing gas exchange problems were investigated for changes in ventilation-perfusion ratios. All patients had significant shunt flow at baseline. Shunt-flow and low V/Q areas were not significantly changed by nitric oxide (NO) inhalation or treprostinil inhalation using a metered dose inhaler (MDI-TRE). MDI-TRE applied at high treprostinil concentrations did not negatively affect ventilation-perfusion matching and gas-exchange. Data are given as mean value ± 95% confidence intervals.

[0018] FIG. 5 presents response of pulmonary vascular resistance (PVR) to inhaled treprostinil vs. iloprost - period effects. a) First inhalation with treprostinil (n=22) vs. first inhalation with iloprost (n=22); b) second inhalation with treprostinil (n=22) vs.

second inhalation with iloprost (n=22). The PVR decrease with treprostinil was delayed and prolonged, compared to iloprost. Due to carryover effects from the first period, in the second period, the effects of both drugs appeared shortened. Data are shown as percent of baseline values (mean value ± 95% confidence interval).

[0019] FIG. 6 presents response of PVR and systemic arterial pressure (SAP) to inhalation of treprostinil vs. iloprost – dose effects. a) Inhalation of 7.5 µg iloprost (in 6 min) vs. 7.5 µg treprostinil (6 min) (n=14, in a randomized order). b) Inhalation of 7.5 µg iloprost (6 min) vs. 15 µg treprostinil (6 min) (n=14, in randomized order). c) Inhalation of 7.5 µg iloprost (6 min) vs. 15 µg treprostinil (3 min) (n=16, in randomized order). Data are shown as percent of baseline values (mean ± 95% confidence interval). Iloprost, filled circles; Treprostinil, open triangles.

[0020] FIG. 7 presents hemodynamic response to inhalation of treprostinil vs. iloprost. Data from n=44 patients, who inhaled both drugs in randomized order, shown as percent of baseline values (mean value ± 95% confidence interval). PVR, pulmonary vascular resistance; PAP, mean pulmonary arterial pressure; SAP, mean systemic arterial pressure; CO, cardiac output.

[0021] FIG. 8 presents pharmacodynamics after treprostinil inhalation vs. placebo. Placebo or treprostinil in doses of 30µg, 60µg or 90µg were inhaled (means ± 95 % confidence intervals). Maximal decrease of PVR was comparable for all doses. The duration of pulmonary vasodilation (PVR-decrease) appeared to be dose dependent. PVR, pulmonary vascular resistance; PAP, mean pulmonary arterial pressure; SAP, mean systemic arterial pressure; CO, cardiac output; SaO2, arterial oxygen saturation; SvO2, mixed venous oxygen saturation.

[0022] FIG. 9 presents Areas Between the placebo and the treprostinil Curves (ABC). ABCs were calculated for a 3-hour period after inhalation of TRE or placebo from the relative changes of hemodynamic parameters (means ± 95 % confidence intervals). PVR, pulmonary vascular resistance; PAP, mean pulmonary arterial pressure; SAP, mean systemic arterial pressure; SVR, systemic vascular resistance.

[0023] FIG. 10 presents hemodynamic responses to the inhalation of 15µg treprostinil. The inhalation time by increasing treprostinil concentration. A pulse of aerosol was generated every 6 seconds. TRE aerosol was inhaled in concentrations of 100µg/ml (18 pulses; n=6), 200µg/ml (9 pulses; n=6), 600µg/ml (3 pulses; n=21), 1000µg/ml (2 pulses; n=7) and 2000µg/ml (1 pulse; n=8). Placebo data correspond to Figure 8. Data are shown as means ± 95 % confidence intervals. PVR, pulmonary vascular resistance; PAP, mean pulmonary arterial pressure; SAP, mean systemic arterial pressure; CO, cardiac output.

[0024] FIG. 11 presents areas between the placebo curve and the responses to 15µg treprostinil applied at increasing concentrations to minimize inhalation time. Mean ± SEM of relative changes of hemodynamic parameters (observation time 120 min). PAP, pulmonary arterial pressure, SAP, systemic arterial pressure, PVR, pulmonary vascular resistance, CO, cardiac output, SaO2, systemic arterial oxygen saturation, SvO2, pulmonary arterial oxygen saturation.

[0025] FIG. 12 presents pharmacokinetics of treprostinil after a single inhalation. Treprostinil plasma levels after inhalation of 30µg, 60µg, 90µg or 120µg treprostinil (6 min inhalation period; experiments correspond to those shown in figure 8 and 9). Data with error bars represent mean values ± SEM.

DETAILED DESCRIPTION OF THE INVENTION

[0026] Unless otherwise specified, the term "a" or "an" used herein shall mean "one or more."

[0027] The present application incorporates herein by reference in its entirety Voswinckel R, *et al.* J. Am. Coll. Cardiol. 2006; 48:1672-1681.

[0028] The inventors discovered that a therapeutically effective dose of treprostinil can be administered in a few single inhalations using a compact inhalation device, such as a metered dose inhaler. Furthermore, the inventors discovered that such administering does not cause significant side effects, especially no significant side

effects related to systemic blood pressure and circulation as well as no gas exchange deteriorations or disruptions.

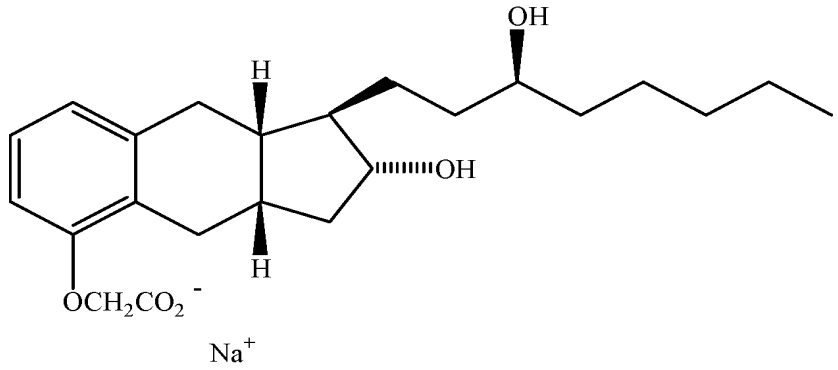
[0029] Accordingly, one embodiment of the invention is a method of delivering to a subject in need thereof, such as a human being, a therapeutically effective amount of treprostinil comprising administering to the subject a formulation comprising a therapeutically effective amount of treprostinil, its derivative or a pharmaceutically acceptable salt thereof using a metered dose inhaler. Treprostinil can be administered via a metered dose inhaler to a subject affected with a condition or disease, which can be treated by treprostinil, such as asthma, pulmonary hypertension, peripheral vascular disease or pulmonary fibrosis.

[0030] Another embodiment of the invention is a method for treating pulmonary hypertension, comprising administering to a subject in need thereof, such as a human being, treprostinil or its derivative, or a pharmaceutically acceptable salt using a metered dose inhaler.

[0031] Treprostinil, or 9-deoxy-2',9-alpha-methano-3-oxa-4,5,6-trinor-3,7-(1'3'-interphenylene)-13,14-dihydro-prostaglandin F1, is a prostacyclin analogue, first described in US patent 4,306,075. US 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. US 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. US 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. US patent application publication No. 2005/0165111 discloses treprostinil treatment of ischemic lesions. US patent No. 7,199,157 discloses that treprostinil treatment improves kidney functions. US patent application publication No. 2005/0282903 discloses treprostinil treatment of neuropathic foot ulcers. US provisional application No. 60/900,320 filed February 9, 2007, discloses treprostinil treatment of pulmonary fibrosis.

[0032] The term "acid derivative" is used herein to describe C1-4 alkyl esters and amides, including amides wherein the nitrogen is optionally substituted by one or two C1-4 alkyl groups.

[0033] The present invention also encompasses methods of using Treprostinil or its derivatives, or pharmaceutically acceptable salts thereof. In one embodiment, a method uses Treprostinil sodium, currently marketed under the trade name of REMODULIN®. The FDA has approved Treprostinil sodium for the treatment of pulmonary arterial hypertension by injection of dose concentrations of 1.0 mg/mL, 2.5 mg/mL, 5.0 mg/mL and 10.0 mg/mL. The chemical structure formula for Treprostinil sodium is:



[0034] Treprostinil sodium is sometimes designated by the chemical names: (a) [(1*R*,2*R*,3a*S*,9a*S*)-2,3,3a,4,9,9a-hexahydro-2-hydroxy-1-[(3*S*)-3-hydroxyoctyl]-1*H*-benz[*f*]inden-5-yl]oxy]acetic acid; or (b) 9-deoxy-2',9-α-methano-3-oxa-4,5,6-trinor-3,7-(1',3'-interphenylene)-13,14-dihydro-prostaglandin F_1. Treprostinil sodium is also known as: UT-15; LRX-15; 15AU81; UNIPROST™; BW A15AU; and U-62,840. The molecular weight of Treprostinil sodium is 390.52, and its empirical formula is $C_{23}H_{34}O_5$.

[0035] In certain embodiments, treprostinil can be administered in combination with one or more additional active agents. In some embodiments, such one or more additional active agents can be also administered together with treprostinil using a metered dose inhaler. Yet in some embodiments, such one or more additional active agents can be administered separately from treprostinil. Particular additional active

agents that can be administered in combination with treprostinil may depend on a particular disease or condition for treatment or prevention of which treprostinil is administered. In some cases, the additional active agent can be a cardiovascular agent such as a calcium channel blocker, a phosphodiesterase inhibitor, an endothelial antagonist, or an antiplatelet agent.

[0036] The present invention extends to methods of using physiologically acceptable salts of Treprostinil, as well as non-physiologically acceptable salts of Treprostinil that may be used in the preparation of the pharmacologically active compounds of the invention.

[0037] The term "pharmaceutically acceptable salt" refers to a salt of Treprostinil with an inorganic base, organic base, inorganic acid, organic acid, or basic or acidic amino acid. Salts of inorganic bases can be, for example, salts of alkali metals such as sodium or potassium; alkaline earth metals such as calcium and magnesium or aluminum; and ammonia. Salts of organic bases can be, for example, salts trimethylamine, triethylamine, pyridine, picoline, ethanolamine, diethanolamine, and triethanolamine. Salts of inorganic acids can be, for example, salts of hydrochloric acid, hydroboric acid, nitric acid, sulfuric acid, and phosphoric acid. Salts of organic acids can be, for example, salts of formic acid, acetic acid, trifluoroacetic acid, fumaric acid, oxalic acid, lactic acid, tartaric acid, maleic acid, citric acid, succinic acid, malic acid, methanesulfonic acid, benzenesulfonic acid, and p-toluenesulfonic acid. Salts of basic amino acids can be, for example, salts of arginine, lysine and ornithine. Salts of acidic amino acids can include, for example, salts of aspartic acid and glutamic acid. Quaternary ammonium salts can be formed, for example, by reaction with lower alkyl halides, such as methyl, ethyl, propyl, and butyl chlorides, bromides, and iodides, with dialkyl sulphates, with long chain halides, such as decyl, lauryl, myristyl, and stearyl chlorides, bromides, and iodides, and with aralkyl halides, such as benzyl and phenethyl bromides.

[0038] Preferred pharmaceutically acceptable salts are disclosed, for example, in US patent application publication No. 20050085540.

[0039] Treprostinil can be administered by inhalation, which in the present context refers to the delivery of the active ingredient or a combination of active ingredients through a respiratory passage, wherein the subject in need of the active ingredient(s) through the subject's airways, such as the subject's nose or mouth.

[0040] A metered dose inhaler in the present context means a device capable of delivering a metered or bolus dose of respiratory drug, such as treprostinil, to the lungs. One example of the inhalation device can be a pressurized metered dose inhaler, a device which produces the aerosol clouds for inhalation from solutions and/or suspensions of respiratory drugs in chlorofluorocarbon (CFC) and/or hydrofluoroalkane (HFA) solutions.

[0041] The inhalation device can be also a dry powder inhaler. In such case, the respiratory drug is inhaled in solid formulation, usually in the form of a powder with particle size less than 10 micrometers in diameter or less than 5 micrometers in diameter.

[0042] The metered dose inhaler can be a soft mist inhaler (SMI), in which the aerosol cloud containing a respiratory drug can be generated by passing a solution containing the respiratory drug through a nozzle or series of nozzles. The aerosol generation can be achieved in SMI, for example, by mechanical, electromechanical or thermomechanical process. Examples of soft mist inhalers include the Respimat® Inhaler (Boeringer Ingelheim GmbH), the AERx® Inhaler (Aradigm Corp.), the Mystic™ Inhaler (Ventaira Pharmaceuticals, Inc) and the Aira™ Inhaler (Chrysalis Technologies Incorporated). For a review of soft mist inhaler technology, see *e.g.* M. Hindle, The Drug Delivery Companies Report, Autumn/Winter 2004, pp. 31-34. The aerosol for SMI can be generated from a solution of the respiratory drug further containing pharmaceutically acceptable excipients. In the present case, the respiratory drug is treprostinil, its derivative or a pharmaceutically acceptable salt thereof, which can be formulated in SMI is as a solution. The solution can be, for example, a solution of treprostinil in water, ethanol or a mixture thereof. Preferably, the diameter of the treprostinil-containing aerosol particles is less than about 10 microns, or less than about 5 microns, or less than about 4 microns.

[0043] Treprostinil concentration in an aerosolable formulation, such as a solution, used in a metered dose inhaler can range from about 500 μg/ml to about 2500 μg/ml, or from about 800 μg/ml to about 2200 μg/ml, or from about 1000 μg/ml to about 2000 μg/ml.

[0044] The dose of treprostinil that can be administered using a metered dose inhaler in a single event can be from about 15 μg to about 100 μg or from about 15μg to about 90 μg or from about 30 μg to about 90 μg or from about 30 μg to about 60μg.

[0045] Administering of treprostinil in a single event can be carried out in a limited number of breaths by a patient. For example, treprostinil can be administered in 20 breaths or less, or in 10 breaths or less, or than 5 breaths or less. Preferably, treprostinil is administered in 3, 2 or 1 breaths.

[0046] The total time of a single administering event can be less than 5 minutes, or less than 1 minute, or less than 30 seconds.

[0047] Treprostinil can be administered a single time per day or several times per day.

[0048] In some embodiments, the method of treatment of pulmonary hypertension can further comprise administering at least one supplementary agent selected from the group consisting of sildenafil, tadalafil, calcium channel blockers (diltiazem, amlodipine, nifedipine), bosentan, sitaxsentan, ambrisentan, and pharmaceutically acceptable salts thereof. In some embodiments, the supplementary agents can be included in the treprostinil formulation and, thus, can be administered simultaneously with treprostinil using a metered dose inhaler. In some embodiments, the supplementary agents can be administered separately from treprostinil. In some embodiments, the application of intravenous prostacyclin (flolan), intravenous iloprost or intravenous or subcutaneous treprostinil can be administered in addition to treprostinil administered via inhalation using a metered dose inhaler.

[0049] The present invention also provides a kit that includes a metered dose inhaler containing a pharmaceutical formulation comprising treprostinil or its derivative, or a pharmaceutically acceptable salt thereof. Such a kit can further include instructions on how to use the metered dose inhaler for inhaling treprostinil. Such instructions can include, for example, information on how to coordinate patient's breathing, and actuation of the inhaler. The kit can be used by a subject, such as human being, affected with a disease or condition that can be treated by treprostinil, such as asthma, pulmonary hypertension, peripheral vascular disease or pulmonary fibrosis.

[0050] In some cases, the kit is a kit for treating pulmonary hypertension, that includes (i) a metered dose inhaler containing a pharmaceutical formulation comprising treprostinil or its derivative, or a pharmaceutically acceptable salt thereof; and (ii) instructions for use of the metered dose inhaler containing treprostinil in treating pulmonary hypertension.

[0051] As used herein, the phrase "instructions for use" shall mean any FDA-mandated labeling, instructions, or package inserts that relate to the administration of Treprostinil or its derivatives, or pharmaceutically acceptable salts thereof, for treatment of pulmonary hypertension by inhalation. For example, instructions for use may include, but are not limited to, indications for pulmonary hypertension, identification of specific symptoms associated with pulmonary hypertension, that can be ameliorated by Treprostinil, recommended dosage amounts for subjects suffering from pulmonary hypertension and instructions on coordination of individual's breathing and actuation of the metered dose inhaler.

[0052] The present invention can be illustrated in more detail by the following example, however, it should be understood that the present invention is not limited thereto.

EXAMPLE 1

OPEN LABEL STUDY UPON ACUTE SAFETY, TOLERABILITY AND HEMODYNAMIC EFFECTS OF INHALED TREPROSTINIL DELIVERED IN SECONDS.

[0053] A study was conducted of acute vasodilator challenge during right heart catheter investigation to determine the safety, tolerability and pulmonary vasodilatory potency of inhaled treprostinil applied in seconds by a soft mist inhaler (SMI-TRE). The study produced evidence for a long lasting favourable effect of SMI-TRE on pulmonary hemodynamics in absence of systemic side effects and gas exchange disruptions.

Summary:

[0054] Inhaled nitric oxide (20 ppm; n=45) and inhaled treprostinil sodium (TRE; n=41) or placebo (n=4) were applied once during right heart catheter investigation. TRE was delivered in 2 breaths (1000µg/ml aerosol concentration; 30µg dose; n=12), 3 breaths (1000µg/ml; 45µg; n=9) or 2 breaths (2000µg/ml; 60µg; n=20) from a Respimat® SMI. Pulmonary hemodynamics and blood gases were measured at defined time points, observation time following TRE application was 120 minutes. TRE doses of 30µg, 45µg and 60µg reduced pulmonary vascular resistance (PVR) to 84.4 ± 8.7 %, 71.4 ± 17.5 % and 77.5 ± 7.2 % of baseline values, respectively (mean ± 95% confidence interval). The 120 minute area under the curve for PVR for placebo, 30µg, 45µg and 60µg TRE was 1230 ± 1310, -870 ± 940, -2450 ± 2070 and -2000 ± 900 min %, respectively. Reduction of PVR by a single inhalation of the two higher doses outlasted the observation period of 120 minutes. Reduction of systemic vascular resistance and pressure was negligible, showing a high pulmonary selectivity for SMI-TRE. Intrapulmonary selectivity was also provided by SMI-TRE as ventilation/perfusion matching, assessed by the multiple inert gas elimination technique in 5 patients with gas exchange problems, was not significantly different after SMI-TRE compared to inhaled nitric oxide or no treatment. No significant side effects were observed.

[0055] Conclusions: The acute application of inhaled treprostinil with a metered dose inhaler in 2-3 breaths was safe, well tolerated and induced a strong and sustained pulmonary selective vasodilation.

Methods and Patients

[0056] A total number of 45 patients with moderate to severe precapillary pulmonary hypertension were enrolled. Patient characteristics were: female to male ratio (f/m) = 29/16, age 59 ± 2.3 years, pulmonary artery pressure (PAP) 45 ± 1.8 mmHg, pulmonary vascular resistance (PVR) 743 ± 52 dynes·s·cm^{-5}, pulmonary artery wedge pressure (PAWP) 8.6 ± 0.5 mmHg, central venous pressure (CVP) 6.4 ± 0.7 mmHg, cardiac output (CO) 4.5 ± 0.2 l/min, central venous oxygen saturation (SvO2) 62.3 ± 1.2 mmHg (mean ± Standard Error of the Mean). Disease etiologies were idiopathic PAH (iPAH) (n=13), PAH other (n=11), chronic thromboembolic pulmonary hypertension (CTEPH) (n=17) and pulmonary fibrosis (n=4). Table 1 presents the patient characteristics of the different groups.

Table 1.

[0057] Patient characteristics of the different treatment groups. Data are given as mean ± Standard Error of the Mean (SEM). PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; CO = cardiac output; SAP = systemic arterial pressure; SaO2 = arterial oxygen saturation; SvO2 = central venous oxygen saturation.

	Placebo (n=4)	30µg TRE (n=12)	45µg TRE (n=9)	60µg TRE (n=20)
Age [years]	61 ± 8	53.9 ± 3.9	54.2 ± 5.7	65.5 ± 3.1
PAP [mmHg]	49.5 ± 10.1	45 ± 3.1	54.3 ± 2.8	39.7 ± 2.0
PVR [Dynes]	896 ± 163	597 ±53.9	1049 ± 107	663 ± 81
CO [l/min]	4.46 ± 0.9	5.2 ± 0.4	3.9 ± 0.4	4.4 ± 0.3
SAP [mmHg]	98 ± 8.1	90.1 ± 3.2	82.8 ± 3.9	86.1 ± 2.0
SaO2 [%]	85.3 ± 4.5	90.0 ± 1.1	89.6 ± 1.1	90.6 ± 0.5
SvO2 [%]	57.5 ±3.9	66.0 ± 1.6	59.1 ± 3.4	62.5 ± 1.6

[0058] Baseline values were determined 20-30 minutes after placement of the catheter. Heart rate, pulmonary and systemic blood pressure and cardiac output were measured and blood gases were taken during each pharmacological intervention at defined time points. Pharmacological interventions included the inhalation of 20 ppm nitric oxide (NO) after evaluation of baseline parameters (n=45) and the consecutive inhalation of placebo (n=4), 30µg SMI-TRE (n=12), 45µg SMI-TRE (n=9) or 60µg (n=20) SMI-TRE. Placebo and treprostinil was applied with the Respimat® SMI. For filling of this device with treprostinil sodium, the placebo solution was withdrawn from the device with a syringe and treprostinil solution was injected into the device under sterile conditions. Aerosol quality was controlled before and after refilling of the SMI devices by laser diffractometry, see e.g. Gessler T., Schmehl T., Hoeper M.M., Rose F., Ghofrani H.A., Olschewski H. et al. Ultrasonic versus jet nebulization of iloprost in severe pulmonary hypertension. Eur. Respir. J. 2001;17:14-19 incorporated herein in its entirety. The aerosol sizes before (placebo) and after filling (treprostinil) were unchanged. The aerosol particles mass median aerodynamic diameter of treprostinil-aerosol was 4-5µm, which can be at the upper limit for alveolar deposition. The aerosol volume delivered by one cycle from the SMI was 15µl. The solution used for aerosol generation was prepared from treprostinil sodium salt using a standard protocol. The SMI was either filled with a concentration of 1000µg/ml treprostinil sodium (one aerosol puff = 15µg TRE) or with 2000µg/ml (one puff = 30µg TRE). The different doses were applied as 2 puffs 1000µg/ml (30µg), 3 puffs 1000µg/ml (45µg) and 2 puffs 2000µg/ml (60µg). The placebo was inhaled as 2 puffs from a placebo-SMI. Hemodynamics and gas-exchange parameters were recorded for 120 minutes after TRE inhalation. This study used the Respimat®

device, because the implemented "soft mist" technology was well suited for the deposition of such highly active drugs like prostanoids.

[0059] The impact of SMI-TRE on ventilation-perfusion matching was assessed in five patients (30µg TRE, n=2; 45µg TRE, n=1; 60µg TRE, n=2) with pre-existing gas exchange problems by use of the multiple inert gas elimination technique (MIGET), see e.g. Wagner PD, Saltzman HA, West JB. Measurement of continuous distributions of ventilation-perfusion ratios: theory. J Appl Physiol. 1974; 36:588-99; Ghofrani HA, Wiedemann R, Rose F, Schermuly RT, Olschewski H, Weissmann N et al. Sildenafil for treatment of lung fibrosis and pulmonary hypertension: a randomised controlled trial. Lancet. 2002;360:895-900, both incorporated herein in their entirety.

Statistics:

[0060] Mean values, standard deviation, standard error of the mean and 95% confidence intervals were calculated. Statistical analysis was done by use of a paired t-test.

Results:

[0061] The inhalation of treprostinil sodium from the metered dose inhaler (SMI-TRE) was well tolerated, only mild and transient cough for a maximum of one minute was reported. No systemic side effects like headache, flush, nausea or dizziness were observed.

[0062] Two to three breaths of SMI-TRE induced a strong pulmonary vasodilation that outlasted the observation time of 120 minutes (45 and 60µg). The lower dose of 30µg TRE induced a somewhat shorter effect on pulmonary vascular resistance; however, the maximal pulmonary vasodilation was comparable. In contrast, placebo inhalation did not induce pulmonary vasodilation. In fact a slight increase in PVR over the time of the right heart catheter investigation could be recorded following placebo inhalation (Figure 1). The effect of SMI-TRE on systemic vascular resistance and pressure was very small and not clinically significant. Cardiac output was significantly increased over the whole observation period, whereas heart rate was

rather unchanged. Gas exchange was not influenced by SMI-TRE (Figure 2). The maximal changes in hemodynamic and gas-exchange parameters compared to baseline values are depicted in Table 2.

Table 2.

[0063] Extremes of the relative changes of hemodynamic and gas exchange parameters compared to baseline after inhalation of Placebo (n=4), 30µg treprostinil (n=12), 45µg treprostinil (n=9) and 60µg treprostinil (n=20). Highest (max) and lowest (min) values during the observation period are shown. Data are given as percent of baseline values (mean ± SEM). PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance; CO = cardiac output; SAP = systemic arterial pressure; HR = heart rate; SaO2 = arterial oxygen saturation; SvO2 = central venous oxygen saturation.

	Placebo	30µg TRE	45µg TRE	60µg TRE
PAP (min)	99.4 ± 3.0	83.4 ± 3.2	77.6 ± 6.8	79.5 ± 2.4
PVR (min)	101.4 ± 1.9	84.4 ± 4.4	71.4 ± 8.9	77.5 ± 3.7
CO (max)	99.7 ± 1.1	108.8 ± 3.8	108.6 ± 5.6	103.8 ± 2.0
SVR (min)	104.3 ± 4.3	97.7 ± 4.2	92 ± 3.9	91.3 ± 2.1
SAP (min)	102.7 ± 1.7	97.3 ± 1.9	96.1 ± 1.5	93.6 ± 2.9
HR (max)	105 ± 2.1	106.1 ± 2.9	99.1 ± 2.4	101.1 ± 0.9
SaO2 (min)	98.2 ± 0.4	101 ± 0.3	94.4 ± 1.8	95.8 ± 0.9
SvO2 (max)	104.5 ± 1.4	102.4 ± 1.3	104.5 ± 4.4	102 ± 1.0

[0064] The areas under the curve for PVR were calculated for placebo and the different SMI-TRE doses over the 120 minute observation period (figure 3). A dose effect of SMI-TRE with a trend to a more sustained effect with the two highest doses could be observed.

[0065] The inhalation of a highly concentrated aerosol can be in theory prone to disturbances of gas exchange because the deposition of even small amounts of aerosol may deliver high doses locally and thereby antagonize the hypoxic pulmonary vasoconstriction in poorly ventilated areas. This would then lead to increased shunt flow or increase of low ventilation/perfusion (V/Q) areas. This question was addressed in five patients with the multiple inert gas elimination technique (MIGET), the gold-standard for intrapulmonary V/Q ratio determination. The MIGET patients

were selected for pre-existing gas exchange limitations. Characteristics of these patients were: PAP 54.6 ± 3.2 mmHg, PVR 892 ± 88 dynes, SaO2 91.7 ± 0.5 %, SvO2 65.2 ± 1.8 %. Etiologies were iPAH (n=1), CTEPH (n=3), pulmonary fibrosis (n=1). The maximal relative reduction of SaO2 after inhalation of SMI-TRE in these patients was -3.8 ± 1.5 % compared to baseline values. Shunt flow at baseline, NO-inhalation and 60 minutes after SMI-TRE was 6.4 ± 4.3 %, 5.4 ± 3.0 % and 8.3 ±3.4 %, respectively (mean ± 95% confidence interval; figure 4).

[0066] No significant increase in low V/Q areas or shunt fraction after inhalation of SMI-TRE was observed, in fact the distribution of perfusion was not different to that at baseline and during nitric oxide inhalation. This proves an excellent intrapulmonary selectivity of SMI-TRE, which is also reflected by unchanged arterial oxygen saturation.

Conclusion:

[0067] Treprostinil is tolerated at high doses with no systemic side effects. The application of an effective amount of treprostinil in only few or even one single breath was achieved with a highly concentrated treprostinil sodium solution. Treprostinil can be applied by a metered dose inhaler, such as Respimat® soft mist inhaler.

EXAMPLE 2

INVESTIGATION OF THE EFFECTS OF INHALED TREPROSTINIL ON PULMONARY HEMODYNAMICS AND GAS EXCHANGE IN SEVERE PULMONARY HYPERTENSION

[0068] This study investigated the effects of inhaled treprostinil on pulmonary vascular resistance in severe pulmonary hypertension and addressed systemic effects and gas exchange as well as tolerability and efficacy of high doses of treprostinil given in short time. A total of 123 patients with a mean pulmonary artery pressure of about 50 mmHg were investigated in three separate randomized studies. Inhaled treprostinil exerted potent sustained pulmonary vasodilation with excellent tolerability and could be safely applied in a few breaths or even one breath.

Summary:

[0069] Three different studies were conducted on a total of 123 patients by means of right heart catheterization: i) a randomized crossover-design study (44 patients), ii) a dose escalation study (31 patients) and iii) a study of reduction of inhalation time while keeping the dose fixed (48 patients). The primary endpoint was the change in pulmonary vascular resistance (PVR).

[0070] The mean pulmonary artery pressure of the enrolled patients was about 50 mmHg. Hemodynamics and patient characteristics were similar in all studies. In study i) TRE and Iloprost (ILO), at an inhaled dose of 7.5 μg, displayed comparable PVR decrease, with a significantly different time course ($p<0.001$), TRE exhibiting a more sustained effect on PVR ($p<0.0001$) and less systemic side effects. In study ii) placebo, 30μg, 60μg, 90μg or 120μg TRE were applied with drug effects being observed for 3 hours after inhalation. A near-maximal acute PVR decrease was observed at 30μg TRE. In study iii) TRE was inhaled with a pulsed ultrasonic nebulizer, mimicking a metered dose inhaler. 15μg TRE was inhaled with 18 pulses (TRE concentration 100μg/ml), 9 pulses (200μg/ml), 3 pulses (600μg/ml), 2 pulses (1000μg/ml) or 1 pulse (2000μg/ml), each mode achieving comparable, sustained pulmonary vasodilation.

[0071] Inhaled treprostinil exerts sustained pulmonary vasodilation with excellent tolerability at doses, which may be inhaled in a few or even one breath. Inhaled treprostinil is advantageous to inhaled iloprost in terms of duration of effect and systemic side effects. Inhaled treprostinil is well tolerated in concentrations up to 2000 mg/ml (bringing down inhalation time to a single breath) and in high doses (up to 90 μg).

Methods:

[0072] All inhalations were performed with the OPTINEB® ultrasonic nebulizer (Nebutec, Elsenfeld, Germany).

[0073] Study i) was a randomized, open-label, single-blind crossover study. The primary objective was to compare the acute hemodynamic effects and the systemic side effects of inhaled treprostinil with inhaled iloprost at comparable doses. A total number of 44 patients with moderate to severe precapillary pulmonary hypertension were enrolled. Patient characteristics and hemodynamic as well as gas exchange parameters are outlined in Table 3.

Table 3

[0074] Patient characteristics, hemodynamic parameters and gas exchange values at baseline, before challenge with inhalative prostanoids.

[0075] Group 1 corresponds to study i); randomized crossover study comparing inhaled iloprost (ILO) and inhaled treprostinil (TRE). a = 7.5g ILO vs. 7.5µg TRE, b = 7.5g ILO vs. 15µg TRE (6 min inhalation time), c = 7.5g ILO vs. 15µg TRE (3 min inhalation time). Group 2 corresponds to study ii); evaluation of maximal tolerated dose of TRE. a = placebo inhalation, b = 30µg TRE, c = 60µg TRE, d = 90 µg TRE, e = 120µg TRE. Group 3 corresponds to study iii); reduction of inhalation time by increase of TRE concentration, aiming at a total inhaled dose of 15 µg. a = 18 pulses of 100µg/ml TRE, b = 9 pulses of 200µg/ml TRE, c = 3 pulses of 600µg/ml TRE, d = 2 pulses of 1000µg/ml TRE, e = 1 pulse 2000µg/ml TRE. Etiology of pulmonary hypertension was classified as idiopathic PAH (i), PAH of other causes (o), chronic thromboembolic PH (t), and pulmonary fibrosis (f).

	N	Age	Gender f/m	Etiology i/o/t/f	PAP [mmHg]	PVR [dyn*s*cm^{-5}]	SAP [mmHg]	CVP [mmHg]	PAWP [mmHg]	CO [l/min]	SaO2 [%]	SvO2 [%]
1a	14	55.1±4.8	11/3	4/4/2/4	53.8±3.1	911±102	95.4±3.6	7.4±1	8.0±0.8	4.3±0.4	93.8±2	63.9±2.4
1b	14	54.1±3.3	10/4	1/6/5/2	47.4±3.8	716±80	90.6±3.3	5.9±1.4	6.4±0.7	4.7±0.4	92±1	64.4±2.3
1c	16	56±2.9	7/9	6/3/6/1	47.5±4.5	777±102	92±4.5	8,3±1.4	8.6±1.4	4.4±0.5	91.4±0.9	59.8±2.6
2a	8	60.8±4	4/4	2/2/3/1	51.9±4.9	849±152	95.9±4.8	7.6±1.4	11.1±1.7	4.4±0.6	89.6±2.8	60.1±2.8
2b	8	52.8±6.6	6/2	1/3/3/1	49±4	902±189	92.4±2.4	4.8±1.1	7.2±1.3	4.0±0.4	92.4±2.4	62.5±1.7
2c	6	56.8±5.9	4/2	0/2/2/2	44.2±3.5	856±123	96.3±3.9	5±1.1	6±1	3.8±0.3	92.8±1.5	63.6±1.8
2d	6	51.2±3.8	4/2	2/2/2/0	55.5±4.9	940±110	91.2±8.1	11.2±1.2	10±0.7	3.9±0.4	92±1.9	62±5.8
2e	3	57.3±9.1	1/2	0/1/0/2	45.3±5.2	769±267	99±3.2	5±2.1	9±0.6	4.5±0.6	94.2±1.3	66.3±1.5
3a	6	52.7±6.6	4/2	2/4/0/0	53.8±6.7	928±145	92.7±7.9	8.7±2.7	8.8±1.3	4.2±0.6	90.4±2.8	64.8±4.3
3b	6	58.3±3.5	4/2	3/1/1/1	54.2±6.1	808±156	94.3±2.8	7±1.4	10±1.3	5±0.7	91.9±0.7	63.5±2.9
3c	21	57.4±5.6	8/3	7/7/6/1	46.1±2.5	900±99	88±2.8	9±1.4	9.2±0.5	3.7±0.3	91.7±0.5	59.7±2
3d	7	55.6±5.8	3/4	0/4/3/0	53.1±7.1	732±123	91.4±5.6	7.9±3.1	8.6±1.3	5±0.4	90.7±1.4	61.3±3.7
3e	8	59±5.2	7/1	0/4/4/0	45.1±3.9	733±114	92.8±6.8	4.6±0.8	8.1±1.1	4.3±0.2	90.7±0.8	66.3±2.8

[0076] Each patient inhaled both iloprost and treprostinil on the same day during right heart catheter investigation; the drugs were administered consecutively with a one hour interval between the drug applications. One half of the study patients initially inhaled treprostinil and then inhaled iloprost (n=22), while the other half initially inhaled iloprost and then inhaled treprostinil (n=22). Patients were randomized to one of the two groups and blinded as to the study drugs. Drug effects were monitored for 60 minutes after each inhalation. Iloprost was inhaled at 4 µg/ml (6 min inhalation time; n=44) and treprostinil was inhaled at a concentration of 4 µg/ml (6 min inhalation ; n=14), 8 µg/ml (6 min inhalation; n=14) or 16 µg/ml (3 min inhalation; n=16). Based on previous biophysical characterization of the ultrasonic device with iloprost- and treprostinil-solution, this corresponds to a total inhaled dose of 7.5µg iloprost and treprostinil (4µg/ml) and 15µg treprostinil (8µg/ml and 16µg/ml), respectively.

[0077] Study ii) was a randomized, open-label, single blind, placebo controlled study. The primary objectives were to describe the pharmacodynamic and pharmacokinetic effects of inhaled treprostinil at a well tolerated dose (30µg) and to explore the highest tolerated single dose. A total number of 31 patients inhaled either placebo or treprostinil; each patient received one inhalation. The first 16 patients were randomized to 30µg TRE (16µg/ml, n=8) or placebo (stock solution in a concentration corresponding to TRE 16µg/ml). Subsequent patients received 60µg TRE (32µg/ml; n=6), 90µg TRE (48µg/ml; n=6) and 120µg TRE (64µg/ml; n=3). Inhalation time was 6 minutes in all groups. Hemodynamics and gas-exchange as well as arterial treprostinil concentrations were recorded for 180 minutes.

[0078] Study iii) was a randomized, open-label, single blind study. The primary objective was to explore the shortest possible inhalation time for a 15µg dose of inhaled treprostinil. A total of 48 patients inhaled one dose of TRE during right heart catheter investigation. The drug was applied in 18, 9, 3, 2 or 1 breaths. The aerosol was generated by a pulsed ultrasonic nebulizer (OPTINEB®, Nebutec, Elsenfeld, Germany) in cycles consisting of 2 seconds aerosol production (pulse) and 4 seconds pause. The device included an opto-acoustical trigger for the patient to synchronize

the inspiration to the end of the aerosol pulse, thereby providing exact dosage. The TRE dose of 15µg was either generated during 18 cycles (OPTINEB® filled with 100µg/ml TRE, n=6), 9 cycles (200µg/ml TRE, n=6), 3 cycles (600µg/ml TRE, n=21), 2 cycles (1000µg/ml TRE, n=7) or 1 cycle (2000µg/ml TRE, n=8). Hemodynamics and gas exchange were recorded for 120 - 180 minutes.

[0079] Treprostinil plasma concentrations were assessed in study ii) at 10, 15, 30, 60 and 120 minutes after inhalation. Treprostinil quantification was done by Alta Analytical Laboratory (El Dorado Hills, California, USA) with a validated liquid chromatography atmospheric-pressure ionization tandem mass spectrometry as previously described Wade M., *et al.* J. Clin. Pharmacol. 2004;44:503-9. Mixed venous blood was drawn at the depicted time points (Figure 11) after inhalation, centrifuged and the plasma frozen at -80°C until temperature controlled shipping on dry ice.

Statistics:

[0080] For statistical analysis of study i) the repeated PVR measurements after inhaled iloprost and treprostinil were subjected to a three-factorial analysis of variance (ANOVA; factors: time (A), drug (B), treprostinil concentration (C)) to avoid multiple testing. The time to maximum PVR decrease after inhalation of iloprost versus treprostinil was compared by paired t-test. Area under the curve (AUC) was calculated from start of inhalation until 60 min after inhalation. Means, standard error of the mean (SEM) and 95% confidence intervals were calculated. For study ii) and iii) areas between curves (ABC) were calculated between placebo inhalation (study ii) and the respective treprostinil inhalation until 180 min (study ii)) and 120 min (study iii)) after end of inhalation.

Results:

[0081] The inhalation of iloprost as well as treprostinil in study i) resulted in a rapid decrease in PVR and PAP (Figure 5-7). No significant differences were observed for the areas under the curve (AUC) of PVR decrease after inhalation of 7.5 µg TRE in 6 minutes (AUC -12.6 ± 7.0 %), 15 µg TRE in 6 minutes (AUC -13.3 ± 3.2 %) and 15

µg TRE in 3 minutes (AUC -13.6 ± 4.3 %). The AUC for PVR after the inhalation of 7.5 µg iloprost in 6 minutes was – 7.7 ± 3.7% (mean ± 95 % confidence interval). An overview of the pooled data of treprostinil inhalation as compared to iloprost inhalation is given in Figure 7. The maximum effect of iloprost and treprostinil on PVR was comparable but this effect was reached significantly later after treprostinil inhalation (18 ± 2 min) compared to iloprost (8 ± 1 min; mean ± SEM, $p<0.0001$) and lasted considerably longer (after 60 min, PVR values in the treprostinil group had not yet returned to baseline). The increase in cardiac output was less acute but prolonged after treprostinil inhalation. Systemic arterial pressure (SAP) was unaffected by treprostinil inhalation, whereas a transient decrease was observed after iloprost inhalation. Iloprost and treprostinil did not affect gas exchange. Three-factorial ANOVA for PVR demonstrated a significant difference between repeated measurements after inhalation ($p_{(A)}<0.0001$), no significant difference between drugs ($p_B=0.1$), no difference between treprostinil concentrations ($p_{(C)}=0.74$) and a significant drug x time interaction ($p_{(AxB)}<0.0001$). This translates into a significant effect of both drugs on PVR with comparable drug potency but a prolonged drug effect of treprostinil compared to iloprost.

[0082] In this study the occasionally observed mild side effects of iloprost inhalation at the given dose (transient flush, headache) were not observed with inhaled treprostinil. Bad taste was reported by most of the patients after inhalation of TRE. This was later found to be attributable to the metacresol preservative contained in the treprostinil solution.

[0083] In study ii) pharmacodynamics of inhaled placebo or treprostinil were observed for 180 minutes. Placebo inhalation was followed by a gradual increase in PVR over the entire observation time. Due to reduced patient numbers in the 120µg TRE group (because of side effects, see below), the hemodynamic values for this group were not included in the graphs of this study (Figure 8-9). All TRE doses lead to comparable maximal decreases of PVR to 76.5±4.7% (30µg), 73.7±5.8% (60µg), 73.3±4.3% (90µg) and 65.4±4.1% (120µg) of baseline values. An extended duration of pulmonary vasodilation was noted, surpassing the 3 hour observation period for the

60µg and 90µg (and 120 µg) TRE doses, whereas in the 30 µg dose group the hemodynamic changes had just returned to baseline within this period. Even at the highest doses, TRE had only minor effects on systemic arterial pressure (Figure 8). Cardiac output was increased to a maximum of 106.8±3.2% (30µg), 122.9±4.3% (60µg), 114.3±4.8% (90µg) and 111.3±3.9% (120µg TRE). The areas between the response curves after placebo versus TRE inhalation were calculated for PVR, PAP, SVR and SAP (Figure 9). Areas between the curves for PVR were not significantly different for 30µg, 60µg and 90µg TRE, a nearly maximal effect on PVR was already observed with 30µg TRE. Effects on PAP and SAP were small and did not show a dose-response relationship. Gas exchange was not affected at doses up to 90µg TRE, but arterial oxygen saturation was significantly decreased at a dose of 120µg TRE in all 3 patients. Further dose increments were omitted due to this side effect and severe headache in one patient.

[0084] Again, bad taste of the TRE aerosol was reported by most patients. Other side effects were flushing (n=1; 30µg TRE), mild transient cough (n=3; 60µg TRE), mild transient bronchoconstriction that resolved after one inhalation of fenoterol (n=1; 30µg TRE), moderate bronchoconstriction that resolved after one inhalation of fenoterol (n=1; 120µg TRE), and severe headache (n=1; 120µg TRE). The bad taste, the bronchoconstriction and the drop in SaO2 was attributed to metacresol in the original TRE solution. With the use of a metacresol-free solution of TRE (University Hospital Giessen, Germany; produced according to the manufacturer's protocol) in the following study, these side effects did no longer occur.

[0085] Study iii) was performed with metacresol-free TRE solution, having no specific taste and smell. A total of 48 patients were enrolled. This study aimed at the reduction of inhalation time and aerosol volume needed for pulmonary drug delivery. A modified OPTINEB® inhalation device was programmed to produce a constant amount of aerosol during repeatable pulses of aerosol generation. With this device, treprostinil could be safely utilized up to a concentration of 2000µg/ml without considerable side effects. No relationship of number or type of side effects to TRE

concentration was observed. Reported side effects were mild transient cough (n=6), mild headache (n=2) and mild jaw pain (n=1).

[0086] The reduction of PVR and PAP was comparable between all groups (Figure 10). TRE inhalation reduced PVR to 76.3±5.6% (18 pulses, 100µg/ml), 72.9±4.9% (9 pulses, 200µg/ml), 71.2±6.0% (3 pulses, 600µg/ml), 77.4±4.5% (2 pulses, 1000µg/ml) and 80.3±5.2% (1 pulse, 2000µg/ml). PAP was reduced to 84.2±4.5% (18 pulses, 100µg/ml), 84.2±4.1% (9 pulses, 200µg/ml), 81.1±4.1% (3 pulses, 600µg/ml), 86±4% (2 pulses, 1000µg/ml) and 88±5.4% (1 pulse, 2000µg/ml). Cardiac output was moderately increased in all groups, whereas systemic arterial pressure was not significantly affected.

[0087] The areas between the curves (ABC) for changes in hemodynamic and gas-exchange parameters after inhalation of 15µg TRE versus placebo were calculated for an observation time of 120 minutes (Figure 11). The ABC for both PVR and PAP was comparable between all groups.

[0088] Pharmakokinetic results from study ii): Peak plasma concentrations of treprostinil were found 10-15 minutes after inhalation. Maximal treprostinil plasma concentrations (C_{max}) for the 30µg, 60µg, 90µg and 120µg doses were 0.65 ± 0.28 ng/ml (n=4), 1.59 ± 0.17 ng/ml (n=4), 1.74 ng/ml (n=1) and 3.51 ± 1.04 ng/ml (n=2), respectively (mean ± SEM; Figure 12).

Discussion:

[0089] These studies investigated whether i) the acute effects of inhaled treprostinil would be comparable to or possibly advantageous over inhaled iloprost in pulmonary hypertensive patients, ii) the inhaled prostanoid dose might be increased without substantial local or systemic side effects, and iii) if the time of inhalation, which is 6 – 12 minutes for iloprost, could be reduced significantly by increasing the concentration of treprostinil aerosol.

[0090] The patient population in these studies included different forms of precapillary pulmonary hypertension. All these patients had a need for therapy of

pulmonary hypertension and reflected the typical population of a pulmonary hypertension center. No major differences in patient characteristics or hemodynamic baseline values existed between the different groups (table 3).

[0091] In study i) it was shown that the inhalation of treprostinil and iloprost in similar doses resulted in a comparable maximum pulmonary vasodilatory effect. However, marked differences in the response profile were noted. The onset of the pulmonary vasodilatory effect of inhaled treprostinil was delayed compared to iloprost, but lasted considerably longer, with the PVR decrease continuing beyond the one-hour observation period. Although the average dose of treprostinil was higher than the iloprost dose, no systemic effects were noted after treprostinil inhalation, whereas flush and transient SAP decrease, accompanied by more prominent cardiac output increase, occurred after iloprost inhalation. Such side effects were more prominent than in previous studies with inhaled iloprost. This may have been caused by the fact that the iloprost dose used in this study was 50% higher than the recommended single inhalation dose (5μg) and that the preceding treprostinil inhalation may have added to the systemic side effects caused by the iloprost inhalation. Surprisingly, with TRE there was no such systemic side effect, although the average effect on PVR was as potent as with iloprost.

[0092] This study used a cross-over design in order to minimize the effects of inter-individual differences in response to prostanoids. The short observation period of 1 hour was used to avoid an uncomfortably long catheter investigation. As a study limitation, the short observation interval may have caused carryover effects of the first to the second period as suggested by Figure 5. However, this still allowed for the interpretation of the study, that both drugs are potent pulmonary vasodilators and that treprostinil effects are significantly sustained compared to the iloprost effects.

[0093] The longer duration of action and the virtual absence of side effects (except the bitter taste of treprostinil aerosol, later attributed to metacresol) encouraged increasing the applied treprostinil dose in study ii). Observation time was extended to 3 hours to obtain precise pharmacodynamic data. Inhaled treprostinil resulted in a strong pulmonary vasodilation that outlasted the observation time of 3 hours when

compared to placebo inhalation. Surprisingly, inhaled treprostinil was tolerated in doses up to 90µg.

[0094] Study iii) successfully demonstrated that the inhalation time could be reduced to literally one single breath of 2000µg/ml treprostinil solution, thereby applying a dose of 15µg. This drug administration with a single breath induced pulmonary vasodilation for longer than 3 hours compared to placebo inhalation. Side effects were minor, of low frequency and not related to drug concentration. It was a surprising finding that such high concentrations of treprostinil were so well tolerated.

Conclusion:

[0095] Inhaled treprostinil can be applied in high doses (up to 90 µg) with a minimal inhalation time. Inhaled treprostinil exerts high pulmonary selectivity and leads to a long-lasting pulmonary vasodilation.

[0096] 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.

[0097] 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 method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device, wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

2. The method of claim 1, wherein the inhalation device is a soft mist inhaler.

3. The method of claim 1, wherein the inhalation device is a pulsed ultrasonic nebulizer.

4. The method of claim 1, wherein the inhalation device is a dry powder inhaler.

5. The method of claim 1, wherein the inhalation device is a pressurized metered dose inhaler.

6. The method of claim 4, wherein the formulation is a powder.

7. The method of claim 6, wherein the powder comprises particles less than 5 micrometers in diameter.

8. The method of claim 1, wherein the formulation contains no metacresol.

ABSTRACT

Treprostinil can be administered using a metered dose inhaler. Such administration provides a greater degree of autonomy to patients. Also disclosed are kits that include a metered dose inhaler containing a pharmaceutical formulation containing treprostinil.

FIGURE 1

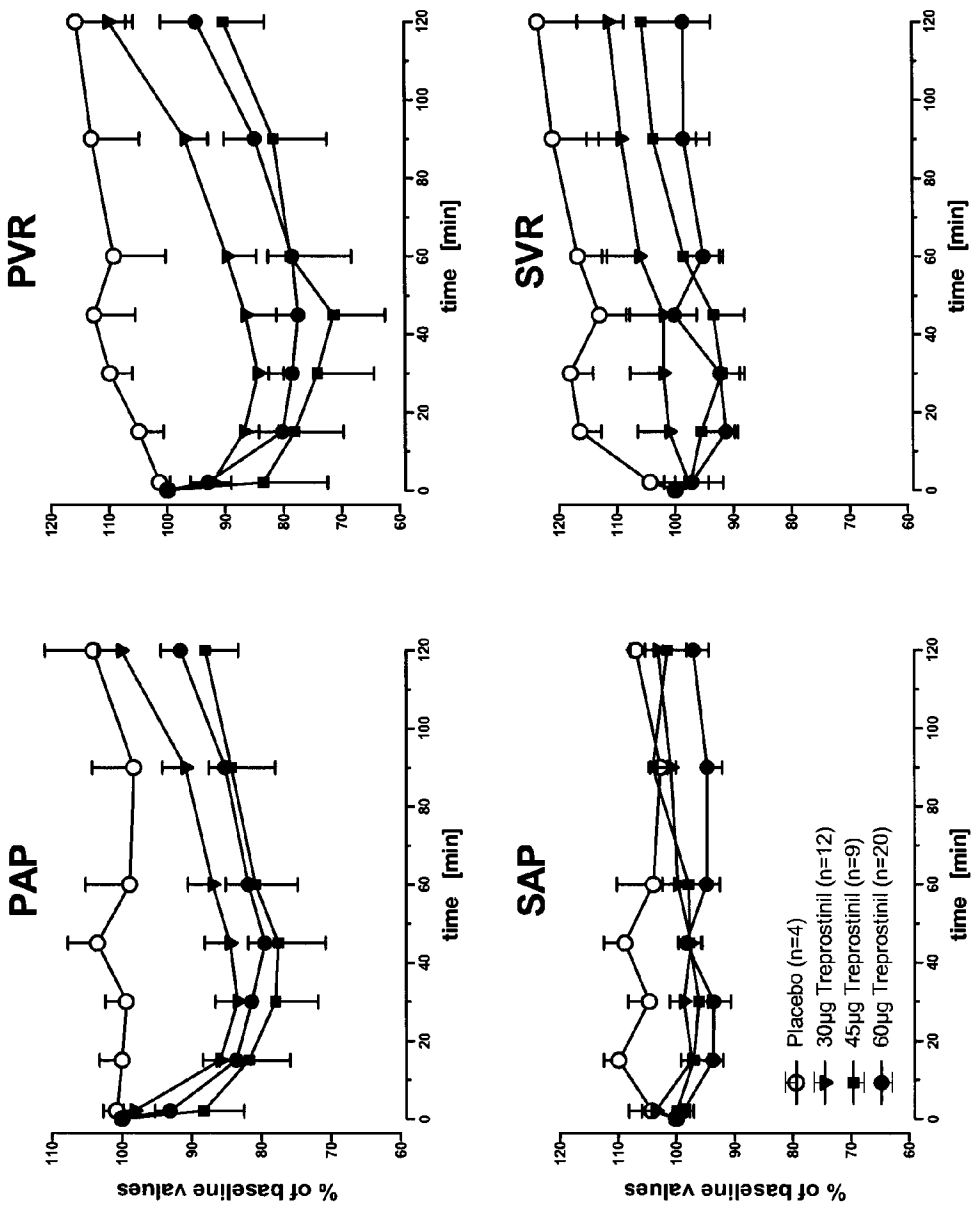

PAP
PVR
SAP
SVR
% of baseline values
time [min]
Placebo (n=4)
30µg Treprostinil (n=12)
45µg Treprostinil (n=9)
60µg Treprostinil (n=20)

FIGURE 2

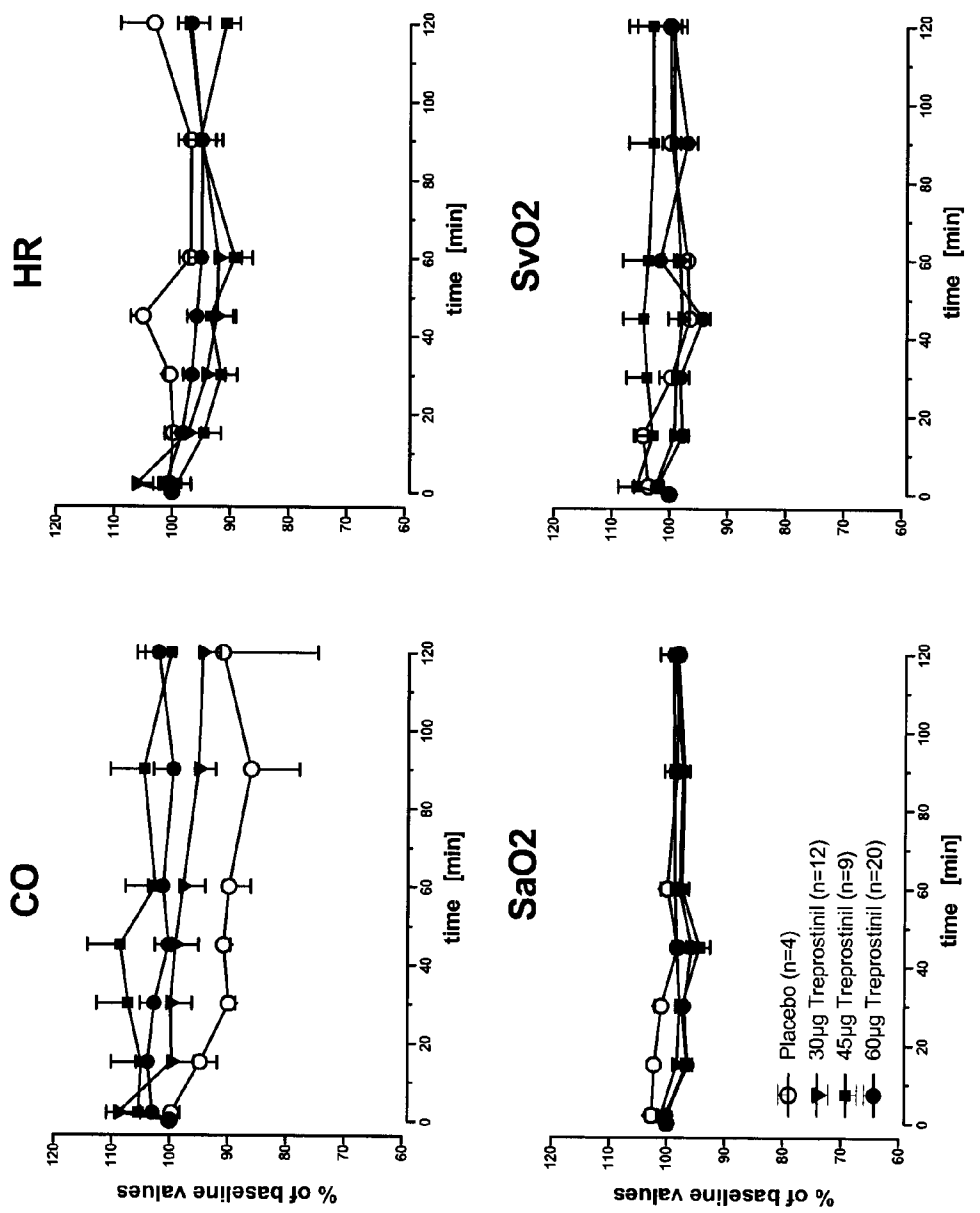

HR
CO
SvO2
SaO2
% of baseline values
time [min]
Placebo (n=4)
30µg Treprostinil (n=12)
45µg Treprostinil (n=9)
60µg Treprostinil (n=20)

FIGURE 3

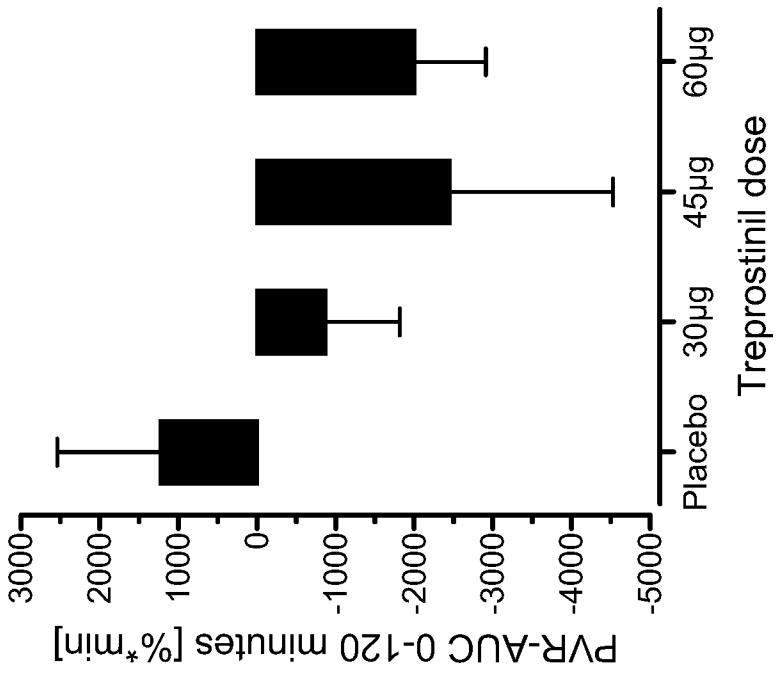

PVR-AUC 0-120 minutes [%*min]
3000
2000
1000
0
-1000
-2000
-3000
-4000
-5000
Placebo
30µg
45µg
60µg
Treprostinil dose

FIGURE 4

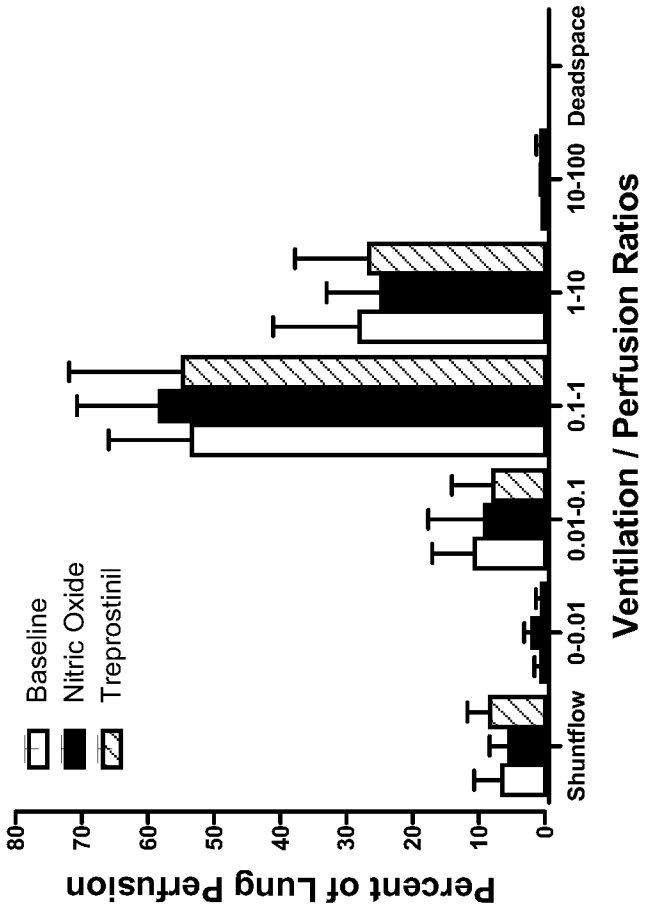

Baseline
Nitric Oxide
Treprostinil
Percent of Lung Perfusion
0
10
20
30
40
50
60
70
80
Shuntflow
0-0.01
0.01-0.1
0.1-1
1-10
10-100
Deadspace
Ventilation / Perfusion Ratios

FIGURE 5

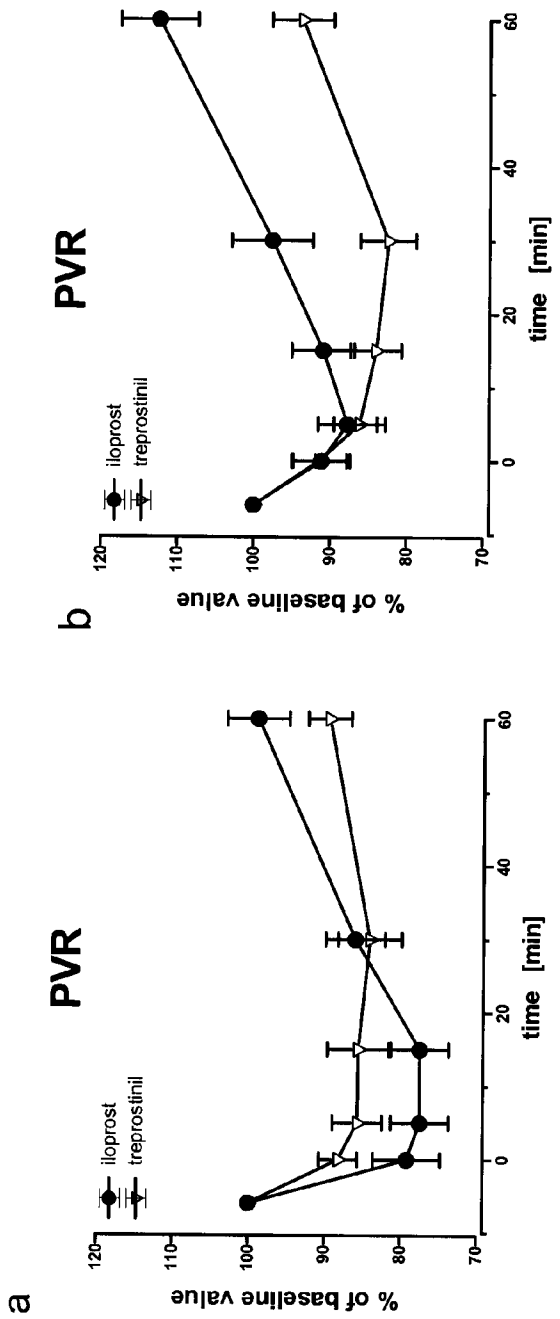

a
PVR
iloprost
treprostinil
% of baseline value
120
110
100
90
80
70
0
20
40
60
time [min]
b
PVR
iloprost
treprostinil
% of baseline value
120
110
100
90
80
70
0
20
40
60
time [min]

FIGURE 6

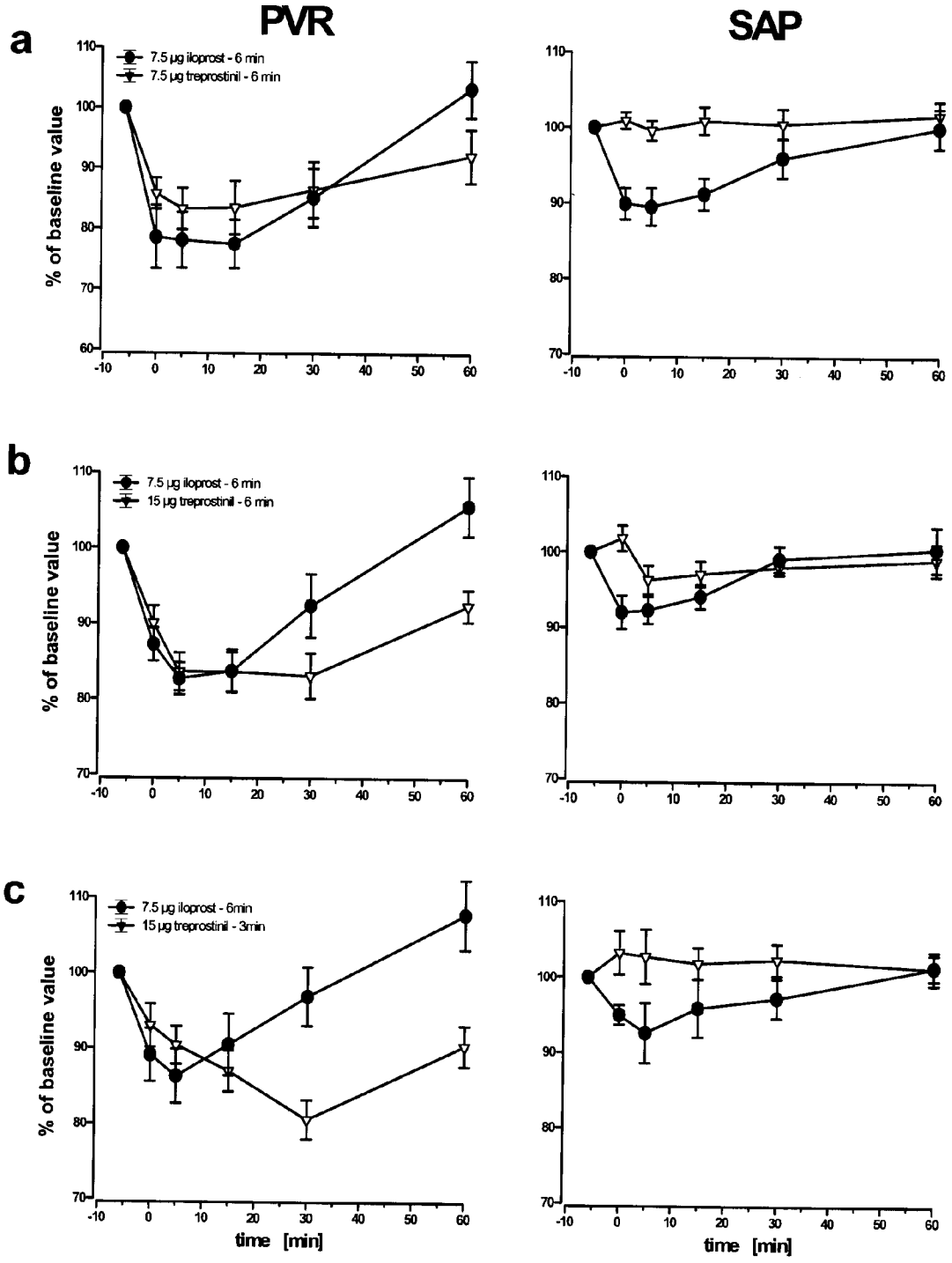

PVR
SAP
a
b
c
7.5 µg iloprost - 6 min
7.5 µg treprostinil - 6 min
15 µg treprostinil - 6 min
7.5 µg iloprost - 6min
15 µg treprostinil - 3min
% of baseline value
time [min]

FIGURE 7

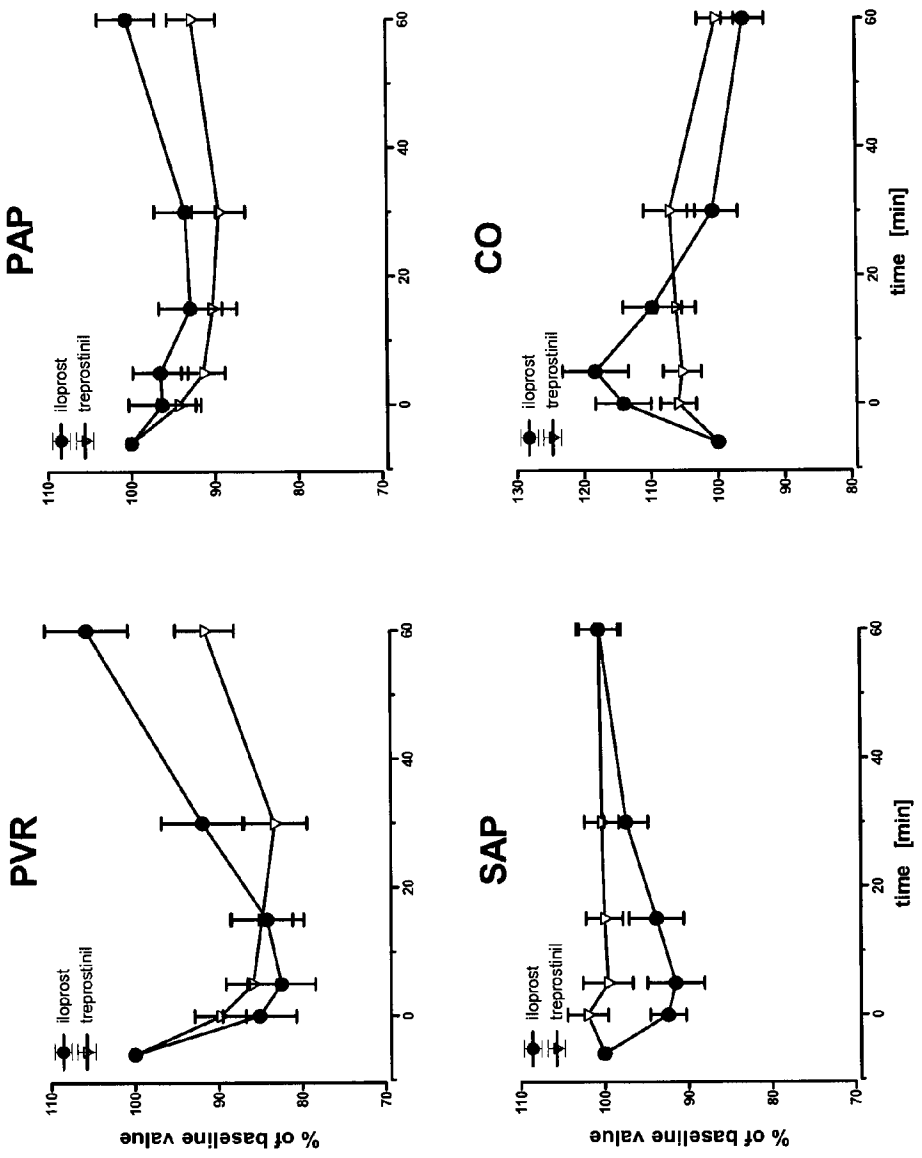

PVR
PAP
SAP
CO
iloprost
treprostinil
% of baseline value
time [min]

FIGURE 8

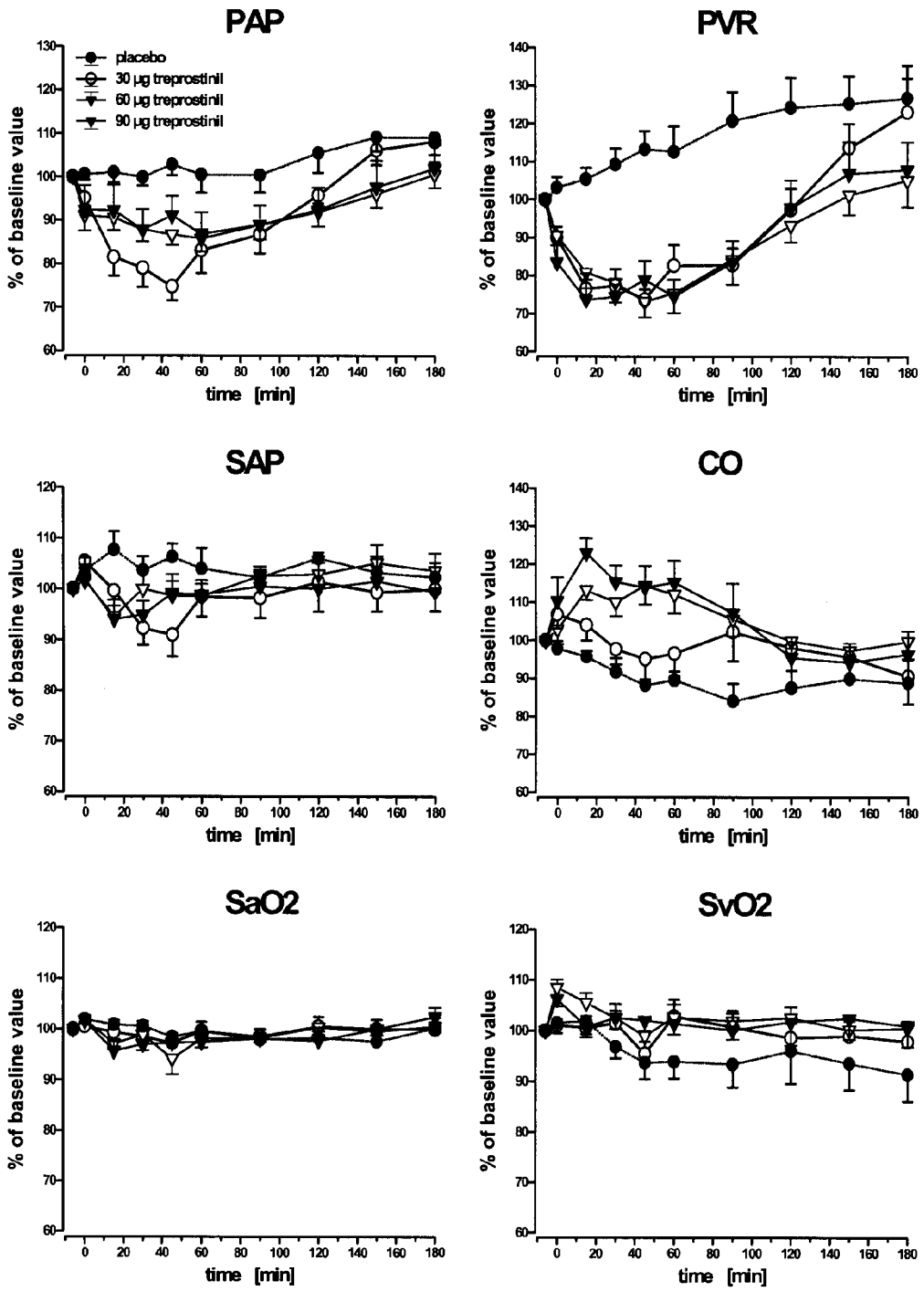

PAP
PVR
SAP
CO
SaO2
SvO2
placebo
30 µg treprostinil
60 µg treprostinil
90 µg treprostinil
% of baseline value
time [min]

FIGURE 9

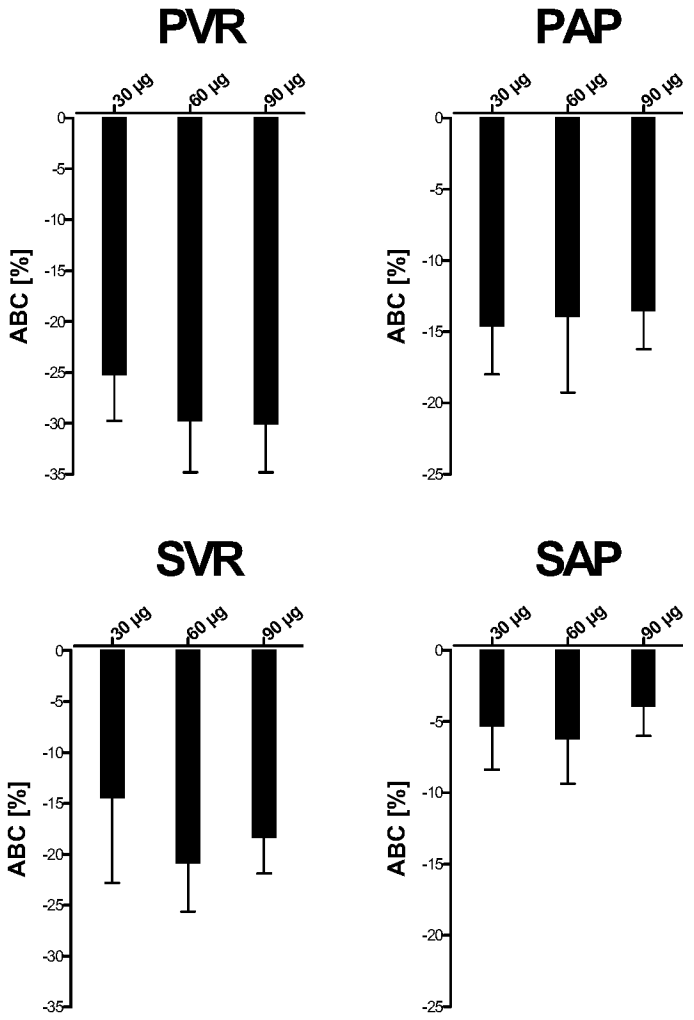


FIGURE 10

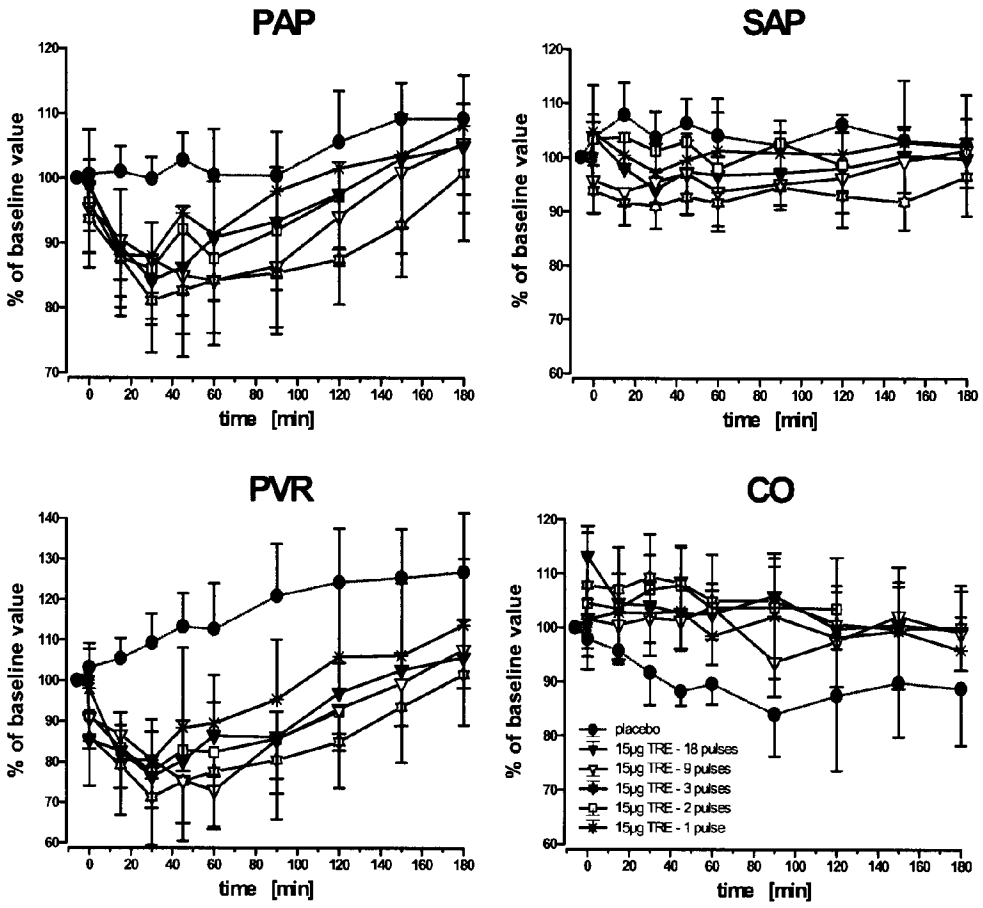

PAP
SAP
PVR
CO
% of baseline value
time [min]
placebo
15µg TRE - 18 pulses
15µg TRE - 9 pulses
15µg TRE - 3 pulses
15µg TRE - 2 pulses
15µg TRE - 1 pulse

FIGURE 11

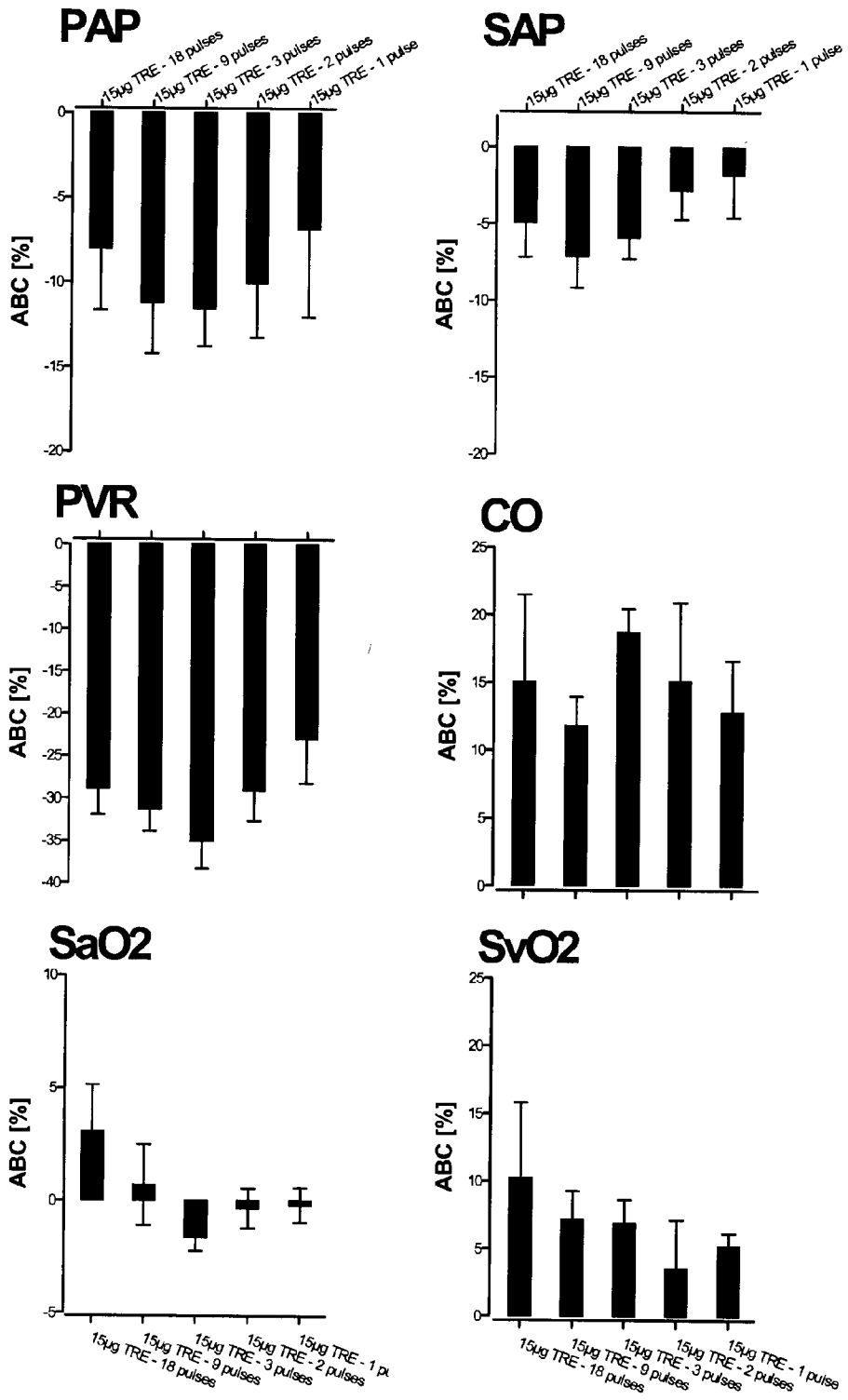
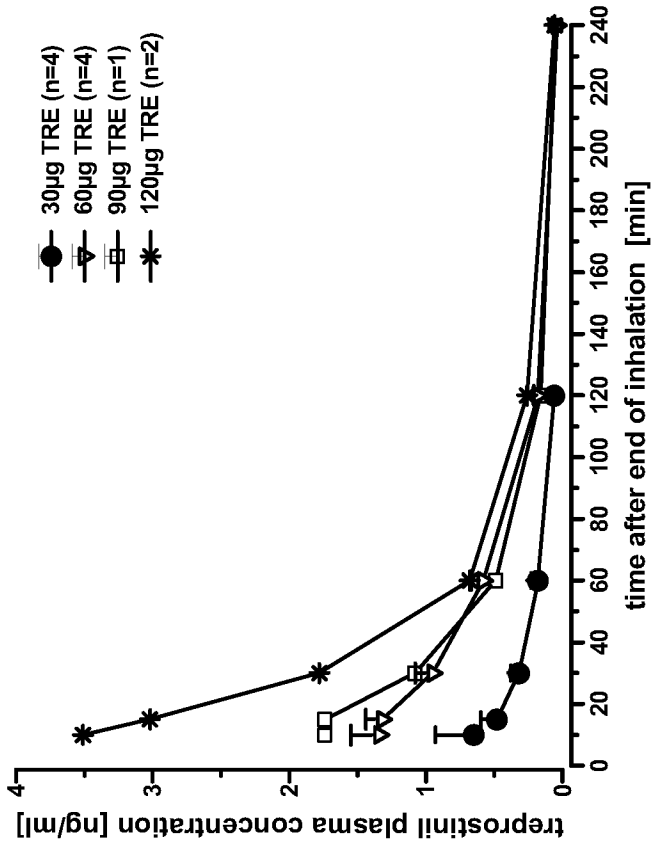

PAP
SAP
PVR
CO
SaO2
SvO2
ABC [%]
15µg TRE - 18 pulses
15µg TRE - 9 pulses
15µg TRE - 3 pulses
15µg TRE - 2 pulses
15µg TRE - 1 pulse

FIGURE 12


30µg TRE (n=4)
60µg TRE (n=4)
90µg TRE (n=1)
120µg TRE (n=2)
treprostinil plasma concentration [ng/ml]
time after end of inhalation [min]
0
1
2
3
4
0
20
40
60
80
100
120
140
160
180
200
220
240

PTO/AIA/01 (modified)

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)	080618-1639

Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 15/011,999 filed on 2/1/2016.

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:

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

LEGAL NAME OF INVENTOR

Inventor: Horst OLSCHEWSKI Date (Optional): 16 juin 2016

Signature: Dr. Horst Olschewski

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.

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

080618-1639

Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 15/011,999 filed on 2/1/2016.

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:

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

LEGAL NAME OF INVENTOR

Inventor: Robert ROSCIGNO Date (Optional): 2/3/2016

Signature: Robert Rosciano

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.

PTO/AIA/01 (modified)

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)	080618-1639

Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 15/011,999 filed on 2/1/2016.

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:

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

LEGAL NAME OF INVENTOR

Inventor: Lewis J. RUBIN Date (Optional): 3/4/16

Signature: Lewis J Rubin

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.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)	080618-1639

Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 15/011,999 filed on 2/1/2016.

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:

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

LEGAL NAME OF INVENTOR

Inventor: Werner SEEGER Date (Optional): 2016-2-3

Signature: _____

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.

Doc code: Oath
Document Description: Oath or declaration filed

PTO/AIA/02 (07-13)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

SUBSTITUTE STATEMENT IN LIEU OF AN OATH OR DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (35 U.S.C. 115(d) AND 37 CFR 1.64)

Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION

This statement is directed to:

☐ The attached application,

OR

☒ United States application or PCT international application number 15/011,999 filed on 02-01-2016

LEGAL NAME of inventor to whom this substitute statement applies:

(*E.g.*, Given Name (first and middle (if any)) and Family Name or Surname)

Thomas SCHMEHL

Residence (except for a deceased or legally incapacitated inventor):

City	State	Country
Giessen		DE

Mailing Address (except for a deceased or legally incapacitated inventor):

City	State	Zip	Country

I believe the above-named inventor or joint inventor to be the original inventor or an original joint inventor of a claimed invention in the application.

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

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

Relationship to the inventor to whom this substitute statement applies:

- ☐ Legal Representative (for deceased or legally incapacitated inventor only),
- ☒ Assignee,
- ☐ Person to whom the inventor is under an obligation to assign,
- ☐ Person who otherwise shows a sufficient proprietary interest in the matter (petition under 37 CFR 1.46 is required), or
- ☐ Joint Inventor.

PTO/SB/AIA02 (07-13)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

SUBSTITUTE STATEMENT

Circumstances permitting execution of this substitute statement:

- [x] Inventor is deceased,
- [ ] Inventor is under legal incapacity,
- [ ] Inventor cannot be found or reached after diligent effort, or
- [ ] Inventor has refused to execute the oath or declaration under 37 CFR 1.63.

If there are joint inventors, please check the appropriate box below:

- [x] An application data sheet under 37 CFR 1.76 (PTO/AIA/14 or equivalent) naming the entire inventive entity has been or is currently submitted.

OR

- [ ] An application data sheet under 37 CFR 1.76 (PTO/AIA/14 or equivalent) has not been submitted. Thus, a Substitute Statement Supplemental Sheet (PTO/AIA/11 or equivalent) naming the entire inventive entity and providing inventor information is attached. See 37 CFR 1.64(b).

WARNING:

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

PERSON EXECUTING THIS SUBSTITUTE STATEMENT:

Name: Shaun R. Snader | Date (Optional): 01 July 2019

Signature:

APPLICANT NAME AND TITLE OF PERSON EXECUTING THIS SUBSTITUTE STATEMENT:

If the applicant is a juristic entity, list the applicant name and the title of the signer:

Applicant Name: United Therapeutics Corporation

Title of Person Executing This Substitute Statement: Vice President, Associate General Counsel, IP

The signer, whose title is supplied above, is authorized to act on behalf of the applicant.

Residence of the signer (unless provided in an application data sheet, PTO/AIA/14 or equivalent):

City Falls Church | State VA | Country United States

Mailing Address of the signer (unless provided in an application data sheet, PTO/AIA/14 or equivalent)

United Therapeutics Corporation, 1735 Connecticut Avenue, NW

City Washington | State DC | Zip 20009 | Country United States

Note: Use an additional PTO/AIA/02 form for each inventor who is deceased, legally incapacitated, cannot be found or reached after diligent effort, or has refused to execute the oath or declaration under 37 CFR 1.63.

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.

Doc code: Oath
Document Description: Oath or declaration filed

PTO/AIA/02 (07-13)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

SUBSTITUTE STATEMENT IN LIEU OF AN OATH OR DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (35 U.S.C. 115(d) AND 37 CFR 1.64)

Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION

This statement is directed to:

☐ The attached application,

OR

☒ United States application or PCT international application number 15/011,999 filed on 02-01-2016.

LEGAL NAME of inventor to whom this substitute statement applies:

(*E.g.*, Given Name (first and middle (if any)) and Family Name or Surname)

Carl STERRITT

Residence (except for a deceased or legally incapacitated inventor):

City	State	Country
Weybridge		GB

Mailing Address (except for a deceased or legally incapacitated inventor):

c/o Shield Therapeutics, 16 Upper Woburn Place, Euston

City	State	Zip	Country
London		WC1H 0AF	GB

I believe the above-named inventor or joint inventor to be the original inventor or an original joint inventor of a claimed invention in the application.

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

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

Relationship to the inventor to whom this substitute statement applies:

☐ Legal Representative (for deceased or legally incapacitated inventor only),

☒ Assignee,

☐ Person to whom the inventor is under an obligation to assign,

☐ Person who otherwise shows a sufficient proprietary interest in the matter (petition under 37 CFR 1.46 is required), or

☐ Joint Inventor.

PTO/SB/AIA02 (07-13)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

SUBSTITUTE STATEMENT

Circumstances permitting execution of this substitute statement:

- ☐ Inventor is deceased,
- ☐ Inventor is under legal incapacity,
- ■ Inventor cannot be found or reached after diligent effort, or
- ☐ Inventor has refused to execute the oath or declaration under 37 CFR 1.63.

If there are joint inventors, please check the appropriate box below:

- ■ An application data sheet under 37 CFR 1.76 (PTO/AIA/14 or equivalent) naming the entire inventive entity has been or is currently submitted.

OR

- ☐ An application data sheet under 37 CFR 1.76 (PTO/AIA/14 or equivalent) has not been submitted. Thus, a Substitute Statement Supplemental Sheet (PTO/AIA/11 or equivalent) naming the entire inventive entity and providing inventor information is attached. See 37 CFR 1.64(b).

WARNING:

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

PERSON EXECUTING THIS SUBSTITUTE STATEMENT:

Name: Shaun R. Snader | Date (Optional): 01 July 2019

Signature: 

APPLICANT NAME AND TITLE OF PERSON EXECUTING THIS SUBSTITUTE STATEMENT:

If the applicant is a juristic entity, list the applicant name and the title of the signer:

Applicant Name: United Therapeutics Corporation

Title of Person Executing This Substitute Statement: Vice President, Associate General Counsel, IP

The signer, whose title is supplied above, is authorized to act on behalf of the applicant.

Residence of the signer (unless provided in an application data sheet, PTO/AIA/14 or equivalent):

City Falls Church | State VA | Country United States

Mailing Address of the signer (unless provided in an application data sheet, PTO/AIA/14 or equivalent)

United Therapeutics Corporation, 1735 Connecticut Avenue, NW

City Washington | State DC | Zip 20009 | Country United States

Note: Use an additional PTO/AIA/02 form for each inventor who is deceased, legally incapacitated, cannot be found or reached after diligent effort, or has refused to execute the oath or declaration under 37 CFR 1.63.

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.

Doc code: Oath
Document Description: Oath or declaration filed

PTO/AIA/02 (07-13)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

SUBSTITUTE STATEMENT IN LIEU OF AN OATH OR DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (35 U.S.C. 115(d) AND 37 CFR 1.64)

Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION

This statement is directed to:

☐ The attached application,

OR

■ United States application or PCT international application number 15/011,999 filed on 02-01-2016.

LEGAL NAME of inventor to whom this substitute statement applies:

(*E.g.*, Given Name (first and middle (if any)) and Family Name or Surname)

Robert VOSWINCKEL

Residence (except for a deceased or legally incapacitated inventor):

City Giessen | State | Country DE

Mailing Address (except for a deceased or legally incapacitated inventor):

c/o Justus-Liebig Universitaet Giessen, Parkstrasse 1

City Bad Nauheim | State | Zip D-61231 | Country DE

I believe the above-named inventor or joint inventor to be the original inventor or an original joint inventor of a claimed invention in the application.

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

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

Relationship to the inventor to whom this substitute statement applies:

- ☐ Legal Representative (for deceased or legally incapacitated inventor only),
- ■ Assignee,
- ☐ Person to whom the inventor is under an obligation to assign,
- ☐ Person who otherwise shows a sufficient proprietary interest in the matter (petition under 37 CFR 1.46 is required), or
- ☐ Joint Inventor.

PTO/SB/AIA02 (07-13)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

SUBSTITUTE STATEMENT

Circumstances permitting execution of this substitute statement:

- ☐ Inventor is deceased,
- ☐ Inventor is under legal incapacity,
- ■ Inventor cannot be found or reached after diligent effort, or
- ☐ Inventor has refused to execute the oath or declaration under 37 CFR 1.63.

If there are joint inventors, please check the appropriate box below:

- ■ An application data sheet under 37 CFR 1.76 (PTO/AIA/14 or equivalent) naming the entire inventive entity has been or is currently submitted.

OR

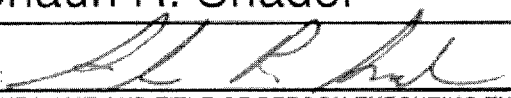
- ☐ An application data sheet under 37 CFR 1.76 (PTO/AIA/14 or equivalent) has not been submitted. Thus, a Substitute Statement Supplemental Sheet (PTO/AIA/11 or equivalent) naming the entire inventive entity and providing inventor information is attached. See 37 CFR 1.64(b).

WARNING:

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

PERSON EXECUTING THIS SUBSTITUTE STATEMENT:

Name: Shaun R. Snader | Date (Optional): 01 July 2019

Signature: 

APPLICANT NAME AND TITLE OF PERSON EXECUTING THIS SUBSTITUTE STATEMENT:

If the applicant is a juristic entity, list the applicant name and the title of the signer:

Applicant Name: United Therapeutics Corporation

Title of Person Executing This Substitute Statement: Vice President, Associate General Counsel, IP

The signer, whose title is supplied above, is authorized to act on behalf of the applicant.

Residence of the signer (unless provided in an application data sheet, PTO/AIA/14 or equivalent):

City Falls Church | State VA | Country United States

Mailing Address of the signer (unless provided in an application data sheet, PTO/AIA/14 or equivalent)

United Therapeutics Corporation, 1735 Connecticut Avenue, NW

City Washington | State DC | Zip 20009 | Country United States

Note: Use an additional PTO/AIA/02 form for each inventor who is deceased, legally incapacitated, cannot be found or reached after diligent effort, or has refused to execute the oath or declaration under 37 CFR 1.63.

Privacy Act Statement

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

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

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

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Horst		OLSCHEWSKI	

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

City	Graz	Country of Residence	AT

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation
Address 2	1040 Spring Street

City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 2 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Robert		ROSCIGNO	

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

City	Chapel Hill	State/Province	NC	Country of Residence	US

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation
Address 2	1040 Spring Street

City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 3 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Lewis	J.	RUBIN	

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

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

City	LaJolla	State/Province	CA	Country of Residence	US

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 4 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Thomas		SCHMEHL	

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

City	Giessen	Country of Residence	DE

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 5 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Werner		SEEGER	

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

City	Giessen	Country of Residence	DE

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	State/Province	MD
Postal Code	20910	Country	

Inventor 6 Remove

Legal Name

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Prefix	Given Name	Middle Name	Family Name	Suffix
	Carl		STERRITT	

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

City	Weybridge	Country of Residence ⓘ	GB

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	**State/Province**	MD
Postal Code	20910	**Country** ⓘ	

Inventor 7 Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Robert		VOSWINCKEL	

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

City	Giessen	Country of Residence ⓘ	DE

Mailing Address of Inventor:

Address 1	c/o United Therapeutics Corporation		
Address 2	1040 Spring Street		
City	Silver Spring	**State/Province**	MD
Postal Code	20910	**Country** ⓘ	

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

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

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

Customer Number	22428		
Email Address	IPDocketing@foley.com	Add Email	Remove Email

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Application Information:

Title of the Invention	TREPROSTINIL ADMINISTRATION BY INHALATION		
Attorney Docket Number	080618-1916	**Small Entity Status Claimed** ☐	
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	12	**Suggested Figure for Publication (if any)**	

Filing By Reference:

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

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

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

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	◉ Customer Number	○ US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	22428		

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	16/536954	2019-08-09
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
16/536954	Continuation of	15/011999	2016-02-01
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15/011999	Division of	13/469854	2012-05-11
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
13/469854	Division of	12/591200	2009-11-12
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
12/591200	Continuation of	11/748205	2007-05-14
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
11/748205	Claims benefit of provisional	60/800016	2006-05-15

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

Foreign Priority Information:

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove

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

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

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

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

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Authorization or Opt-Out of Authorization to Permit Access:

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

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

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

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

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

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

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

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

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

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

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

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

Applicant Information:

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

Applicant 1

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

Clear

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

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

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	United Therapeutics Corporation		
Mailing Address Information For Applicant:			
Address 1	1040 Spring Street		
Address 2			
City	Silver Spring	**State/Province**	MD
Country		Postal Code	20910
Phone Number		Fax Number	
Email Address			

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

Assignee Information including Non-Applicant Assignee Information:

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

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

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. ☒

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

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

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

Signature	/Stephen B. Maebius			Date (YYYY-MM-DD)	2020-01-31
First Name	Stephen B.	Last Name	Maebius	Registration Number	35264

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

PTO/AIA/14 (02-18)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	080618-1916
	Application Number	
Title of Invention	TREPROSTINIL ADMINISTRATION BY INHALATION	

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

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

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

1 The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3 A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent CooperationTreaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

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

PTO/AIA/80 (07-12)
Approved for use through 11/30/2014. OMB 0651-0035
U.S. Patent and Trademark Office; U.S DEPARTMENT OF COMMERCE

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 ssigned only to the undersigned according to the USPTO assignment records or assignments docu ments 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

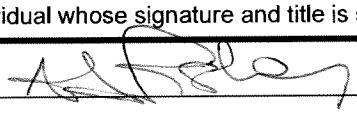
☐	Firm or Individual Name		
	Address		
	City		
	Country		
	Telephone		Email

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		

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name:	Horst OLSCHEWSKI
Title:	TREPROSTINIL ADMINISTRATION BY INHALATION
Application No.:	Unassigned (CON of 16/536,954)
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. 11/748,205, filed 5/14/2007; Application No. 12/591,200, filed 11/12/2009; Application No. 13/469,854, filed 5/11/2012; Application No. 15/011,999, filed 2/1/2016; Application No. 16/536,954, filed 8/9/2019, 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). Applicant does 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 Jan. 31, 2020

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

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.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	1	of	11	Attorney Docket Number	080618-1916

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	2003/0192532 A1	10/16/2003	Hopkins	
	A2	2004/0063912 A1	04/01/2004	Blumberg et al.	
	A3	2004/0105819 A1	06/03/2004	Hale et al.	
	A4	2004/0149282 A1	08/05/2004	Hickle	
	A5	2004/0265238 A1	12/30/2004	Chaudry, Imtiaz	
	A6	2005/0165111 A1	07/28/2005	Wade et al.	
	A7	2005/0166913 A1	08/04/2005	Sexton et al.	
	A8	2005/0183719 A1	08/25/2005	Wuttke et al.	
	A9	2005/0282901 A1	12/22/2005	Phares et al.	
	A10	2006/0147520 A1	07/06/2006	Ruegg, Curtis	
	A11	2006/0201500 A1	09/14/2006	Von Hollen et al.	
	A12	2008/0200449 A1	08/21/2008	Olschewski et al.	
	A13	2008/0280986A1	11/13/2008	Wade et al.	
	A14	2009/0036465 A1	02/05/2009	Roscigno et al.	
	A15	2010/0076083 A1	03/25/2010	Olschewski et al.	
	A16	2010/0236545 A1	09/23/2010	Kern	
	A17	2010/0282622 A1	11/11/2010	Phares, Kenneth R.	
	A18	2012/0177693 A1	07/12/2012	Cipolla et al.	
	A19	3,664,337	05/23/1972	Lindsey et al.	
	A20	4,001,650 A	01/04/1977	Romain	
	A21	4,281,113 A	07/28/1981	Axen et al.	
	A22	4,306,075	12/15/1981	Aristoff	
	A23	4,306,076 A	12/15/1981	Nelson, Norman A.	
	A24	4,349,689 A	09/14/1982	Aristoff, Paul A.	
	A25	4,473,296	09/25/1984	Shofner et al.	
	A26	4,486,598 A	12/04/1984	Aristoff, Paul A.	
	A27	4,495,944	01/29/1985	Brisson et al.	
	A28	4,635,647	01/13/1987	Choksi	
	A29	4,668,814 A	05/26/1987	Aristoff, Paul A.	
	A30	4,677,975	07/07/1987	Edgar et al.	
	A31	4,683,330 A	07/28/1987	Aristoff, Paul A.	
	A32	4,692,464 A	09/08/1987	Skuballa et al.	
	A33	4,708,963 A	11/24/1987	Skuballa et al.	
	A34	4,976,259	12/11/1990	Higson et al.	
	A35	4,984,158	01/08/1991	Hillsman	
	A36	5,063,922	11/12/1991	Hakkinen	
	A37	5,080,093 A	01/14/1992	Raabe et al.	
	A38	5,153,222	10/06/1992	Tadepalli et al.	
	A39	5,234,953 A	08/10/1993	Crow et al.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	2	of	11	Attorney Docket Number	080618-1916

U.S. PATENT DOCUMENTS

Examiner	Cite No.[1]	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant
	A40	5,322,057 A	06/21/1994	Raabe et al.	
	A41	5,361,989 A	11/08/1994	Merchat et al.	
	A42	5,363,842 A	11/15/1994	Mishelevich et al.	
	A43	5,497,763 A	03/12/1996	Lloyd et al.	
	A44	5,551,416 A	09/03/1996	Stimpson et al.	
	A45	5,727,542 A	03/17/1998	King	
	A46	5,865,171 A	02/02/1999	Cinquin	
	A47	5,881,715 A	03/16/1999	Shibasaki	
	A48	5,908,158 A	06/01/1999	Cheiman	
	A49	6,054,486 A	04/25/2000	Crow et al.	
	A50	6,123,068 A	09/26/2000	Lloyd et al.	
	A51	6,357,671	03/19/2002	Cewers, Goran	
	A52	6,521,212 B1	02/18/2003	GILLES et al.	
	A53	6,626,843 B2	09/30/2003	Hillsman	
	A54	6,756,033	06/29/2004	Cloutier et al.	
	A55	6,765,117 B2	07/20/2004	Moriarty et al.	
	A56	6,803,386 B2	10/12/2004	Shorr et al.	
	A57	6,809,223 B2	10/26/2004	Moriarty et al.	
	A58	7,172,557 B1	02/06/2007	Parker	
	A59	7,199,157 B2	04/03/2007	Wade et al.	
	A60	7,384,978 B2	06/10/2008	Phares et al.	
	A61	7,417,070 B2	08/26/2008	Phares et al.	
	A62	7,544,713 B2	06/09/2009	Phares et al.	
	A63	7,726,303 B2	07/01/2010	Tyvoll et al.	
	A64	4,007,238	02-08-1977	Glenn	
	A65	7,261,102	08-28-2007	Barney et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3]-Number[4]-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]
	A66	AU1999959533 B2	02/03/2000	Toray Industries, Inc.		
	A67	DE 19838711 C1	06/2000	Gessler		✓
	A68	DE 19934582 A1	01/2001	Buff		✓
	A69	FR 2783431 A1	03/24/2000	Systen Assistance Medical		A
	A70	JP 2003-522003 A	07/22/2003		=WO01/58514	✓
	A71	JP 2004-512101 A	04/22/2004	Glaxo Group Limited	=WO02/34318	✓
	A72	JP 2005-034341 A	02/10/2005	Teijin Ltd.		A
	A73	WO 93/00951 A1	01/21/1993	Inhale, Inc.		
	A74	WO 01/58514 A1	08/16/2001	Medic-Aid Limited		

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

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.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	3	of	11	Attorney Docket Number	080618-1916

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3]-Number[4]-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]
	A75	WO 01/85241 A1	11/15/2001	Pari GmbH		
	A76	WO 02/34318 A2	05/02/2002	Glaxo Group Limited		

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]
	A77	Abe et al., "Effects of inhaled prostacyclin analogue on chronic hypoxic pulmonary hypertension," J. Cardiovascular Pharmacology, 2001, 37, 239 251.	
	A78	Agnew JE, Bateman RM, Pavia D, Clarke SW. (1984) Radionuclide demonstration of ventilatory abnormalities in mild asthma. Clinical Science; 66: 525-531.	
	A79	Annals of the International Commission on Radiological Protection (ICRP) Vol 28, No. 3, 1998, Publication 80, Radiation Dose to Patients from Radiopharmaceuticals.	
	A80	Aradigm Corporation news release October 24, 2005, "Aradigm and United Therapeutics Sign Development and Commercialization Agreement Targeting Pulmonary Hypertension," Red Orbit News, http://www.redorbit.com/modules/news/tools.php?tool=print&id=281787, 2 pages.	
	A81	Aristoff et al., "Synthesis of benzopyran prostaglandins, potent stable prostacyclin analogs, via an intermolecular mitsunobu reaction," Tetrahedron Letters, 1984, 25(36):3955-3958.	
	A82	Badesch et al., "Prostanoid Therapy for Pulmonary Arterial Hypertension," Journal of the American College of Cardiology, 2004, 43(12:Suppl.S):56S-61S.	
	A83	Bein et al., "Cardiovascular and pulmonary effects of aerosolized prostacyclin administration in severe respiratory failure using a ventilator nebulization system," J. Cardiovascular Pharmacology, 1996, 27, 583-586.	
	A84	Benedict et al., "Evidence-based pharmacologic management of pulmonary arterial hypertension," Clinical Therapeutics, 2007, 29, 2134-2153.	
	A85	Bindl et al., "Aerosolised prostacyclin for pulmonary hypertension in neonates," Archives of disease in childhood, Fetal and neonatal edition, 1994, 71(3), F214-6.	
	A86	Blanchard, J.D., Cipolla, D., Liu, K., Morishige, R., Mudumba, S., Thipphawong, J., Taylor, G., Warren, S., Radhakrishnan, R., Van Vlasselaer, R., Visor , G. and Starko, K. (2003) Lung Deposition of Interferon Gamma-1b following Inhalation via AERx® System vs. Respirgard II™ Nebulizer Proc. ATS Annual Meeting (Abstract A373), Seattle.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	4	of	11	Attorney Docket Number	080618-1916

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]
	A87	Booke et al., "Prostaglandins in Patients with Pulmonary Hypertension: The Route of Administration," Anesth. Analg., 1998, 86:917, Letter to the Editor.	
	A88	Boyd, B., Noymer, P., Liu, K., Okikawa, J., Hasegawa, D., Warren, S., Taylor, G., Ferguson, E., Schuster, J., Farr, S., and Gonda, I. (2004) Effect of Gender and Device Mouthpiece Shape on Bolus Insulin Aerosol Delivery Using the AERx Pulmonary Delivery System. Pharmaceutical Research. 21 (10) 1776-1782.	
	A89	BYRON, Peter R., "Drug Delivery Devices, Issues in Drug Development," Proc. Am. Thorac. Soc., 2004, 1:321-328.	
	A90	Channick et al., "Safety and efficacy of inhaled treprostinil as add-on therapy to bosentan in pulmonary arterial hypertension," J. American College of Cardiology, 2006, 48, 1433-1437.	
	A91	Colthorpe P, Taylor G, Farr SJ. (1997) A comparison of two non-invasive methods for quantifying aerosol deposition in the lungs of rabbits. J. Aerosol Med.; 10:255	
	A92	Defendant Watson Laboratories, Inc.'s Invalidity Contentions for U.S. Patent Nos. 9,339,507 and 9,358,240, in The United States District Court for the District of New Jersey, Civil Action No. 3.15:cv-05723-PGS-LHG, August 5, 2016, 56 pages.	
	A93	Doyle et al., "Inhaled prostacyclin as a selective pulmonary vasodilator," Anaesthesia and Intensive Care, August 1996, 24(4):514-515.	
	A94	Dumas et al,. "Hypoxic pulmonary vasoconstriction," General Pharmacology, 1999, 33, 289-297.	
	A95	Dworetz et al., "Survival of infants with persistent pulmonary hypertension without extracorporeal membrane oxygenation," Pediatrics, 1989, 84, 1-6.	
	A96	EPA Integrated Risk Information System (IRIS): data sheet for 3-methylphenol (m-cresol). Accessed at http://www.epa.gov/iris/subst/0301/htm on 3/9/2014.	
	A97	EU Community Register, Annexes to Commission Decision C(2005)3436, September 5, 2005, http://ec.europa.eu/health/documents/communityregister/2005/2005090510259/anx_10259_en.pdf (Annex III –Ventavis® Labelling and Package Leaflet), 30 pages.	
	A98	Ewert et al., "Aerosolized iloprost for primary pulmonary hypertension," New England Journal of Medicine, 2000, 343, 1421-1422.	
	A99	Ewert et al., "Iloprost als inhalative bzw. Intravenose langzeitbehandlung von patienten mit primarer pulmonaler hypertonie," Z. Kardiol., 2000, 89, 987-999.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	5	of	11	Attorney Docket Number	080618-1916

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]
	A100	Farr et al., "Comparison of in vitro and in vivo efficiencies of a novel unit-dose liquid aerosol generator and a pressurized metered dose inhaler," International Journal of Pharmaceutics, 2000, 198:63-70.	
	A101	Final Office Action dated 10/10/2014 in US SN 12/591,200.	
	A102	Final Office Action dated 10/17/2012 in US SN 12/591,200.	
	A103	Final Office Action dated 11/4/2013 in US SN 12/303,877.	
	A104	Final Office Action dated 12/22/2011 in US SN 12/591,200.	
	A105	Final Office Action dated 7/2/2013 in US SN 13/120,015.	
	A106	Final Office Action dated 7/20/2015 in US SN 13/120,015.	
	A107	Final Office Action dated 8/1/2012 in US SN 12/303,877.	
	A108	Findlay et al., "Radioimmunoassay for the Chemical Stable Prostacyclin Analog, 15AU81: a Preliminary Pharmacokinetics Study in the Dog," Prostaglandins Leukot. Essent. Fatty Acids, February 1993, 48(2):167-174.	
	A109	Fink et al., "Use of Prostacyclin and its Analogues in the Treatment of Cardiovascular Disease," Heart Disease, 1999, 1:29-40.	
	A110	Gessler et al., "Ultrasonic versus jet nebulization of iloprost in severe pulmonary hypertension," Eur. Respir. J., 2001, 17, 14-19.	
	A111	GHOFRANI et al., "Hypoxia- and non-hypoxia-related pulmonary hypertension -- Established and new therapies," Cardiovascular Research, 2006, 72:30-40.	
	A112	Ghofrani et al., "New therapies in the treatment of pulmonary hypertension," Herz (Heart), 2005, 4:296-302, with English translation.	✓

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

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.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	6	of	11	Attorney Docket Number	080618-1916

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]
	A113	Hallioglu et al., "Comparison of Acute Hemodynamic Effects of Aerosolized and Intravenous *Iloprost* in Secondary Pulmonary Hypertension in Children With Congenital Heart Disease," Am. J. Cardiol., 2003, 92:1007-1009.	
	A114	Haraldsson et al., "Comparison of inhaled nitric oxide and inhaled aerosolized prostacyclin in the evaluation of heart transplant candidates with elevated pulmonary vascular resistance," Chest, 1998, 114, 780-786.	
	A115	Hoeper et al., "A comparison of the acute hemodynamic effects of inhaled nitric oxide and aerosolized iloprost in primary hypertension," J. American College of Cardiology, 2000, 35, 176-182.	
	A116	Hoeper et al., "Effects of inhaled nitric oxide and aerosolized iloprost in pulmonary veno-occlusive disease," Respiratory Medicine, 1999, 93, 62-70.	
	A117	Hoeper et al., "Long term treatment of primary pulmonary hypertension with aerosolized iloprost, a prostacyclin analogue," New England Journal of Medicine, 2000, 342, 1866-1870.	
	A118	Horn et al., "Treprostinil therapy for pulmonary artery hypertension," Expert Opinion on Investigational Drugs, 2002, 11(11):1615-1622.	
	A119	Howarth, P.H., "Why particle size should affect clinical response to inhaled therapy," Journal of Aerosol Medicine, 2001, 14 Supp. 1, S-27-S-34.	
	A120	Ichida et al., "Additive effects of beraprost on pulmonary vasodilation by inhaled nitric oxide in children with pulmonary hypertension," American Journal of Cardiology, 1997, 80, 662-664.	
	A121	Konorza et al., "Klinisch-pharmakologische Austestung bei pulmonaler Hypertonie zur Therapiefuehrung," Herz, 2005, 30:286-295, English abstract on first page.	A
	A122	Krause et al., "Pharmacokinetics and pharmacodynamics of the prostacyclin analogue iloprost in man," Eur. J. Clin. Pharmacol., 1986, 30, 61-68.	
	A123	Labiris et al., "Pulmonary drug delivery. Part II: The role of inhalant delivery devices and drug formulations in therapeutic effectiveness of aerosolized medications," Br. J. Clin. Pharmacol., 2003, 56(6):600-612.	
	A124	Lee et al., "Current strategies for pulmonary arterial hypertension," J. Internal Medicine, 2005, 258, 199-215.	
	A125	MARTIN, John C., "Inhaled Form of Remodulin in the Pipeline," http://www.phneighborhood.com/content/in_the_news/archive_2320,aspx, ph Neighborhood, October 28, 2005, 2 pages.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	7	of	11	Attorney Docket Number	080618-1916

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]
	A126	Max et al., "Inhaled prostacyclin in the treatment of pulmonary hypertension," Eur. J. Pediatr., 1999, 158 Suppl 1, S23-S26.	
	A127	McNulty et al., "The Pharmacokinetics and Pharmacodynamics of the Prostacyclin Analog 15AU81 in the Anesthetized Beagle Dog," Prostaglandins Leukot. Essent. Fatty Acids, February 1993, 48(2):159-166.	
	A128	Miller et al., "Standardisation of spirometry. Series ATS/ERS Task Force: Standardisation of Lung Function Testing'' Eur Respir J 2005; 26: 319–338.	
	A129	Mueller et al., "Inhaled iloprost in the management of pulmonary hypertension in infants undergoing congenital heart surgery," European Journal of Anaesthesiology, June 2004, 21(Suppl.33):3, Abstract No. 084.	
	A130	National Radiological Protection Board. Doses to Patients from Medical Radiological Examinations in Great Britain. (1986) Radiological Protection Bulletin No. 77.	
	A131	Nebu-Tec med. Produkte Eike Kern GmbH, VENTA-NEB®-ir A-I-C-I® Operating Instrutions, Sep. 2005.	
	A132	Non-Final Office Action dated 1/29/2015 in US SN 13/120,015.	
	A133	Non-Final Office Action dated 10/11/2011 in US SN 12/303,877.	
	A134	Non-Final Office Action dated 10/31/2012 in US SN 13/120,015.	
	A135	Non-Final Office Action dated 12/30/2014 in US SN 12/303,877.	
	A136	Non-Final Office Action dated 3/15/2013 in US SN 12/303,877.	
	A137	Non-Final Office Action dated 3/9/2014 in US SN 12/591,200.	
	A138	Notes for Guidance on the Clinical Administration of Radiopharmaceuticals and Use of Sealed Radioactive Sources. Administration of Radioactive Substances Advisory Committee (ARSAC) (March 2006). ARSAC Secretariat, Chilton, Didcot, Oxon. OX11 0RQ.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	8	of	11	Attorney Docket Number	080618-1916

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]
	A139	Notice of Allowance dated 6/11/2015 in US SN 12/303,877.	
	A140	Olschewski et al. for the German PPH Study Group, "Inhaled iloprost to treat severe pulmonary hypertension – An uncontrolled trial," Annals of Internal Medicine, 2000, 132, 435-443.	
	A141	Olschewski et al., "Aerosolized prostacyclin and iloprost in severe pulmonary hypertension,: Annals of Internal Medicine, 1996, 124, 820 824.	
	A142	Olschewski et al., "Inhaled Iloprost for Severe Pulmonary Hypertension," N. Eng. J. Med., August 1, 2002, 347(5):322-329.	
	A143	Olschewski et al., "Inhaled prostacyclin and iloprost in severe pulmonary hypertension secondary to lung fibrosis," Am. Respir. Crit. Care Med., 1999, 160, 600-607.	
	A144	Olschewski et al., "Pharmacodynamics and pharmacokinetics of inhaled iloprost, aerosolized by three different devices, in severe pulmonary hypertension," Chest, 2003, 124, 1294-1304.	
	A145	Olschewski et al., "Prostacyclin and its analogues in the treatment of pulmonary hypertension," Pharmacology and Therapeutics, 2004, 102, 139-153.	
	A146	Olschewski et al., "Recovery from circulatory shock in severe primary pulmonary hypertension (PPH) with aerosolization of iloprost," Intensive Care Med., 1998, 24, 631-634.	
	A147	Olschewski, Horst, "Therapie der pulmonalen Hypertonie," Pneumologe, 2004, 1:95-101.	
	A148	OPTINEB®-ir Operating Instructions, Unit Type ON-100/2-2.4 MHz, 2005, 33 pages, verified English translation.	
	A149	Pappert et al., "Aerosolized Prostacyclin Versus Inhaled Nitric Oxide in Children with Severe Acute Respiratory Distress Syndrome," Anesthesiology, June 1995, 82(6):1507-1511.	
	A150	Publications of the International Commission on Radiological Protection (ICRP) (1977) Recommendations of the International Commission on Radiological Protection 26.	
	A151	Pulmonary Delivery, ONdrugDelivery, 2006, 5 pages.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

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.

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	9	of	11	Attorney Docket Number	080618-1916

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]
	A152	RIGBY, Jonathan, Aradigm Corporation, "Technological advances for success: Product pipeline in targeted pulmonary delivery," Pulmonary Delivery Innovative Technologies Breathing New Life into Inhalable Therapeutics, ONdrugDelivery, http://www.ondrugdelivery.com/publications/Pulmonary.pdf, 2006, 17-19.	
	A153	Rubin et al., "Pulmonary Arterial Hypertension: A Look to the Future," Journal of the American College of Cardiology, June 18, 2004, 43(12,Suppl.S):89S-90S.	
	A154	Saini et al., "Effect of Electrostatic Charge and Size Distributions on Respirable Aerosol Deposition in Lung Model," Industry Applications Conference, 2004, 39th IAS Annual Meeting, Conference Record of the 2004 IEEE Seattle, WA, October 3-7, 2004, 2:948-952.	
	A155	Sandifer et al., "Effects of Aerosol vs IV UT-15 on Prostaglandin H_2 Analog-Induced Pulmonary Hypertension in Sheep," Chest, 2005, 128:616S.	
	A156	SANDIFER et al., "Potent effects of aerosol compared with intravenous treprostinil on the pulmonary circulation," J. Appl. Physiol., 2005, 99:2363-2368.	
	A157	Santak et al., "Prostacyclin aerosol in an infant with pulmonary hypertension," Eur. J. Pediatr., 1995, 154, 233-235.	
	A158	Scientific discussion for the approval of Ventavis, European Medicines Agency (EMEA), October 20, 2004, 30 pages.	
	A159	Soditt et al., "Improvement of oxygenation induced by aerosolized prostacyclin in a preterm infant with persistent pulmonary hypertension of the newborn," Intensive Care Med., 1997, 23, 1275-1278.	
	A160	Steffen et al., "The Effects of 15AU81, a Chemically Stable Prostacyclin Analog, on the Cardiovascular and Renin-Angiotensis Systems of Anesthetized Dogs," Prostaglandins, Leukotrienes and Essential Fatty Acids," 1991, 43:277-286.	
	A161	Stricker et al., "Sustained improvement of performance and haemodynamics with long-term aerosolized prostacyclin therapy in severe pulmonary hypertension," Schweiz Med. Wochenschr., 1999, 129, 923-927.	
	A162	Van Heerden et al., "Inhaled aerosolized prostacyclin as a selective pulmonary vasodilator for the treatment of severe hypertension," Anaesthesia and Intensive Care, 1996, 24, 87-90.	
	A163	Van Heerden et al., "Re: Delivery of inhaled aerosolized prostacyclin (IAP)," Anaesthesia and Intensive Care, 1996, 24, 624-625.	
	A164	Voswinckel et al., "Acute effects of the combination of sildenafil and inhaled treprostinil on haemodynamics and gas exchange in pulmonary hypertension," Pulmonary Pharmacology & Therapeutics, 2008, 21, 824-832.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	10	of	11	Attorney Docket Number	080618-1916

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]
	A165	VOSWINCKEL et al., "Favorable Effects of Inhaled Treprostinil in Severe Pulmonary Hypertension," Journal of the American College of Cardiology, 2006, 48(8):1672-1681.	
	A166	VOSWINCKEL et al., "Inhaled Treprostinil for Treatment of Chronic Pulmonary Arterial Hypertension," Annals of Internal Medicine, January 17, 2006, 144(2):149-150.	
	A167	Voswinckel et al., "Inhaled treprostinil is a potent pulmonary vasodilator in severe pulmonary hypertension," European Heart Journal, Journal of the European Society of Cardiology, ESC Congress, August 28 - September 1, 2004, Munich, Germany, p. 22, abstract 218.	
	A168	Voswinckel et al., "Inhaled Treprostinil Sodium (TRE) for the Treatment of Pulmonary Hypertension," Circulation, October 2004, Abstract 1414, 110, 17 Supplement.	
	A169	Voswinckel et al., "Inhaled Treprostinil Sodium (TRE) for the Treatment of Pulmonary Hypertension," Circulation, October 26, 2004, Supplement, 110(17):295, abstract 1414.	
	A170	Walmrath et al., "Effects of inhaled versus intravenous vasodilators in experimental pulmonary hypertension," Eur. Respir. J., 1997, 10, 1084-1092.	
	A171	Wasserman et al., "Bronchodilator effects of prostacyclin (PGI2) in dogs and guinea pigs," European Journal of Pharmacology, 1980, 66, 53-63.	
	A172	*Watson Laboratories, Inc. (Petitioner) v. United Therapeutics Corp. (Patent Owner)*, Decision Granting Institute of *Inter Partes* Review 37 C.F.R. 42.108, IRP2017-01621, Patent No. 9,358,240, January 11, 2018.	
	A173	*Watson Laboratories, Inc. (Petitioner) v. United Therapeutics Corp. (Patent Owner)*, Decision Granting Institute of *Inter Partes* Review 37 C.F.R. 42.108, IRP2017-01622, Patent No. 9,339,507, January 11, 2018.	
	A174	*Watson Laboratories, Inc. (Petitioner) v. United Therapeutics, Inc. (Patent Owner)*, Petition for *Inter Partes* Review, IRP2017-01622, Patent No. 9,339,507, with all Exhibits on exhibit list.	
	A175	*Watson Laboratories, Inc. (Petitioner) v. United Therapeutics, Inc. (Patent Owner)*, Petition for *Inter Partes* Review, IRP2017-01621, Patent No. 9,358,240, with only Exhibits 1002, 1059, 1161 and 1164 and not including exhibits already provide with C2.	
	A176	Webb et al., "The use of inhaled aerosolized prostacyclin (IAP) in the treatment of pulmonary hypertension secondary to pulmonary embolism," Intensive Care Med., 1996, 22, 353-355.	
	A177	Wensel et al., "Effects of iloprost inhalation on exercise capacity and ventilator efficiency in patients with primary pulmonary hypertension," Circulation, 2000, 101, 2388-2392.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449/PTO				***Complete if Known***	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Unassigned
				Filing Date	Herewith
Date Submitted: January 31, 2020				**First Named Inventor**	Horst OLSCHEWSKI
				Art Unit	Unassigned
(use as many sheets as necessary)				Examiner Name	Unassigned
Sheet	11	of	11	Attorney Docket Number	080618-1916

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]
	A178	Wetzel, R.C., "Aerosolized prostacyclin: in search of the ideal pulmonary vasodilator," Anesthesiology, 1995, 82, 1315-1317.	
	A179	Wittwer et al., "Inhalative Pre-Treatment of Donor Lungs Using the Aerosolized Prostacyclin Analog Iliprost Ameliorates Reperfusion Injury," J. Heart Lung Transplant, 2005, 24:1673-1679.	
	A180	Zanen et al., "Optimal particle size for beta 2 agonist and anticholinergic aerosols in patients with severe airflow obstruction," Thorax, 1996, 51, 977-980.	
	A181	Zanen et al., "The optimal particle size for β-adrenergic aerosols in mild asthmatics," International Journal of Pharmaceutics, 1994, 107, 211-217.	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst Olschewski
Filer:	Stephen Bradford Maebius/Karen Strawderman
Attorney Docket Number:	080618-1916

Filed as Large Entity

Filing Fees for Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
UTILITY APPLICATION FILING	1011	1	300	300
UTILITY SEARCH FEE	1111	1	660	660
UTILITY EXAMINATION FEE	1311	1	760	760
REQUEST FOR PRIORITIZED EXAMINATION	1817	1	4000	4000
Pages:				
Claims:				
Miscellaneous-Filing:				
PROCESSING FEE, EXCEPT PROV. APPLS.	1830	1	140	140

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**5860**

Electronic Acknowledgement Receipt

EFS ID:	38459522
Application Number:	16778662
International Application Number:	
Confirmation Number:	4471
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION
First Named Inventor/Applicant Name:	Horst Olschewski
Customer Number:	22428
Filer:	Stephen Bradford Maebius/Karen Strawderman
Filer Authorized By:	Stephen Bradford Maebius
Attorney Docket Number:	080618-1916
Receipt Date:	31-JAN-2020
Filing Date:	
Time Stamp:	15:30:40
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$5860
RAM confirmation Number	E20201UF31080102
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	TrackOne Request	Track1Req.pdf	145998 ccc5d2c87131b28878e289072dfc519833056944	no	2
Warnings:					
Information:					
2	Transmittal of New Application	Transmittal.pdf	109118 b47401b3d8c15bbb2cb92eb4573cd88dd86983f9	no	4
Warnings:					
Information:					
3		Specification.pdf	209817 b2ab7c9ebd97efe96dfea59735d29c22f9cc6b11	yes	31

Multipart Description/PDF files in .zip description

Document Description	Start	End
Specification	1	29
Claims	30	30
Abstract	31	31

Warnings:					
Information:					
4	Drawings-only black and white line drawings	Drawings.pdf	159877 b89b4deeb7c6241b3d08d4951f8514d942d760db	no	12
Warnings:					
Information:					
5	Oath or Declaration filed	Declarations.pdf	2517074 5de7f479e5181d68a9f81e3167b9e2a0d4460459	no	13

Warnings:					
Information:					
6	Application Data Sheet	ADS.pdf	113890 83c68b297999654615c99df3d6efc78051f3428f	no	11
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
7	Power of Attorney	POA.pdf	116513 77ebc675ac09a2143d9def4fd3e22d309202a0d0	no	1
Warnings:					
Information:					
8	Transmittal Letter	IDSTM.pdf	116539 e3751f3eee0d241d9a4454db47c606405af7ac7a	no	2
Warnings:					
Information:					
9	Information Disclosure Statement (IDS) Form (SB08)	SB08.pdf	224370 14f6a07d9f844d17be43b3fdeb64660ca18ccd19	no	11
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
10	Fee Worksheet (SB06)	fee-info.pdf	38959 2f04d429c8e773ac44855b430a31749b6b82f64f	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	3752155		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRACK1.REQ
Document Description: TrackOne Request

PTO/AIA/424 (04-14)

CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION UNDER 37 CFR 1.102(e) (Page 1 of 1)

First Named Inventor:	Horst OLSCHEWSKI	Nonprovisional Application Number (if known):	Not yet Assigned
Title of Invention:	TREPROSTINIL ADMINISTRATION BY INHALATION		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

1. The processing fee set forth in 37 CFR 1.17(i)(1) and the prioritized examination fee set forth in 37 CFR 1.17(c) have been filed with the request. The publication fee requirement is met because that fee, set forth in 37 CFR 1.18(d), is currently $0. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.

2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims, and that any request for an extension of time will cause an outstanding Track I request to be dismissed.

3. The applicable box is checked below:

I. ☑ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)

i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.

---OR---

(b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.

ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, **or** the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application.

II. ☐ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)

i. A request for continued examination has been filed with, or prior to, this form.
ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature /Stephen B. Maebius/	Date Jan. 31, 2020
Name (Print/Typed) Stephen B. Maebius	Practitioner Registration Number 35,264

Note: *This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.**

☐ *Total of _____ forms are submitted.

Privacy Act Statement

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

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

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