



No. 14-024164- -00005-0000

Fecha: 2014-08-19 16:53:20

Dep. 2020 DIR.NUEVASCR

Tra. 11 PATENTEIYII

Eve: 378 FASENACIONALI

Act. 457 PROCEDIPPH

Folios: 35

Señor Director

DIRECCION DE NUEVAS CREACIONES

Superintendencia de Industria y Comercio

E. S. D.

Trámite : 011

Evento : 378

Actuación: 457

Referencia : Expediente No. **14.024.164**
Asunto : Solicitud de patente para: **SOLVATOS CRISTALINOS DE
HIDROCLORURO DE 6-(PIPERIDIN-4-ILOXI)-2H-
ISOQUINOLIN-1-ONA**
Solicitante : **SANOFI**
Clase : A61K 031/4725, A61P 009/000, C07D 401/012
Fecha Solicitud : 05 de febrero de 2014

RECONOCIMIENTO DE EXAMEN DE PATENTABILIDAD DE LA USPTO

Yo, **LUZ CLEMENCIA DE PÁEZ**, obrando como apoderada del solicitante en el asunto antes identificado, respetuosamente manifiesto que de conformidad con lo dispuesto en la resolución No. 54093 de 2012, atentamente me permito solicitar el reconocimiento del resultado del examen de patentabilidad proferido por la Oficina de Propiedad Industrial de los Estados Unidos para la solicitud US 13/534,815 cuyas reivindicaciones son equivalentes a las del asunto antes indicado. Lo anterior, teniendo en cuenta los siguientes documentos:

- Formulario de procedimiento acelerado de exámenes de patente (PPH).
- Resultado de examen de fondo proferido por la USPTO junto con su traducción a Español.
- Copia de las reivindicaciones que han sido determinadas como patentables u otorgables en la USPTO junto con su traducción a español.
- Nuevo pliego reivindicatorio conformado por 14 reivindicaciones, correspondiente a las reivindicaciones 1 a 6, 11, y 15 a 21 de la solicitud US 13/534,815 consideradas patentables u otorgables por USPTO como Oficina de primera presentación (OPP).
- Formulario de modificaciones y comprobante de pago por \$128.000 por concepto de modificación del pliego reivindicatorio.

"EXCELENCIA LEGAL EN UN MUNDO SIN FRONTERAS"

BOGOTÁ - Edificio Siski - Carrera 4 No. 72 - 35 - Tel. (57-1) 347 3611 - Fax (57-1) 211 8650 - Fax in U.S.A: (1-305) 675 7743 - COLOMBIA
MEDELLÍN - San Fernando Plaza - Carrera 43 A No. 1 - 50 - Torre Protección Oficina 852 - Tel: (57-4) 520 4760 / (57-4) 326 0789 / (57) 317 365 8663 / (57) 318 532 2365- COLOMBIA

www.cavelier.com
cavelier@cavelier.com

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CAVELIER

A B O G A D O S

- Tabla de correspondencia de las reivindicaciones que han sido determinadas como patentables u otorgables en la USPTO, y aquellas presentadas junto con el presente memorial como modificación voluntaria.

NUEVO PLIEGO DE REIVINDICACIONES PRESENTADAS ANTE LA SIC COMO OSP JUNTO CON EL PRESENTE MEMORIAL	REIVINDICACIONES PATENTABLES U OTORGABLES EN LAS SOLICITUDES DE LA USPTO COMO OPP
Reivindicación No. 1	Reivindicación No. 1
Reivindicación No. 2	Reivindicación No. 2
Reivindicación No. 3	Reivindicación No. 3
Reivindicación No. 4	Reivindicación No. 4
Reivindicación No. 5	Reivindicación No. 5
Reivindicación No. 6	Reivindicación No. 6
Reivindicación No. 7	Reivindicación No. 11
Reivindicación No. 8	Reivindicación No. 15
Reivindicación No. 9	Reivindicación No. 16
Reivindicación No. 10	Reivindicación No. 17
Reivindicación No. 11	Reivindicación No. 18
Reivindicación No. 12	Reivindicación No. 19
Reivindicación No. 13	Reivindicación No. 20
Reivindicación No. 14	Reivindicación No. 21

Cumplido así con lo dispuesto para que una solicitud sea aceptada en el Procedimiento Acelerado de Estudio de Solicitudes de Patentes entre la USPTO como Oficina de Primera Presentación (OPP) y la SIC como Oficina de Segunda Presentación (OSP), atentamente solicito que se continúe con el trámite correspondiente a esta solicitud de Patente de Invención.

Señor Director,


LUZ CLEMENCIA DE PÁEZ
C.C. 35.456.344 de Usaquén
T.P.A. No. 23.555


COLO-00751-0841-077-9
MMS\MMS\ID-270136\WPCL0751
No. M-2014-270136\MMS

 Industria y Comercio SUPERINTENDENCIA	Espacio reservado para el adhesivo de radicación
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DIRECCIÓN DE NUEVAS CREACIONES

Procedimiento acelerado de exámenes de patente (pph)

1	NÚMERO DE SOLICITUD ANTE LA SIC	14.024.164		
2	OFICINA DE PRIMERA PRESENTACIÓN (OPP)	Estados Unidos de América		
3	NÚMERO(S) DE SOLICITUD O PUBLICACIÓN DE LA(S) SOLICITUD(ES) (OPP):	US 13/534,815		
4	☐ REPRESENTANTE LEGAL ☒ APODERADO			
APELLIDOS DE PAEZ		NOMBRES LUZ CLEMENCIA		
		IDENTIFICACIÓN C.C.35.456.344 T.P.23.555		
DIRECCIÓN	Cra 4a No. 72-35	No. TELÉFONO 3473611		
CIUDAD	Bogotá	CORREO ELECTRÓNICO cavelier@cavelier.com		
PAÍS	Colombia	No. RADICACIÓN O PROTOCOLO DE PODER GENERAL		
5	CONDICIONES PARA ACCEDER A ESTE PROCESO:			
5.1.	DATOS DE PRIORIDAD ☒ SI ☐ NO			
(33) PAÍS DE ORIGEN		CÓDIGO PAÍS	(31) NÚMERO	(32) FECHA(AAAA/MM/DD)
EUROPA		EP	11305890.3	2011/07/08
EUROPA		EP	11306033.9	2011/12/29
5.2.	DATOS SOLICITUD INTERNACIONAL PCT ☒ SI ☐ NO			
Solicitud Internacional No.		PCT/EP2012/062431	Fecha	2012/06/27
Publicación Internacional No.		WO/2013/007518 A1	Fecha	2013/01/17
El solicitante presenta una copia de la(s) reivindicación(es) patentable(s) u otorgable(s) de la solicitud de la Oficina de Primera Presentación que profirió el examen de patentabilidad, junto con una traducción al castellano. ☒ SI ☐ NO				
REQUISITOS PARA EL RECONOCIMIENTO DE LOS RESULTADOS DE EXÁMENES DE PATENTABILIDAD EFECTUADOS A SOLICITUDES EXTRANJERAS				
Para que la Superintendencia de Industria y Comercio pueda reconocer los resultados de exámenes de patentabilidad producidos por otras Oficinas de Propiedad Industrial se debe cumplir con las siguientes condiciones:				
(a) Al momento de solicitar el examen de patentabilidad, si el solicitante pide que se reconozcan exámenes de patentabilidad de otras oficinas extranjeras, deberá aportar junto con el pago de la tasa correspondiente, los siguientes anexos:				
(i) Copia de las resoluciones, fallos o decisiones que han sido relevantes para la determinación de la patentabilidad de la(s) solicitud(es) en la Oficina que haya proferido el examen de patentabilidad que contienen reivindicaciones patentables u otorgables que son la base de la petición, y si es del caso, su traducción al castellano. ☒ SI ☐ NO				
(ii) Copia de todas las reivindicaciones determinadas como patentables u otorgables en la Oficina que profirió el examen de patentabilidad y, si es del caso, su traducción al castellano. ☒ SI ☐ NO				
(iii) Copia de los antecedentes, información o documentos citados por el examinador de la Oficina de Primera Presentación del examen de patentabilidad, en las resoluciones, fallos o decisiones correspondientes, incluyendo la literatura no patente. Los documentos de patente deberán presentarse siempre y cuando no estén disponibles para la Superintendencia de Industria y Comercio mediante el simple acceso a bases de datos gratuitas. ☐ SI ☒ NO				
(iv) Una tabla de correspondencias de las reivindicaciones que han sido determinadas como patentables u otorgables en la solicitud de la Oficina que haya proferido el examen de patentabilidad. ☒ SI ☐ NO				

7	FIRMA DEL SOLICITANTE, DEL APODERADO O DEL REPRESENTANTE LEGAL
 LUZ CLEMENCIA DE PAEZ C.C 35.456.344 de Usaquén Tarjeta Profesional 23.555	



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

97464 7590 12/13/2013
Scully, Scott, Murphy & Presser, P.C.
400 Garden City Plaza, Suite 300
Garden City, NY 11530

EXAMINER

NORTHINGTON DAVIS, ZINNA

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 12/13/2013

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/534,815	06/27/2012	Norbert NAGEL	28853	7197

TITLE OF INVENTION: CRYSTALLINE SOLVATES OF 6-(PIPERIDIN-4-YLOXY)-2H-ISOQUINOLIN-1-ONE HYDROCHLORIDE

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1780	\$300	\$0	\$2080	03/13/2014

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

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

HOW TO REPLY TO THIS NOTICE:

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

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

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

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

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

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

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

PART B - FEE(S) TRANSMITTAL

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

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

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

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.

97464 7590 12/13/2013
Scully, Scott, Murphy & Presser, P.C.
400 Garden City Plaza, Suite 300
Garden City, NY 11530

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

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/534,815	06/27/2012	Norbert NAGEL	28853	7197

TITLE OF INVENTION: CRYSTALLINE SOLVATES OF 6-(PIPERIDIN-4-YLOXY)-2H-ISOQUINOLIN-1-ONE HYDROCHLORIDE

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1780	\$300	\$0	\$2080	03/13/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
NORTHINGTON DAVIS, ZINNA	1625	514-309000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

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

2. For printing on the patent front page, list

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

1 _____
2 _____
3 _____

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

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

(A) NAME OF ASSIGNEE

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

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

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

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

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

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

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

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

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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.



UNITED STATES PATENT AND TRADEMARK OFFICE

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/534,815	06/27/2012	Norbert NAGEL	28853	7197

97464 7590 12/13/2013
Scully, Scott, Murphy & Presser, P.C.
400 Garden City Plaza, Suite 300
Garden City, NY 11530

EXAMINER

NORTHINGTON DAVIS, ZINNA

ART UNIT	PAPER NUMBER
----------	--------------

1625

DATE MAILED: 12/13/2013

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

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

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

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

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

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.

**Notices of Allowance and Fee(s) Due mailed between October 1, 2013 and
December 31, 2013**

(Addendum to PTOL-85)

If the "Notice of Allowance and Fee(s) Due" has a mailing date on or after October 1, 2013 and before January 1, 2014, the following information is applicable to this application.

If the issue fee is being timely paid on or after January 1, 2014, the amount due is the issue fee and publication fee in effect January 1, 2014. On January 1, 2014, the issue fees set forth in 37 CFR 1.18 decrease significantly and the publication fee set forth in 37 CFR 1.18(d)(1) decreases to \$0.

If an issue fee or publication fee has been previously paid in this application, applicant is not entitled to a refund of the difference between the amount paid and the amount in effect on January 1, 2014.

Notice of Allowability

Application No.

13/534,815

Applicant(s)

NAGEL ET AL.

Examiner

Zinna Northington Davis

Art Unit

1625

AIA (First Inventor to
File) Status

No

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

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

1. ☒ This communication is responsive to the Amendment filed October 28, 2013.

☐ 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 and 3-22 (now renumbered as 1-21, respectively). 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)

5. ☒ Examiner's Amendment/Comment

2. ☐ Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____

6. ☒ Examiner's Statement of Reasons for Allowance

3. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material

7. ☒ Other The drawings filed September 13, 2012 are approved.

4. ☒ Interview Summary (PTO-413),
Paper No./Mail Date 11/19/2013.

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.
2. Authorization for this examiner's amendment was given in a telephone interview with Mr. Richard Catania on November 19, 2013.
3. The application has been amended as follows:
 - A. At claim 1, after the comma, the phrase "wherein the hydrate contains 1.85 to 2.2 molecules water per molecule (I)." has been amended to read in favor of:
--wherein the hydrate contains 1.85 to 2.2 molecules water per molecule--.
 - B. Claim 3 has been amended to read in favor of:
-- 3. (Currently Amended) The hydrate according to claim 1, wherein the hydrate contains 2.0 molecules water per molecule--.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance:

4. Based upon the response filed October 28, 2013, the rejections under 35 U.S.C. 112, second paragraph and 35 U.S.C. 103(a) based upon Sanofi-Aventis [WO 2008/077550 (Reference 2, cited by Applicants)], Sanofi-Aventis Deutschland GMBH [WO 2007/012421 (Reference 1, cited by Applicants)], Sarnoff- Aventis [WO 2009/080335 (Reference 3, cited by Applicants)] are withdrawn.
5. Claims 1 and 3 have been amended to clearly define the claimed invention.

Application/Control Number: 13/534,815
Art Unit: 1625

Page 3

6. The changes made by Examiner's Amendment are editorial in nature. The changes are not made to avoid any possible rejections based upon prior art.
7. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zinna Northington Davis whose telephone number is (571)272-0682.
9. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571)272-0867.
10. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

[SIGNATURE BLOCK ON NEXT PAGE]

Application/Control Number: 13/534,815
Art Unit: 1625

Page 4

/Zinna Northington Davis/
Zinna Northington Davis
Primary Examiner
Group 1600-AU 1625

Znd
11.19.2013

Examiner-Initiated Interview Summary	Application No.		Applicant(s)	
	13/534,815		NAGEL ET AL.	
	Examiner		Art Unit	
	Zinna Northington Davis		1625	

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

(1) Zinna Northington Davis. (3) _____

(2) Richard Catania. (4) _____

Date of Interview: 19 November 2013.

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

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

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

Claim(s) discussed: All.

Identification of prior art discussed: None.

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

Claims 1 and 3 will be amended. The necessary changes will be made by Examiner's Amendment.

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

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

☐ Attachment



OFICINA DE MARCAS Y PATENTES DE LOS ESTADOS UNIDOS

DEPARTAMENTO DE COMERCIO DE LOS
ESTADOS UNIDOS
Oficina de marcas y patentes de los Estados Unidos
Dirección: Comisionado de patentes
Código postal 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTIFICACIÓN DE APROBACIÓN Y TASA(S) ADEUDADA(S)

97464 7590 12/13/2013

Scully, Scott, Murphy & Presser, P.C.
400 Garden City Plaza, Suite 300
Garden City, NY 11530

EXAMINADOR

NORTHINGTON DAVIS. ZINNA

UNID ART NÚMERO DE DOCUMENTO
1625

FECHA DE ENVÍO; 12/13/2013

SOLICITUD NO.	FECHA DE PRESENTACIÓN	NOMBRE DEL INVENTOR	NO. DE EXPEDIENTE DE ABOGADO	NO. DE CONFIRMACIÓN
13/534,815	06/27/2012	Norbert NAGEL	28853	7197

TÍTULO DE LA INVENCIÓN: SOLVATOS CRISTALINOS DE CLORHIDRATO 6-(PIPERIDINA-4-ILOXI)-2H-ISOQUINOLINA-1-UNO

TIPO DE SOLICITUD	ESTADO DE LA ENTIDAD	TASA DE EMISIÓN ADEUDADA	TASA DE PUBL. ADEUDADA	TASA DE EMISIÓN PREV. PAGO	TOTAL DE TASA(S) ADEUDADA(S)	FECHA DE VENCIMIENTO
No provisional	Sin descontar	\$1780	\$300	\$0	\$2080	13/03/2014

LA SOLICITUD IDENTIFICADA ANTERIORMENTE SE HA EXAMINADO Y ESTÁ APROBADA PARA EMISIÓN COMO UNA PATENTE. EL PROCESO SOBRE LOS MÉRITOS ESTÁ CERRADO. ESTA NOTIFICACIÓN DE APROBACIÓN NO ES UN OTORGAMIENTO DE DERECHOS DE PATENTE. ESTA SOLICITUD ESTÁ SUJETA A RETIRO DE LA EMISIÓN A INICIATIVA DE LA OFICINA O A PETICIÓN DEL SOLICITANTE. VER 37 CFR 1.313 Y MPEP 1308

LA TASA DE EMISIÓN Y LA TASA DE PUBLICACIÓN (DE REQUERIRSE) DEBE PAGARSE DENTRO DE TRES MESES A PARTIR DE LA FECHA DE LA ENTREGA DE ESTA NOTIFICACIÓN O ESTA SOLICITUD SE CONSIDERARÁ ABANDONADA. ESTE PLAZO LEGAL NO PUEDE EXTENDERSE. VER 35 U.S.C. 151. LA TASA DE EMISIÓN ADEUDADA INDICADA ANTERIORMENTE NO REFLEJA UN CRÉDITO POR NINGUNA TASA DE EMISIÓN PAGADA PREVIAMENTE EN ESTA SOLICITUD. SI UNA TASA DE EMISIÓN SE HA PAGADO ANTERIORMENTE EN ESTA SOLICITUD (COMO SE MUESTRA ARRIBA), LA DEVOLUCIÓN DE LA PARTE B DEL PRESENTE FORMATO SE CONSIDERARÁ UNA SOLICITUD PARA RESOLICITAR LA TASA DE EMISIÓN PAGADA PREVIAMENTE HACIA LA TASA DE EMISIÓN AHORA ADEUDADA.

COMO RESPONDER A ESTA NOTIFICACIÓN:

I. Revisar el ESTADO DE LA ENTIDAD que se muestra arriba. Si el ESTADO DE LA ENTIDAD se muestra como PEQUEÑA o MICRO, verificar si todavía aplica el derecho a ese estado de la entidad.

Si el ESTADO DE LA ENTIDAD es el mismo al que se muestra arriba, pagar la TOTALIDAD DE TASA(S) ADEUDADA(S) mostradas arriba.

Si el ESTADO DE LA ENTIDAD cambia por el que se muestra arriba, en la PARTE B – TRANSMISIÓN DE TASA(S), complete la sección número 5 titulada “Cambio en el Estado de la Entidad (del estado indicado arriba)”.

A efectos de la presente notificación, las tasas de pequeña entidad son la mitad de la cantidad de las tasas sin descontar, y las tasas de micro entidad son la mitad de la cantidad de las tasas de pequeña entidad.

II. LA PARTE B – TRANSMISIÓN DE TASA(S), o su equivalente, debe completarse y devolverse a la Oficina de Marcas y Patentes de los Estados Unidos (USPTO) con su TASA DE EMISIÓN y TASA DE PUBLICACIÓN (si se necesita). Si usted está cargando la(s) tasa(s) a su cuenta de depósitos, se debe completar la sección “4b” de la Parte B – Transmisión de Tasa(s) y se debe entregar una copia extra del formato. Si se presenta un equivalente de la Parte B, se debe realizar claramente una solicitud para reaplicar una tasa de emisión previamente pagada y puede haber retrasos en el procesamiento debido a la dificultad en reconocer el documento como un equivalente de la Parte B.

III. Toda la comunicación relacionada a la presente solicitud debe dar el número de solicitud. Por favor dirija todas las comunicaciones a la oficina de la dirección interna de TASA DE EMISIÓN y marcas que se indica la cantidad.

PARTE B – TRANSMISIÓN DE TASA(S)

Complete y envíe este formato, junto con la(s) tasa(s) aplicables, a: **Correo** Dirección interna TASA DE EMISIÓN
Comisionado de patentes
Apartado de correos 1450
Alexandria, Virginia 22313-1450
o **Fax** (571)-273-2885

INSTRUCCIONES: Este formato debe usarse para transmitir la TASA DE EMISIÓN y TASA DE PUBLICACIÓN (si se requiere). Los campos 1 a 5 deben completarse cuando sea apropiado. Toda la correspondencia posterior, incluyendo la Patente, órdenes de anticipo y notificación de tasas de mantenimiento serán enviadas a la dirección de correspondencia actual como se indica, a menos que se corrija a continuación o se indique lo contrario en el Campo 1, (a) indicando una nueva dirección de correspondencia; y/o (b) indicando una "DIRECCIÓN DE TASA" separada para notificaciones de tasa de mantenimiento.

DIRECCIÓN DE CORRESPONDENCIA ACTUAL (Nota: use el Campo 1 para cualquier cambio de dirección)

Nota: Solamente se puede usar un certificado de envío para envíos nacionales de la Transmisión de Tasa(s). Este certificado no puede usarse para ningún otro documento adjunto. Cada documento adicional, tal como una cesión o dibujo formal, debe tener su propio certificado de envío o transmisión.

Certificado de envío o transmisión

Por la presente certifico que esta Transmisión de Tasa(s) está siendo depositada en el Servicio Postal de los Estados Unidos con suficiente franqueo para correo de primera clase en un sobre dirigido a la Dirección Interna de TASA DE EMISIÓN, dirección arriba, o transmitida por fax a la USPTO (571) 273-2885, en la fecha indicada a continuación.

(Nombre del depositante)

(Firma)

(Fecha)

SOLICITUD NO.	FECHA DE PRESENTACIÓN	NOMBRE DEL INVENTOR	NO. DE EXPEDIENTE DE ABOGADO	NO. DE CONFIRMACIÓN		
B/534,815	06/27/2012	Norbert NAGEL	28853	7197		
TÍTULO DE LA INVENCIÓN: SOLVATOS CRISTALINOS DE CLORHIDRATO 6-(P-PIPERIDINA-4-ILOXI)-2H-ISQUINOLINA-1-UNO						
TIPO DE SOLICITUD	ESTADO DE LA ENTIDAD	TASA DE EMISIÓN ADEUDADA	TASA DE PUBL. ADEUDADA	TASA DE EMISIÓN PREV. PAGO	TOTAL DE TASA(S) ADEUDADA(S)	FECHA DE VENCIMIENTO
No provisional	Sin descontar	\$ 1780	\$ 300	\$ 0	\$ 2,080	12/03/2014
EXAMINADOR		UNID. ART.	CLASE-SUBCLASE			
NORTHINGTON DAVIS, ZENNA		1625	514-309000			

1. Cambio de dirección de correspondencia o indicación de "Dirección de Tasas" (37 CFR 1.363).

☐ Cambio de dirección de correspondencia (o formato de Cambio de Dirección de Correspondencia PTO/SB/122) adjunto.

☐ Indicación de "Dirección de Tasa" (o formato de indicación "Dirección de Tasa" PTO/SB/47; Rev 03-02 o más reciente) adjunta. Se requiere el uso de un Número de Cliente.

2. Para impresión en la primera página de la patente, lista

(1) los nombres de hasta 3 abogados de patente registrados o agentes O, de manera alternativa,

(2) el nombre de una sola firma (que tenga como miembro un abogado o agente registrado) y los nombres de hasta 2 abogados de patente registrados o agentes. Si no hay ningún nombre enumerado, no se imprimirá ningún nombre.

1. _____

2. _____

3. _____

2. NOMBRE DEL CESIONARIO Y DATOS DE RESIDENCIA A IMPRIMIR EN LA PATENTE (en imprenta o a máquina)

POR FAVOR TENGA EN CUENTA: A menos que abajo se identifique un cesionario, no aparecerán datos del cesionario en la patente. Si abajo se identifica un cesionario, el documento se ha presentado para su registro como se establece en 37 CFR 3.11. Completar este formato NO es un sustituto para presentar una cesión.

(A) NOMBRE DEL CESIONARIO

(E) RESIDENCIA: (CIUDAD y ESTADO O PAÍS)

Por favor marque la categoría o categorías de cesionario apropiada (no estará impreso en la patente): ☐ Individual ☐ Sociedad u otro grupo empresarial privado ☐ Gobierno

3a. Se entrega(n) la(s) siguiente(s) tasa(s):

☐ Tasa de emisión

☐ Tasa de publicación (no se permite descuento de entidad pequeña)

☐ Orden de avance - # de copias _____

4b. Pago de tasa(s): (Por favor primero reemplace cualquier tasa de emisión pagada previamente mostrada antes)

☐ Se adjunta un cheque.

☐ Pago con tarjeta de crédito. Formato PTO-2038 se encuentra adjunto.

☐ Por la presente el Director está autorizado a cobrar la(s) tasa(s) requeridas, cualquier deficiencia, o acreditar cualquier pago excesivo al Número de Cuenta de Depósito _____ (adjunte una copia extra de este formato).



OFICINA DE MARCAS Y PATENTES DE LOS ESTADOS UNIDOS

DEPARTAMENTO DE COMERCIO DE LOS EE.UU.
Oficina de Marcas y Patentes de los Estados Unidos
Dirección: COMISIONADO DE PATENTES
Apartado de correos 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

SOLICITUD NO.	FECHA DE SOLICITUD	NOMBRE DEL INVENTOR	NO. DE EXPEDIENTE DE ABOGADO	NO. DE CONFIRMACIÓN
13/534,815	06/27/2012	Norbert NAGEL	28853	7197
97464	7590	13/12/2013	EXAMINADOR	
Scully, Scott, Murphy & Presser, P.C. 400 Garden City Plaza, Suite 300 Garden City, NY 11530			NORTHINGTON DAVIS, ZINNA	
			UNIT ART	NÚMERO DE DOCUMENTO
			1625	

FECHA DE ENVÍO: 13/12/2013

Determinación de ajuste de término de patente bajo 35 U.S.C. 154 (b)
(solicitud presentada en o después del 29 de mayo de 2000)

El Ajuste del Término de Patente hasta la fecha es 0 días. Si la tasa de emisión se paga en la fecha que es tres meses después de la fecha de envío de esta notificación y la patente es emitida el martes antes de la fecha que es 28 semanas (seis meses y medio) después de la fecha de envío de esta notificación, el Ajuste del Término de Patente será de 0 días.

Si se presentó una Solicitud de Continuación de Proceso (CPA) en la solicitud identificada anteriormente, la fecha de presentación que determina el Ajuste del Término de Patente es la fecha de presentación de la CPA más reciente.

El Solicitante podrá obtener mayor información detallada accediendo a la Recuperación de Información de Solicitud de Patente (PAIR) sitio web (<http://pair.uspto.gov>).

Cualquier pregunta relacionada con la determinación de la Extensión o Ajuste del Término de Patente debe dirigirse a la Oficina de Administración Legal de Patentes en (571)-272-7702. Las preguntas relacionadas a los pagos de cuotas de emisión y publicación deben dirigirse al Centro de Servicio al Cliente de la Oficina de Publicación de Patente al 1-(888)-786-0101 o (571)-272-4200.

Notificaciones de aprobación y tasa(s) adeudada(s) enviadas entre el 1 de octubre de 2013 y el 31 de diciembre de 2013

(Adenda a PTOL-85)

Si la "Notificación de aprobación y tasa(s) adeudada(s)" tiene una fecha de envío de o después del 1 de octubre de 2013, y antes del 1 de enero de 2014, la siguiente información aplica a la presente solicitud.

Si la tasa de emisión está siendo pagada oportunamente el o antes del 1 de enero de 2014, la cantidad adeudada es la tasa de emisión y tasa de publicación efectiva para el 1 de enero de 2014. El 1 de enero de 2014, las tasas de emisión establecidas en 37 CFR 1.18 disminuyen significativamente y la tasa de publicación establecida en 37 CFR 1.18 (d)(1) disminuyen a \$0.

Si una tasa de emisión o tasa de publicación ha sido pagada previamente en esta solicitud, el solicitante no tiene derecho a una devolución de la diferencia entre la cantidad pagada y la cantidad efectiva el 1 de enero de 2014.

MODIFICACIÓN DEL EXAMINADOR

1. A continuación aparece una modificación al registro por parte del examinador. Si los cambios y/o adiciones no son aceptables para el solicitante, se puede presentar una modificación según lo dispuesto por 37 CFR 1.312. Para asegurar la consideración de tal modificación, DEBE enviarse a más tardar en el pago de la tasa de emisión.

2. Se dio autorización para esta modificación del examinador en una entrevista telefónica con el Sr. Richard Catania el 19 de noviembre de 2013.

3. La solicitud se ha modificado de la siguiente manera:

A. En la reivindicación 1, después de la coma, la frase "en donde el hidrato contiene 1,85 a 2,2 moléculas de agua por molécula (I)." se ha modificado para leerse: -- en donde el hidrato contiene 1,85 a 2,2 moléculas de agua por molécula.--.

B. La reivindicación 3 se ha modificado para leerse:

-- 3. (Actualmente modificada) El hidrato de acuerdo con la reivindicación 1, en donde el hidrato contiene 2,0 moléculas de agua por molécula--.

RAZONES PARA APROBACIÓN

La siguiente es una declaración del examinador de las razones para aprobación:

4. Con base en la respuesta presentada el 28 de octubre de 2013, se retiran los rechazos en virtud de 35 U.S.C. 112, párrafo segundo y 35 U.S.C. 103(a) con base en Sanofi-Aventis [WO 2008/077550 (Referencia 2, citada por los Solicitantes)], Sanofi-Aventis Deutschland GMBH [WO 2007/012421 (Referencia 1, citada por los

privado como el PAIR público. La información del estado para solicitudes no publicadas está disponible a través del PAIR privado únicamente. Para más información sobre el sistema PAIR, ver <http://pair-direct.uspto.gov>. Si tiene preguntas para acceder al PAIR privado, contacte el Centro de Negocios Electrónico (EBC) al 866-217-9197 (número gratuito).

[CAMPO PARA LA FIRMA EN LA SIGUIENTE HOJA]

Examinador-Resumen de Entrevista iniciado	Solicitud No. 13/534,815	Solicitante(s) NAGEL ET AL.	
	Examinador Zinna Northington Davis	Unidad Art 1625	

Todos los participantes (solicitante, representante del solicitante, personal de la PTO):

(1) Zinna Northington Davis. (3) _____.

(2) Richard Catania. (4) _____.

Fecha de la entrevista : 19 de noviembre de 2013.

Tipo: ☒ Telefónica ☐ Video Conferencia
☐ Personal [copia entregada a: ☐ solicitante ☐ representante del solicitante]

Prueba documental presentada o demostración realizada: ☐ Yes ☒ No.
De ser sí, descripción breve: _____

Asuntos discutidos ☐ 101 ☒ 112 ☐ 102 ☐ 103 ☐ Otros
(Para cada una de las cajas marcadas arriba, por favor describa abajo el asunto y descripción detallada de la discusión)

Reivindicación(es) discutidas: Todas.

Identificación de anterioridad discutida: Ninguna.

Fundamento de la entrevista
(Para cada asunto discutido, proporcione una descripción detallada e indique si se logró un acuerdo. Algunos temas pueden incluir: identificación o aclaración de una referencia o una parte de la misma, interpretación de reivindicación, modificaciones propuestas, argumentos de alguna referencia aplicada, etc...)

Se modificarán las reivindicaciones 1 y 3. Se realizarán los cambios necesarios por la Modificación del Examinador.

Instrucciones de inscripción del solicitante: No es necesario que el solicitante proporcione un registro separado del fundamento de la entrevista.

Instrucciones de inscripción del examinador: Los examinadores deben resumir el fundamento de cualquier entrevista de registro. Una inscripción completa y adecuada del fundamento de una entrevista debe incluir los ítems enumerados en MPEP 713.04 para inscripción completa y adecuada incluyendo la identificación de la orientación general de cada argumento o asunto discutido, una indicación general de cualquier otro asunto pertinente discutido en relación a la patentabilidad y los resultados generales o resultado de la entrevista, para incluir una indicación en cuanto a si se alcanzó un acuerdo o no en los asuntos abordados.

☐ Adjunto

MAINTENANCE FEE NOTICE

If the application for this patent was filed on or after December 12, 1980, maintenance fees are due three years and six months, seven years and six months, and eleven years and six months after the date of this grant, or within a grace period of six months thereafter upon payment of a surcharge as provided by law. The amount, number and timing of the maintenance fees required may be changed by law or regulation. Unless payment of the applicable maintenance fee is received in the United States Patent and Trademark Office on or before the date the fee is due or within a grace period of six months thereafter, the patent will expire as of the end of such grace period.

PATENT TERM NOTICE

If the application for this patent was filed on or after June 8, 1995, the term of this patent begins on the date on which this patent issues and ends twenty years from the filing date of the application or, if the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121, or 365(c), twenty years from the filing date of the earliest such application ("the twenty-year term"), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b), and any extension as provided by 35 U.S.C. 154(b) or 156 or any disclaimer under 35 U.S.C. 253.

If this application was filed prior to June 8, 1995, the term of this patent begins on the date on which this patent issues and ends on the later of seventeen years from the date of the grant of this patent or the twenty-year term set forth above for patents resulting from applications filed on or after June 8, 1995, subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b) and any extension as provided by 35 U.S.C. 156 or any disclaimer under 35 U.S.C. 253.



US008710078B2

(12) **United States Patent**
Nagel et al.

(10) **Patent No.:** US 8,710,078 B2
(45) **Date of Patent:** Apr. 29, 2014

(54) **CRYSTALLINE SOLVATES OF
6-(PIPERIDIN-4-YLOXY)-2H-
ISOQUINOLIN-1-ONE HYDROCHLORIDE**

(58) **Field of Classification Search**
None
See application file for complete search history.

(75) **Inventors:** Norbert Nagel, Frankfurt am Main (DE); Bruno Baumgartner, Frankfurt am Main (DE); Harald Berchtold, Frankfurt am Main (DE); Oliver Plettenburg, Frankfurt am Main (DE); Dieter Kadereit, Frankfurt (DE); Mandy Mohuicke, Frankfurt am Main (DE); Simon Gessler, Frankfurt am Main (DE); Joachim Tillner, Frankfurt (DE)

(56) **References Cited**

FOREIGN PATENT DOCUMENTS

WO WO2007/012421 A1 2/2007
WO WO2008/077550 A1 7/2008
WO WO2009/080335 A1 7/2009

OTHER PUBLICATIONS

Morissette et al, Advanced Drug Delivery Reviews, 56 (2004), pp. 275-300.*
West, Anthony R., Solid State Chemistry and its Applications, Wiley, New York, 1988, pp. 358 & 365.*
Caira, Mino R., "Crystalline Polymorphism of Organic Compounds," Topics in Current Chemistry (1998), vol. 198, pp. 163-208.
Ray, Peter et al., "Optimisation of 6-substituted isoquinolin-1-amine based ROCK-1 inhibitors," Bioorganic and Medicinal Chemistry Letters (2011), vol. 21, 1084-1088.
European Search Report dated Oct. 11, 2011 issued in EP11305890.
European Search Report dated Feb. 3, 2012 issued in EP11306033.
International Search Report dated Aug. 7, 2012 issued in PCT/EP2012/062431.

* cited by examiner

Primary Examiner — Zinna Northington Davis
(74) **Attorney, Agent, or Firm** — Scully, Scott, Murphy & Presser, P.C.

ABSTRACT

The present invention relates to crystalline solvates of 6-(Piperidin-4-yloxy)-2H-isoquinolin-1-one hydrochloride, processes for their preparation and the use thereof.

21 Claims, 14 Drawing Sheets

(73) **Assignee:** Sanofi, Paris (FR)

(*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) **Appl. No.:** 13/534,815

(22) **Filed:** Jun. 27, 2012

(65) **Prior Publication Data**
US 2013/0012444 A1 Jan. 10, 2013

(30) **Foreign Application Priority Data**

Jul. 8, 2011 (EP) 11305890
Dec. 29, 2011 (EP) 11306033

(51) **Int. Cl.**
C07D 401/12 (2006.01)
A61K 31/4725 (2006.01)

(52) **U.S. Cl.**
CPC C07D 401/12 (2013.01); A61K 31/4725 (2013.01)
USPC 514/309; 546/141

mixture was chilled to ambient temperature. The crystalline material was collected, washed with water/acetone (1/3) and dried to yield 4.54 g (purity>99.9%) of 6-(Piperidin-4-yloxy)-2H-isquinolin-1-one hydrochloride dihydrate.

Water content (Karl Fischer) 10.6%

¹H NMR (500 MHz, d₆-DMSO) δ 1.85-1.95 (m, 2H), 2.13-2.22 (m, 2H), 3.04-3.14 (m, 2H), 3.20-3.29 (m, 2H), 4.79-4.86 (m, 1H), 6.44 (d, J=7.1 Hz, 1H), 7.10 (dd, J=8.9, 2.5 Hz, 1H), 7.14 (dd, J=7.2, 6.7 Hz, 1H), 7.22 (d, J=2.5 Hz, 1H), 8.09 (d, J=8.6 Hz, 1H), 8.97-9.13 (bs, 2H) 11.09 (bd, J=5 Hz, 1H).

c) 0.205 g compound (I) (dihydrate) were dissolved in 20 mL ethanol and 3 mL water at about 65° C. The solvent was allowed to evaporate from the stirred solution at the same temperature over night.

d) 0.200 g of compound (I) (dihydrate) were dissolved in 20 mL ethanol and 4 mL water at 65° C. The solution was rapidly cooled to 0° C. After 45 minutes the product was isolated by vacuum filtration and dried.

In the same manner the dihydrate was obtained if ethanol was replaced by tetrahydrofuran or methyl ethyl ketone in examples c) and d).

e) 0.204 g of compound (I) (dihydrate) were dissolved in 3 mL water at 65° C. The solution was rapidly cooled to 0° C. After 30 minutes the product was isolated by vacuum filtration and dried.

2) Formation of Polymorph 1

C₁₄H₁₇N₂O₂Cl, MW=280.76

1.2 g of 6-(Piperidin-4-yloxy)-2H-isquinolin-1-one hydrochloride were suspended in isopropanol and stirred for 6 h. The solid material (1.14 g) was isolated by filtration. 60.7 mg thereof were suspended in a mixture of 0.352 mL isopropanol and 0.647 mL methanol. The mixture was heated until a clear solution was obtained. Upon cooling the crystalline product was obtained which was isolated by filtration.

3) Formation of Polymorph 2

C₁₄H₁₇N₂O₂Cl, MW=280.76

About 3 mg of compound (I) (dihydrate) were at 25° C. exposed to a dry nitrogen atmosphere (stream of nitrogen) for at least 6 hours. After this treatment, the X-ray diffraction pattern of the sample corresponds to phase 2.

4) Formation of Polymorph 3

C₁₄H₁₇N₂O₂Cl, MW=280.76

a) 0.201 g of compound (I) (dihydrate) were dissolved in 20 mL acetonitril and 3 mL water at 65° C. The solvent was allowed to evaporate from the stirred solution at the same temperature over night. Polymorph 3 and traces of the dihydrate were obtained.

b) 0.208 g of compound (I) (dihydrate) were dissolved in 10 mL methanol at 65° C. The stirred solution was rapidly cooled to 0° C. After 30 minutes the product was isolated by vacuum filtration and dried.

c) 0.203 g of compound (I) (dihydrate) were suspended in 1.2 mL methanol at 20° C. and stirred for 35 days. The product was isolated by vacuum filtration and dried.

The same product (polymorph 3) was obtained, if the dihydrate of compound (I) was suspended in ethanol, 1-propanol or 2-propanol.

5) Formation of Polymorph 4

C₁₄H₁₇N₂O₂Cl, MW=280.76

a) 0.202 g of compound (I) (dihydrate) were suspended in 2.0 mL 2-butanol at 20° C. and stirred for 35 days. The product was isolated by vacuum filtration and dried.

6) Formation of Methyl Acetate Solvate

a) 0.208 g of compound (I) (dihydrate) were suspended in 2.5 mL of methyl acetate. The solution was stirred in a closed vessel at room temperature for 35 days. The solid present in the suspension was the methyl acetate solvate as determined by XRPD in suspension.

After vacuum filtration and drying the dihydrate containing forms 1 and 3 was obtained.

7) Formation of 1,4 Dioxane Solvate

a) 0.204 g of compound (I) (dihydrate) were dissolved in 2.5 mL of 1,4-dioxane at 20° C. for 35 days with continuous stirring. The solid present in the suspension was the methyl acetate solvate as determined by XRPD in suspension.

After vacuum filtration and drying the solvate containing dihydrate were obtained

8) Formation of Acetonitrile Solvate

a) 0.206 g of compound (I) (dihydrate) were suspended in 2.5 mL of acetonitrile. The suspension was stirred at 20° C. for 35 days. The solid present in the suspension was the acetonitrile solvate as determined by XRPD in suspension.

The solid present in the suspension was isolated via vacuum filtration and dried overnight at reduced pressure at room temperature.

After vacuum filtration and drying the dihydrate containing forms 1 and 3 was obtained.

9) Maturation Examples

By maturation experiments (slurry conversion) at the given temperature the relative stability of the polymorphs of compound (I) and the hydrate was investigated.

The following maturation experiment was performed by stirring the suspension under the specified conditions, starting from the dihydrate. The sample was investigated by XRPD in suspension, after vacuum filtration as well as after drying over night at 40° C. in vacuum (<50 mbar). The isolated material was also investigated by DSC and TGA.

a) Maturation of 0.210 g dihydrate of compound (I) in 0.4 mL of water at 20° C. for 35 days. Similar, maturation of the dihydrate was done in water/methanol (vol/vol 1:1) and in water/ethanol (vol/vol 1:1). In all maturation experiments the solid remained as dihydrate.

The following maturation experiments were performed by stirring the suspension under the specified conditions and isolating the solid by vacuum filtration, starting from dihydrate of compound (I). The sample was investigated by XRPD in suspension, after vacuum filtration as well as after drying. The isolated material was also investigated by DSC and TGA.

(b) Maturation of 0.203 g of dihydrate of compound (I) in 1.2 mL of methanol at 20° C. for 35 days.

(c) Maturation was also done as in (b) by using ethanol, 1-propanol or 2-propanol.

In all experiments (b) and (c) polymorph 3 was obtained.

d) Maturation of 0.202 of dihydrate of compound (I) in 2.0 mL of 2-butanol at 20° C. for 35 days. Polymorph 4 was obtained after drying.

The following maturation experiments of suspensions of phase mixtures of the dihydrate of compound (I) and phases consisting of polymorphs 1, 3 and 4 were performed at 0, and 40° C. The product was isolated by vacuum filtration and analyzed after drying.

e) Maturation of a mixture of 0.3 mg phase 1, 23.9 mg phase 3, 29.9 mg phase 4 and 27.9 mg of the dihydrate in 0.7 mL 2-propanol at 0° C. for 2 weeks.

f) Maturation of a mixture of 0.3 mg phase 1, 27.2 mg phase 3, 18.1 mg phase 4 and 29.6 mg of the dihydrate in 2.0 mL 2-butanol at 0° C. for 2 weeks.

g) Similar experiments as in c) and f) were done with corresponding mixtures of phase 1, phase 3, phase 4 and the dihydrate in 2-propanol and 2-butanol at 20° C. and at 40° C., respectively

In all experiments e), f) and g) polymorph 3 was obtained after filtration and drying.

The performed maturation experiments prove that among the found polymorphs phase 3 is the thermodynamically most stable anhydrous form in the investigated temperature range.

10) Formation of Amorphous Compound (I)

80 mg of 6-(Piperidin-4-yloxy)-2H-isquinolin-1-one hydrochloride were dissolved in 40 mL of water and the solution was subjected to lyophilisation: The solution was frozen in liquid nitrogen and exposed to a high vacuum for about 16 hours. The obtained lyophilisate was then subjected to X-ray powder diffraction, which proved that the obtained sample is amorphous as determined by X-ray (FIG. 12).

The invention also relates to new crystalline solvates of 6-(Piperidin-4-yloxy)-2H-isquinolin-1-one hydrochloride, in which one or more non-acidic hydrogen atom(s) were replaced by Deuterium, processes for their preparation and their use, in particular for the preparation of medicaments. The processes for their preparation can be analogue to the processes described above using the respective deuterated compounds.

Analytical Methods and Operation Conditions

X-Ray Powder Diffraction (XRPD)

All X-ray powder diffraction was performed with Stoe Stadi-P transmission diffractometers using CuKα radiation (Lambda is 1.54060 Angstrom). For room temperature powder diffraction, linear position sensitive detectors were used; while for temperature-resolved XRPD image plate position sensitive detectors (IP-PSDs) were used. Unless stated otherwise, X-ray powder diffraction was performed at room temperature. Dry samples were investigated in a flat preparation whereas suspensions were investigated in quartz glass capillaries. The measured data were evaluated and plotted with the Software WinXPOW V2.12.

The observed X-ray powder diffractograms of phases 1, 2, 3 and 4, the dihydrate as well as of the methyl-acetate solvate, 1,4-dioxane solvate and acetonitrile solvate of compound (I) are displayed in the Figures. The X-ray powder diffraction patterns shown in the Figures are background-subtracted.

The 2θ (2theta) angles in ° (degree) are specified. The specified 2θ (2theta) angles in ° (degree) were understood with a potential variance of ±0.6 degrees 2theta.

The relative intensities of characteristic reflections are specified as follows. The relative intensity of a reflection is designated as "strong" if it is more than 75% of the intensity of the most intense reflection or it is the most intense reflection itself, and as "medium" if it is between 20% and 75% of

the intensity of the most intense reflection. Below 20% the intensity is designated "weak".

Temperature-resolved X-ray powder diffractograms showed that phases 1, 2, 3, and 4 of compound (I) melted without preceding solid-solid transitions.

Thermogravimetric Analysis (TGA)
The thermogravimetric analyses were performed with a Mettler TGA851c (module TGA/SDTA851c/SP1100/042). 100 µl Al crucibles sealed with lid were used. The sample changer punches a pinhole into the lid immediately before the start of the measurement. The oven cell is purged with a nitrogen gas flow of about 50 mL/min. The measurements typically start with a hold time of about 25 min at 25° C., followed by heating of the sample with a rate of 10°/min.

Temperature and weight loss were checked by a calcium oxalate hydrate reference sample.

Differential Scanning Calorimetry (DSC)

All DSC measurements were performed with a Mettler DSC822c (module DSC822c/700/109/414935/0025). If not indicated differently, 40 µl Al crucibles with sealed lid and hole were used. All measurements were carried out in a nitrogen gas flow of 50 mL/minute. The heating rate was 10° C./minute unless indicated otherwise. Temperature and heat flow were calibrated via the melting peak of an indium reference. The measured data were evaluated with the software STARe V6.1.

Dynamic Vapor Sorption (DVS)

Moisture sorption/desorption isotherms were recorded on a DVS-1 from Surface Measurement Systems. Two cycles were run at 25° C., in which the sample was first treated with dry nitrogen gas and then the relative humidity was stepwise increased from 0 to 95% and subsequently decreased again back to 0% and the weight of the sample was measured. Typical total measurement times for both cycles are about 20-30 hours.

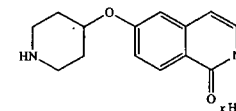
The data were evaluated with the software DVSWin V. 2.15.

Crystal Structures

The crystal structure of the dihydrate of compound (I) was determined by X-ray single crystal structure analysis. Single crystal X-ray diffraction data were collected at room temperature on a Bruker/AXS three circle diffractometer, equipped with a SMART APEX area detector, and a molybdenum Kα rotating anode generator, operated at 50 kV/120 mA and adjusted to a fine focus of 0.5×5 mm².

The invention claimed is:

1. A crystalline hydrate of 6-(Piperidin-4-yloxy)-2H-isquinolin-1-one hydrochloride having the formula



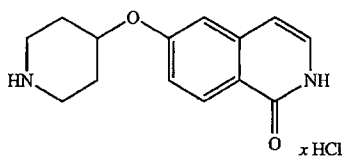
wherein the hydrate contains 1.85 to 2.2 molecules water per molecule.

2. The hydrate according to claim 1, wherein the hydrate contains 2.0 molecules water per molecule.

3. The hydrate according to claim 1, wherein the hydrate contains 10.5-12.5% (w/w) water.

4. A crystalline hydrate of 6-(Piperidin-4-yloxy)-2H-isquinolin-1-one hydrochloride having the formula

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having a reflection in an X-ray powder diffractogram using $\text{CuK}\alpha_1$ radiation at 7.7 ± 0.2 degrees 2θ .

5. The hydrate according to claim 4, having reflections in an X-ray powder diffractogram using $\text{CuK}\alpha_1$ radiation at 7.7, 15.2 and 16.8 degrees $2\theta \pm 0.2$ degrees 2θ .

6. The hydrate according to claim 4, having reflections in an X-ray powder diffractogram using $\text{CuK}\alpha_1$ radiation at 7.7, 15.2, 16.8, 22.4, 25.0, and 26.6 degrees $2\theta \pm 0.2$ degrees 2θ .

7. A pharmaceutical composition comprising the hydrate of 6-(Piperidin-4-yloxy)-2H-isoquinolin-1-one hydrochloride according to claim 1.

8. A method of treating or preventing hypertension, pulmonary hypertension, ocular hypertension, retinopathy, glaucoma, peripheral circulatory disorder, peripheral occlusive arterial disease (PAOD), coronary heart disease, angina pectoris, heart hypertrophy, heart failure, ischemic diseases, end organ damage, fibroid lung, fibroid liver, liver failure, nephropathy, renal failure, fibroid kidney, renal glomerulosclerosis, organ hypertrophy, asthma, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome, thrombotic disorders, stroke, cerebral vasospasm, cerebral ischemia, pain, neuronal degeneration, spinal cord injury, Alzheimer's disease, premature birth, erectile dysfunction, endocrine dysfunctions, arteriosclerosis, prostatic hypertrophy, diabetes and complications of diabetes, metabolic syndrome, blood vessel restenosis, atherosclerosis, inflammation, autoimmune diseases, osteopathy, infection of digestive tracts with bacteria, sepsis or cancer development and progression in a patient in need thereof comprising administering to said patient a therapeutically effective amount of the pharmaceutical composition according to claim 7.

9. A method of treating or preventing nephropathy in a patient in need thereof comprising administering to said patient a therapeutically effective amount of the pharmaceutical composition according to claim 7.

10. The method according to claim 9, wherein nephropathy is diabetic nephropathy.

11. A solid pharmaceutical composition comprising the hydrate of 6-(Piperidin-4-yloxy)-2H-isoquinolin-1-one hydrochloride according to claim 1 and one or more pharmaceutical acceptable excipients.

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12. A method of treating or preventing hypertension, pulmonary hypertension, ocular hypertension, retinopathy, glaucoma, peripheral circulatory disorder, peripheral occlusive arterial disease (PAOD), coronary heart disease, angina pectoris, heart hypertrophy, heart failure, ischemic diseases, end organ damage, fibroid lung, fibroid liver, liver failure, nephropathy, renal failure, fibroid kidney, renal glomerulosclerosis, organ hypertrophy, asthma, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome, thrombotic disorders, stroke, cerebral vasospasm, cerebral ischemia, pain, neuronal degeneration, spinal cord injury, Alzheimer's disease, premature birth, erectile dysfunction, endocrine dysfunctions, arteriosclerosis, prostatic hypertrophy, diabetes and complications of diabetes, metabolic syndrome, blood vessel restenosis, atherosclerosis, inflammation, autoimmune diseases, osteopathy, infection of digestive tracts with bacteria, sepsis or cancer development and progression in a patient in need thereof comprising administering to said patient a therapeutically effective amount of the pharmaceutical composition according to claim 11.

13. A method of treating or preventing nephropathy in a patient in need thereof comprising administering to said patient a therapeutically effective amount of the pharmaceutical composition according to claim 11.

14. The method according to claim 13, wherein nephropathy is diabetic nephropathy.

15. The pharmaceutical composition according to claim 7, further comprising at least one further active ingredient.

16. The pharmaceutical composition as claimed in claim 15, which comprises, as a further active ingredient, one or more antidiabetic agents, active hypoglycemic ingredients or anti-hypertension agents.

17. The pharmaceutical composition as claimed in claim 15, which comprises, as a further active ingredient, one or more beta receptor blockers, calcium channel blockers or inhibitors of the rennin-angiotensin.

18. The pharmaceutical composition as claimed in claim 17, which comprises as a further active ingredient Verapamil, Gallopamil, Fendilin, Diltiazem, Nitrendipin, Felodipin, Amlodipin, Nifedipin, Lercanidipin, Nimodipin, Nicardipin, Lacidipin, Isradipin, Nisoldipin, Nilvadipin or Manidipin.

19. The pharmaceutical composition as claimed in claim 18, which comprises as a further active ingredient Amlodipin.

20. The pharmaceutical composition as claimed in claim 15, which comprises as a further active ingredient, one or more ACE (Angiotensin Converting Enzyme) inhibitors.

21. The pharmaceutical composition as claimed in claim 20, which comprises as a further active ingredient Benazepril, Captopril, Cilazapril, Enalapril, Fosinopril, Imidapril, Lisinopril, Moexipril, Perindopril, Quinapril, Ramipril, Spirapril, Trandolapril or Zofenopril.

* * * * *

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The
United
States
of
America



**The Director of the United States
Patent and Trademark Office**

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America, and if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States of America, or importing into the United States of America, products made by that process, for the term set forth in 35 U.S.C. 154(a)(2) or (c)(1), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b). See the Maintenance Fee Notice on the inside of the cover.

Michelle K. Lee

Deputy Director of the United States Patent and Trademark Office

REIVINDICACIONES

1. Un hidrato cristalino de hidrocloreuro 6-(piperidina-4-iloxi)-2H-isoquinolina-1-ona que tiene la formula en el que el hidrato contiene 1.85 a 2.2 moléculas de agua por molécula.
2. El hidrato de acuerdo con la reivindicación 1, en el que el hidrato contiene 2.0 moléculas de agua por molécula.
3. El hidrato de acuerdo con la reivindicación 1, en el que el hidrato contiene 10.5-12.5% (w/w) de agua.
4. Un hidrato cristalino de hidrocloreuro de 6-(piperidina-4-iloxi)-2H-isoquinolina-1-ona que tiene la fórmula que tiene un reflejo en un difractograma de rayos X de polvo que utiliza radiación $\text{CuK}\alpha_1$ a 7.7 ± 0.2 grados 2θ .
5. El hidrato de acuerdo con la reivindicación 4, que tiene reflejos en un difractograma de rayos X de polvo que utiliza radiación $\text{CuK}\alpha_1$ a 7.7, 15.2 y 16.8 grados $2\theta \pm 0.2$ grados 2θ .
6. El hidrato de acuerdo con la reivindicación 4, que tienen reflejos en un difractograma de rayos X de polvo que utiliza radiación $\text{CuK}\alpha_1$ a 7.7, 15.2, 16.8, 22.4, 25.0 y 26.6 grados $2\theta \pm 0.2$ grados 2θ .
7. Una composición farmacéutica que comprende el hidrato de hidrocloreuro 6-(piperidina-4-iloxi)-2H-isoquinolina-1-ona de acuerdo con la reivindicación 1.
8. Un método para el tratamiento o la prevención de la hipertensión, de la hipertensión pulmonar, de la hipertensión ocular, de la retinopatía, del glaucoma, del trastorno circulatorio periférico, de la enfermedad arterial periférica oclusiva (EAPO), de la enfermedad coronaria, de la angina de pecho, de la hipertrofia cardíaca, de la insuficiencia cardíaca, de la enfermedad isquémica, del daño de los órganos diana, de la fibrosis pulmonar, de la fibrosis hepática, de la insuficiencia hepática, de la nefropatía, de la insuficiencia renal, de la fibrosis renal, de la glomeruloesclerosis renal, de la hipertrofia de órganos, del asma, de la enfermedad pulmonar obstructiva crónica (EPOC), del síndrome de dificultad respiratoria del adulto, de los trastornos trombóticos, del derrame cerebral, del vasoespasma cerebral, de la isquemia cerebral, del dolor, de la degeneración neuronal, de la lesión de la médula espinal, de la enfermedad de Alzheimer, del nacimiento prematuro, de la disfunción eréctil, de las disfunciones endocrinas, de la arteriosclerosis, de la hipertrofia prostática, de la diabetes y de las complicaciones de la diabetes, del síndrome metabólico, de la reestenosis del vaso sanguíneo, de la aterosclerosis, de la inflamación, de las enfermedades autoinmunes, de la osteopatía, de la infección del tracto digestivo con bacterias, de la sepsis o del desarrollo y progresión del cáncer en un paciente

en necesidad del mismo que comprende administrar, a dicho paciente, una cantidad terapéuticamente eficaz de la composición farmacéutica de acuerdo con la reivindicación 7.

9. Un método para el tratamiento o la prevención de la nefropatía en un paciente en necesidad del mismo que comprende administrar a dicho paciente una cantidad terapéuticamente eficaz de la composición farmacéutica de acuerdo con la reivindicación 7.
10. El método de acuerdo a la reivindicación 9, en donde la nefropatía es una nefropatía diabética.
11. Una composición farmacéutica sólida que comprende hidrato de hidrocloreto 6-(piperidina-4-iloxi)-2H-isoquinolina-1-ona de acuerdo con la reivindicación 1 y uno o más excipientes farmacéuticos aceptables.
12. Un método para el tratamiento o la prevención de la hipertensión, de la hipertensión pulmonar, de la hipertensión ocular, de la retinopatía, del glaucoma, del trastorno circulatorio periférico, de la enfermedad arterial periférica oclusiva (EAPO), de la enfermedad coronaria, de la angina de pecho, de la hipertrofia cardíaca, de la insuficiencia cardíaca, de la enfermedad isquémica, del daño de los órganos diana, de la fibrosis pulmonar, de la fibrosis hepática, de la insuficiencia hepática, de la nefropatía, de la insuficiencia renal, de la fibrosis renal, de la glomeruloesclerosis renal, de la hipertrofia de órganos, del asma, de la enfermedad pulmonar obstructiva crónica (EPOC), del síndrome de dificultad respiratoria del adulto, de los trastornos trombóticos, del derrame cerebral, del vasoespasma cerebral, de la isquemia cerebral, del dolor, de la degeneración neuronal, de la lesión de la médula espinal, de la enfermedad de alzhéimer, del nacimiento prematuro, de la disfunción eréctil, de las disfunciones endocrinas, de la arteriosclerosis, de la hipertrofia prostática, de la diabetes y de las complicaciones de la diabetes, del síndrome metabólico, de la reestenosis del vaso sanguíneo, de la aterosclerosis, de la inflamación, de las enfermedades autoinmunes, de la osteopatía, de la infección del tracto digestivo con bacterias, de la sepsis o del desarrollo y progresión del cáncer en un paciente en necesidad del mismo que comprende administrar, a dicho paciente, una cantidad terapéuticamente eficaz de la composición farmacéutica de acuerdo con la reivindicación 11.
13. Un método para el tratamiento o la prevención de la nefropatía en un paciente con la necesidad del mismo que comprende administrar, a dicho paciente, una cantidad farmacéuticamente eficaz de la composición farmacéutica de acuerdo con la reivindicación 11.

14. El método de acuerdo con la reivindicación 13, en donde la nefropatía es nefropatía diabética.
15. La composición farmacéutica de acuerdo con la reivindicación 7, que comprende además al menos un ingrediente activo adicional.
16. La composición farmacéutica como se reivindica en la reivindicación 15, que comprende un ingrediente activo adicional, uno o más agentes antidiabéticos, ingredientes activos hipoglucémicos o agentes antihipertensivos.
17. La composición farmacéutica como se reivindica en la reivindicación 15, que comprende un ingrediente activo adicional, uno o más bloqueadores de los receptores beta, bloqueadores de los canales de calcio o los inhibidores de la renina-angiotensina.
18. La composición farmacéutica como se reivindica en la reivindicación 17, que comprende un ingrediente activo verapamilo, galopamil, fendilin, diltiazem, nitrendipina, Felodipin, amlodipino, nifedipina, lercanidipin, nimodipino, nicardipin, lacidipin, isradipin, nisoldipin, nilvadipin o manidipin adicional,
19. La composición farmacéutica como se reivindica en la reivindicación 18, que comprende un ingrediente amlodipino adicional.
20. La composición farmacéutica como se reivindica en la reivindicación 15, que comprende un ingrediente activo adicional, uno o más inhibidores de enzima convertidora de angiotensina (ECA)
21. La composición farmacéutica como se reivindica en la reivindicación 20, que comprende un ingrediente activo benazepril, captopril, cilazapril, enalapril, fosinopril, imidapril, lisinopril, moexipril, perindopril, quinapril, ramipril, espirapril, trandolapril o zofenopril o adicional.

 Industria y Comercio SUPERINTENDENCIA	Espacio reservado para el adhesivo de radicación
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DIRECCIÓN DE NUEVAS CREACIONES
MODIFICACIONES Y/O CORRECCIONES

1. Identificación del Trámite

☐ Error material

☒ Modificación a una Solicitud en trámite

☒ Patente de Invención

☐ Patente de Modelo de Utilidad

☐ Registro de Diseño Industrial

☐ Esquema de Trazado de Circuitos Integrados

2. Datos del solicitante

Persona Natural

☐

Persona Jurídica

☒

SANOFI

Nombre o denominación / Nombre o razón social completa

Nombre representante legal

Tipo de empresa Micro ☐ Pequeña ☐ Mediana ☐ Otra ☐

Documento de identificación: ☐ C.C. ☐ C.E. ☐ NIT ☐ Otro Número _____

Nacionalidad/País de constitución	Dirección y domicilio del titular	Ciudad
Francia	54, rue La Boétie, F-75008 París, Francia	París
Dirección electrónica	No. Fax	Número telefónico
clientes@cavelier.com	2 11 86 50	3 47 36 11

☐ Autorizo expresamente a la Superintendencia de Industria y Comercio para que todas las comunicaciones sean enviadas a través de la dirección de correo electrónico

3. Datos del apoderado:

Apellidos y Nombre
De Páez Luz Clemencia

Documento de identificación
C.C. 35.456.344

Tarjeta profesional
T.P.A. 23.555

Dirección y domicilio		Ciudad
Carrera 4ª No. 72 –35		Bogotá
Dirección electrónica	No. Fax	Número telefónico
cavelier@cavelier.com	2 11 86 50	3 47 36 11

En caso de haber presentado poder general para asuntos que se adelanten ante la Delegatura de Propiedad Industrial, sírvase indicar el número de su radicación o protocolo de poder general

4. Datos del trámite

Corrección:

Expediente No 14.024.164

Aparece

Debe ser

Modificación:

- ☒ **Modificación al capítulo reivindicatorio.**
Presento nuevo capítulo reivindicatorio compuesto por 14 reivindicaciones y pido respetuosamente que el examen de patentabilidad sea realizado sobre estas nuevas reivindicaciones presentadas. Respetuosamente manifiesto que a pesar de eliminar materia del pliego reivindicatorio originalmente presentado, mi representada no renuncia a la protección que pueda obtener sobre dicha materia y además se reserva el derecho de presentar una solicitud divisional que la contenga durante el trámite de la presente solicitud, beneficiándose de la fecha de prioridad inicialmente reivindicada.
- ☐ **Modificación al capítulo descriptivo.**
- ☐ **Modificación al resumen.**
- ☐ **Modificación a los dibujos.**

5. Anexos

- ☒ Comprobante de pago de la tasa para la presentación de la corrección y/o modificación por \$128.000.
- ☐ Poder, si fuere el caso.
- ☒ Documento que contiene las modificaciones o correcciones.
- ☐ Copia de la solicitud y sus anexos en formato magnético.

6. Firma

Nombre y apellidos

LUZ CLEMENCIA DE PAEZ

C.C. 35.456.344 DE Usaquén

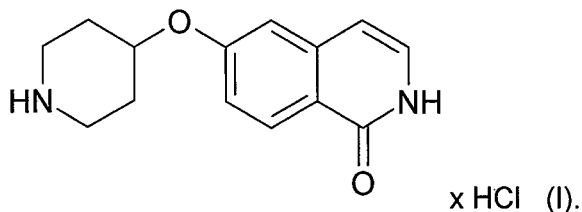
Firma

LUZ CLEMENCIA DE PAEZ

Tarjeta Profesional 23.555

REIVINDICACIONES

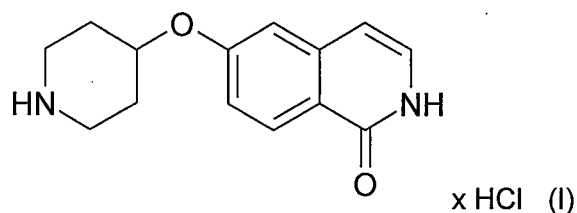
1. Un hidrato cristalino de hidrocloruro de 6-(piperidin-4-iloxi)-2H-isoquinolin-1-ona que tiene la fórmula



En donde el hidrato contiene 1,85 a 2,2 moléculas de agua por molécula (I).

2. El hidrato según la reivindicación 1, en donde el hidrato contiene 2,0 moléculas de agua por molécula (I).
3. El hidrato según la reivindicación 1, en donde el hidrato contiene 10,5 - 12,5 % (p/p) de agua.

4. Un hidrato cristalino de hidrocloruro de 6-(piperidin-4-iloxi)-2H-isoquinolin-1-ona que tiene la fórmula



que tiene una reflexión en un difractograma de rayos X sobre polvo utilizando radiación $\text{CuK}\alpha_1$, a $7,7 \pm 0,2$ grados 2theta.

5. El hidrato según la reivindicación 4, que tiene reflexiones en un difractograma de rayos X sobre polvo utilizando radiación $\text{CuK}\alpha_1$, a

7,7, 15,2 y 16,8 grados $2\theta \pm 0,2$ grados 2θ .

6. El hidrato según la reivindicación 4, que tiene reflexiones en un difractograma de rayos X sobre polvo utilizando radiación $\text{CuK}\alpha_1$, a

7,7, 15,2, 16,8, 22,4, 25,0, y 26,6 grados $2\theta \pm 0,2$ grados 2θ .

7. Una composición farmacéutica sólida que comprende el hidrato de hidrocloruro de 6-(piperidin-4-iloxi)-2H-isoquinolin-1-ona según cualquiera de las reivindicaciones 1 a 6 y uno o más excipientes farmacéuticos aceptables.

8. Un producto farmacéutico que comprende uno o más compuestos como se reivindican en una o más de las reivindicaciones 1 a 6 y al menos un ingrediente activo adicional.

9. El producto farmacéutico como se reivindica en la reivindicación 8, que comprende, como ingrediente activo adicional, uno o más agentes antidiabéticos, ingredientes activos hipoglucémicos o agentes antihipertensivos.

10. El producto farmacéutico como se reivindica en la reivindicación 8, que comprende, como ingrediente activo adicional, uno o más bloqueantes de los receptores beta, bloqueantes de los canales de calcio o inhibidores de la renina-angiotensina.

11. El producto farmacéutico como se reivindica en la reivindicación 10, que comprende como ingrediente activo adicional verapamilo, galopamilo, fendilina, diltiazem, nitrendipino, felodipino, amlodipino, nifedipino, lercanidipino, nimodipino, nicardipino, lacidipino, isradipino, nisoldipino, nilvadipino o manidipino.

12. El producto farmacéutico como se reivindica en la reivindicación 11, que comprende como ingrediente activo adicional amlodipino.

13. El producto farmacéutico como se reivindica en la reivindicación 8, que comprende, como ingrediente activo adicional, uno o más inhibidores de la ACE (enzima convertidora de angiotensina).

14. El producto farmacéutico como se reivindica en la reivindicación 13, que comprende, como ingrediente activo adicional benazepril, captopril, cilazapril, enalapril, fosinopril, imidapril, lisinopril, moexipril, perindopril, quinapril, ramipril, espirapril, trandolapril o zofenopril.

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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Industria y Comercio
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RECIBO DE CAJA

No. 14 - 0085947

Bogotá D.C., Agosto 11 de 2014 - 11:59:04

RECIBIDO DE : CAVELIER ABOGADOS

NI 860.041.367

RE

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR PAGO
RECIBO DE CA	999999999	77407	23/07/2014		1.000.00
RECIBO DE CA	999999999	77421	23/07/2014		5.000.00
RECIBO DE CA	999999999	78335	23/07/2014		41.000.00
RECIBO DE CA	999999999	80324	29/07/2014		62.000.00
RECIBO DE CA	999999999	80327	29/07/2014		52.000.00
RECIBO DE CA	999999999	80339	29/07/2014		106.000.00
RECIBO DE CA	999999999	83843	05/08/2014		21.000.00
RECIBO DE CA	999999999	83861	05/08/2014		278.000.00
RECIBO DE CA	999999999	83862	05/08/2014		520.000.00
RECIBO DE CA	999999999	83866	05/08/2014		515.000.00
RECIBO DE CA	999999999	83874	05/08/2014		5.000.00

*** Conceptos Pagados ***

CANT. RENTISTICO

CONCEPTO

Vr.UNDITARIO Vr.CONCEPTO

1 50005-01-03 CAMBIO DE MODALIDAD Y MODIFICACIONES EN CREACION CORRECCION A SOLICITUD
EN TRAMITE / MODIFICA

128.000.00 128.000.00

\$128.000.00

SON: **CIENTO VEINTIOCHO MIL PESOS MONEDA CORRIENTE***

Responsable: _____

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 14-024164- -00005-0000

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Folios: 35

Código: 00751-841-077-9

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, Agosto 11 de 2014 - 11:59:06