

Clarke, Modet & C°

COLOMBIA

P-3176

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

E. S. D.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Ref.: Expediente No. 11.168.005
Solicitud de Patente a nombre de
XENON PHARMACEUTICALS INC.



No. 11-168005- -00001-0000

Fecha: 2012-02-20 15:48:40 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 329 CTOINFORMACION Folios: 22

Yo, DILIA MARÍA RODRÍGUEZ D'ALEMAN, identificada como aparece al pie de mi firma, domiciliada en la Carrera 11 No. 86-53, piso 6, obrando como apoderada de la sociedad **XENON PHARMACEUTICALS INC.**, con domicilio en Canadá, solicitante de la patente de la referencia, atentamente me permito presentar:

1. Documento donde consta la cesión del derecho a la patente otorgada por los inventores a favor de mi mandante.

Sobre los apartes en inglés, es importante resaltar que de conformidad con las normas legales vigentes, artículo 1 de la Resolución 210 de 2001, expedida por el Superintendente de Industria y Comercio y artículo 2 de la Convención de la Haya, el documento en inglés que se pretenda aportar como parte de los trámites de propiedad industrial ante la Superintendencia de Industria y Comercio no requieren traducción. Por otro lado, la legalización consular y/o diplomática de los documentos expedidos en el extranjero no es necesaria. Por lo tanto, los documentos anexos a este memorial son válidamente presentados en idioma inglés y con la correspondiente apostilla.

2. Documento de poder junto con el Certificado de Existencia y Representación Legal de dicha sociedad y con su respectiva traducción del inglés al español.
3. Examen Preliminar Internacional de Patentabilidad (IPRP) para su consideración en caso de ser necesario.

Señor Superintendente,

DILIA MARÍA RODRÍGUEZ D'ALEMAN
C.C. 41.654.882 de Bogotá.
T.P. 20824 CSJ

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: United States of America

This public document

2. has been signed by T. Wallace

3. acting in the capacity of Certifying Officer

4. bears the seal/stamp of U.S. Patent and Trademark Office

Certified

5. at Washington, D.C.

6. the tenth of January, 2012

7. by Assistant Authentication Officer, United States Department of State

8. No. 12012715-1

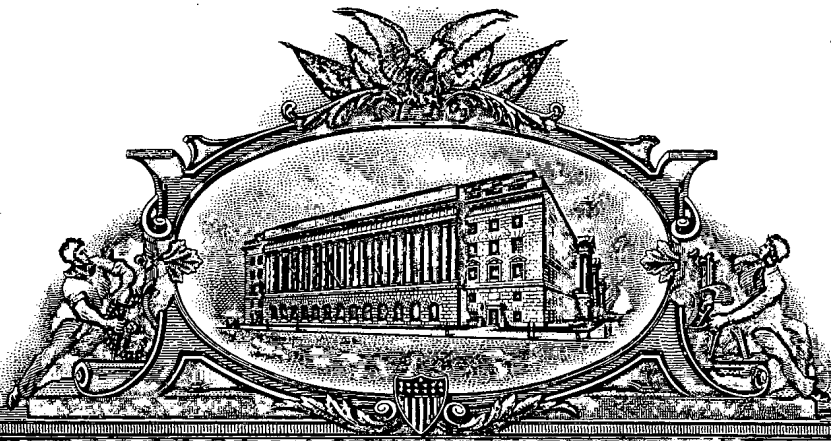
9. Seal/Stamp:

10. Signature:

William F. Finlan

William F. Finlan

A 1866143



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

December 21, 2011

THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE
RECORDS OF THIS OFFICE OF A DOCUMENT RECORDED ON
SEPTEMBER 13, 2010.

By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office




T. WALLACE
Certifying Officer

PATENT ASSIGNMENT

Electronic Version v1.1
Stylesheet Version v1.1

SUBMISSION TYPE:	NEW ASSIGNMENT										
NATURE OF CONVEYANCE:	ASSIGNMENT										
CONVEYING PARTY DATA											
<table border="1"><thead><tr><th>Name</th><th>Execution Date</th></tr></thead><tbody><tr><td>Mikhail Chafeev</td><td>07/29/2010</td></tr><tr><td>Jianmin Fu</td><td>07/29/2010</td></tr><tr><td>Jean-Jacques Cadieux</td><td>07/29/2010</td></tr></tbody></table>		Name	Execution Date	Mikhail Chafeev	07/29/2010	Jianmin Fu	07/29/2010	Jean-Jacques Cadieux	07/29/2010		
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Mikhail Chafeev	07/29/2010										
Jianmin Fu	07/29/2010										
Jean-Jacques Cadieux	07/29/2010										
RECEIVING PARTY DATA											
<table border="1"><tr><td>Name:</td><td>Xenon Pharmaceuticals Inc.</td></tr><tr><td>Street Address:</td><td>3650 Gilmore Way</td></tr><tr><td>City:</td><td>Burnaby</td></tr><tr><td>State/Country:</td><td>CANADA</td></tr><tr><td>Postal Code:</td><td>V5G 4W8</td></tr></table>		Name:	Xenon Pharmaceuticals Inc.	Street Address:	3650 Gilmore Way	City:	Burnaby	State/Country:	CANADA	Postal Code:	V5G 4W8
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PROPERTY NUMBERS Total: 1											
<table border="1"><thead><tr><th>Property Type</th><th>Number</th></tr></thead><tbody><tr><td>Application Number:</td><td>12825168</td></tr></tbody></table>		Property Type	Number	Application Number:	12825168						
Property Type	Number										
Application Number:	12825168										
CORRESPONDENCE DATA											
Fax Number: (206)682-6031 <i>Correspondence will be sent via US Mail when the fax attempt is unsuccessful.</i>											
Phone: 2066224900											
Email: carolw@seedip.com											
Correspondent Name: Carol J. Roth											
Address Line 1: 701 Fifth Avenue											
Address Line 2: Suite 5400											
Address Line 4: Seattle, WASHINGTON 98104-7092											
ATTORNEY DOCKET NUMBER:	980057.472										
NAME OF SUBMITTER:	Carol J. Roth										
Total Attachments: 5 source=980057_472_Assignment#page1.tif											

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PATENT
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PATENT
REEL: 024977 FRAME: 0515

ASSIGNMENT

WHEREAS, we,

Name	Residence Address	
Mikhail Chafeev	1403 – 4788 Hazel Street, Burnaby, British Columbia, Canada V5H 4V9	;
Jianmin Fu	3170 Quintette Crescent, Coquitlam, British Columbia, Canada V3E 3B6	; and
Jean-Jacques Cadieux	#7 – 5090 East Hastings Street, Burnaby, British Columbia, Canada V5B 1P6	

(hereinafter referred to as ASSIGNORS), having residence addresses as listed above next to our names, are the listed inventors/applicants of the patent application entitled "**ENANTIOMERS OF SPIRO-OXINDOLE COMPOUNDS AND THEIR USES AS THERAPEUTIC AGENTS**," as filed with the U.S. Patent and Trademark Office on **June 28, 2010**, and assigned Application No. **12/825,168**. This application claims the benefit of U.S. Provisional Patent Application No. 61/221,424 filed June 29, 2009, and for which an application was filed on June 28, 2010 with the U.S. Receiving Office of the PCT and assigned Application No. PCT/US2010/040187;

WHEREAS, **Xenon Pharmaceuticals Inc.** (hereinafter referred to as ASSIGNEE), a corporation incorporated under the laws of Canada having a place of business at 3650 Gilmore Way, Burnaby, British Columbia, Canada V5G 4W8, is desirous of acquiring the entire right, title and interest in and to the invention and in and to any letters patent that may be granted therefor in the United States and in any and all foreign countries;

NOW, THEREFORE, in exchange for good and valuable consideration, the receipt of which is hereby acknowledged, ASSIGNORS hereby sell, assign and transfer unto said ASSIGNEE the entire right, title and interest in and to said invention, said application and any and all letters patent which may be granted for said invention in the United States of America and its territorial possessions including any extensions or adjustments in term thereof and in any and all foreign countries, and in any and all divisions, reissues and continuations thereof, including the right to file foreign applications directly in the name of ASSIGNEE and to claim priority rights deriving from said United States application to which said foreign applications are entitled by virtue of international convention, treaty or otherwise, said invention, application and all letters patent on said invention to be held and enjoyed by ASSIGNEE and its successors and assigns as fully and entirely as the same would have been held and enjoyed by ASSIGNORS had this assignment, transfer and sale not been made. ASSIGNORS hereby authorize and request the Commissioner of Patents and Trademarks to issue all letters patent on said invention to ASSIGNEE.

ASSIGNORS agree to execute all instruments and documents required for the making and prosecution of applications for United States and foreign letters patent on said invention, for litigation regarding letters patent, or for the purpose of protecting title to said invention or letters patent therefor.

This Assignment is effective as of June 28, 2010.

July 29th, 2010
Date
Mikhail Chafeev
Province of British Columbia
Country of Canada
} ss.

I certify that I know or have satisfactory evidence that **Mikhail Chafeev** is the person who appeared before me, and said person acknowledged that he signed this instrument and acknowledged it to be his free and voluntary act for the uses and purposes mentioned in the instrument.

Dated July 29, 2010
Signature of Notary Public
Printed Name THONG N. TRINH

My Commission is for as long as I remain a practicing member of the Law Society of British Columbia.

THONG NGOC TRINH
BARRISTER & SOLICITOR

July 29, 2010
Date

Jianmin Fu
Jianmin Fu

Province of British Columbia

Country of Canada

} ss.

I certify that I know or have satisfactory evidence that **Jianmin Fu** is the person who appeared before me, and said person acknowledged that he signed this instrument and acknowledged it to be his free and voluntary act for the uses and purposes mentioned in the instrument.

Dated

July 29, 2010

Signature of
Notary Public

Thong Trinh

Printed Name

THONG N. TRINH

My Commission is for as long as I remain a practicing member of the Law Society of British Columbia.

**THONG NGOC TRINH
BARRISTER & SOLICITOR**

Date July 29th, 2010

Jean-Jacques Cadieux
Jean-Jacques Cadieux

Province of British Columbia

Country of Canada

} ss.

I certify that I know or have satisfactory evidence that **Jean-Jacques Cadieux** is the person who appeared before me, and said person acknowledged that he signed this instrument and acknowledged it to be his free and voluntary act for the uses and purposes mentioned in the instrument.

Dated July 29, 2010

Signature of
Notary Public

Thong Trinh

Printed Name

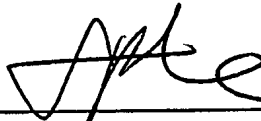
THONG N. TRINH

My Commission is for as long as I remain a practicing member of the Law Society of British Columbia.

**THONG NGOC TRINH
BARRISTER & SOLICITOR**

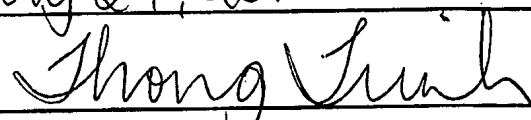
XENON PHARMACEUTICALS INC.

29th July / 2010
Date


Simon N. Pimstone
President and CEO

Province of British Columbia }
Country of Canada } ss.

I hereby certify that I know or have satisfactory evidence that **Simon N. Pimstone**, President and CEO of Xenon Pharmaceuticals Inc., is the person who appeared before me, and said person acknowledged that he signed this instrument, on oath stated that he was authorized to execute the instrument on behalf of Xenon Pharmaceuticals Inc., a corporation organized and existing according to the laws of Canada, and acknowledged it to be his free and voluntary act for the uses and purposes mentioned in the instrument.

Dated July 29, 2010
Signature of Notary Public 
Printed Name THONG N. TRINH

My Commission is for as long as I remain a practicing member of the Law Society of British Columbia.

THONG NGOC TRINH
BARRISTER & SOLICITOR

980057.472 C41.42-US 1653599_1.DOC

COLOMBIA

Carrera 11 N° 86-53 Piso 6 Bogotá Colombia Tel: (57 1) 6181088 Fax: (57 1) 6350824 Email: info@clarkemodet.com.co

PODER

Yo (nosotros), abajo firmante(s)

en mi (nuestro) carácter de representante(s) legales de

XENON PHARMACEUTICALS INC.

una sociedad organizada y existente de acuerdo con las leyes de

y en actual cumplimiento de su objeto social, con domicilio en **3650 Gilmore Way, Burnaby, British Columbia V5G 4W8, Canada.**

por el presente instrumento confiero (conferimos) poder especial a favor de **DILIA MARIA RODRIGUEZ D'ALEMAN**, con Cédula de Ciudadanía N°: 41.654.882 de Bogotá, y tp. 20824 con domicilio en Bogotá, Colombia, para que actuando en su orden en nombre del (de la) otorgante le (la) representen, ante cualquier entidad, autoridad y/o persona, especialmente ante las del orden Administrativo, Contencioso Administrativo, Judicial, Tribunales de Arbitramento y/o cualquier otro en lo referente a los siguientes asuntos:

- 1) Solicitar, tramitar, obtener y/o registrar cualquiera de las modalidades de Propiedad Industrial, tales como: patentes de invención, modelos de utilidad; diseños industriales, variedades vegetales; marcas, lemas, nombres y enseñanzas comerciales y denominaciones de origen; así como sus renovaciones, prórrogas, transferencias, cambios de nombre y/o domicilio, contratos y licencias.
- 2) Solicitar, tramitar, obtener y/o registrar derechos de autor, en cualquiera de sus presentaciones así como la protección de secretos industriales y know-how.
- 3) Solicitar, tramitar, obtener y/o registrar registros sanitarios, permisos y/o licencias de funcionamiento; así como sus renovaciones o prórrogas, transferencias, cambios de nombre y/o domicilio, contratos y licencias.
- 4) Ejercer acciones de oposición, observación, reclamos, reconsideración, reposición, apelación, cancelación administrativa o judicial, nulidad, protección al consumidor, concesión de licencias, protección de secretos industriales y demás acciones y recursos relacionados con derechos derivados de los asuntos arriba indicados y en contra de la competencia desleal, acciones derivadas de la obtención o explotación de licencias, acciones de indemnización de perjuicios. También podrá(n) intervenir en juicios civiles, comerciales, penales, contencioso-administrativos, tutelas y de policía; en acciones o juicios promovidos por el (la) mandante o en contra el (ella).
- 5) Registrar nombres de dominio ante la entidad competente.
- 6) En el ejercicio de este mandato los mandatarios arriba mencionados quedan facultados para: conciliar, cancelar, transigir, comprometer en árbitros, desistir, recibir y tomar posesión de la cosa objeto de litigio y renunciar o desistir a derechos concedidos o en curso de concesión, admitir los hechos del proceso.
- 7) Ratificar o no la agencia oficiosa.
- 8) Así mismo faculto (facultamos) a los mencionados apoderados para recibir notificaciones y designar apoderados judiciales o extrajudiciales, sustituir el presente poder y revocar las sustituciones que hicieren.

Dado y firmado en

a los días de

POWER OF ATTORNEY

I (we), the undersigned **TAREK S. MANSOUR**

legal representative(s) of

XENON PHARMACEUTICALS INC.

an organization existing under the laws of **CANADA**

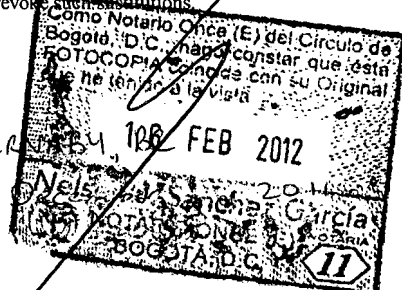
and in present execution of its business activity, domiciled at **3650 Gilmore Way, Burnaby, British Columbia V5G 4W8, CA.**

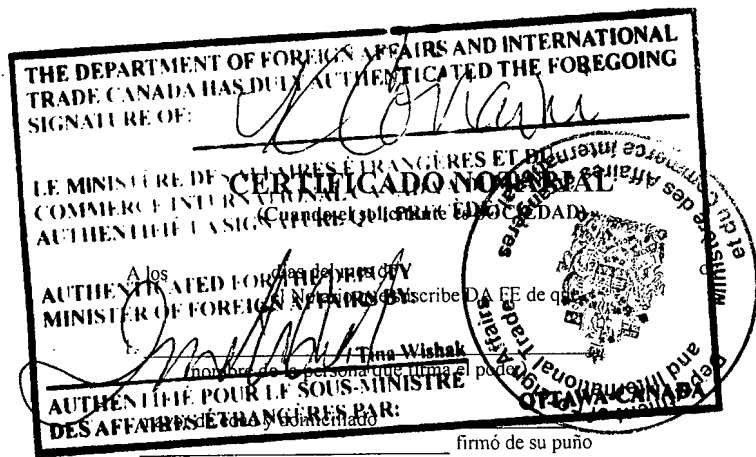
do hereby grant POWER OF ATTORNEY to **DILIA MARIA RODRIGUEZ D'ALEMAN**, identification card No. 41.654.882 of Bogotá, and tp. 20824 residing in Bogotá Colombia, to act in the order of their appointment in behalf of grantor before any entity, authority and/or natural or juridical person, specially before those Administrative, Administrative-Contentious, Judicial, arbitration courts, and/or any other, in all matters concerning the following:

- 1) To apply, process, obtain and/or register any of the modalities of Industrial Property, such as: Patents of Invention, Utility Models; Designs, plant varieties; Marks, Slogans, Trade Names and emblems and appellations of Origin; as well as their renewals, assignments, changes of name and/or domicile, agreements and licenses.
- 2) To apply, process, obtain and/or register copyrights of any kind as well as protection of industrial secrets or know-how.
- 3) To apply, process, obtain and/or register sanitary registrations, operating authorizations and/or licenses; as well as their renewals or assignments, changes of name and/or domicile, agreements and licenses.
- 4) To bring actions of opposition, observations, claims, reconsideration, appeal or legal remedies, cancellations, nullity, protection to the consumer, granting of licenses, protection of trade secrets and other actions related with rights derived from the above-mentioned matters and against the unfair competition, actions resulting from the obtaining or exploitation of licenses, recovering damages actions. They can also intervene or participate in Civil, Commercial, Criminal or Contentious-Administrative Trials; the actions for writ mandamus, police actions; in actions, lawsuits or litigations instituted by the grantor or against him.
- 5) To register domain names before the competent entity.
- 6) To the effect of this mandate the above-named proxy are empowered to: conciliate, cancel, settle, submit to arbitration, withdraw and to receive and take possession of the litigation related objet and waive or renounce the rights granted or in process of granting, admit the facts of the case.
- 7) To ratify or not the officious agency.
- 8) I (we) hereby appoint the afore mentioned attorneys with powers to receive notifications and to designate judicial and extrajudicial attorneys, substitute this Power of Attorney and to revoke such institutions.

Granted and signed at **Burnaby, 18 FEB 2012**
on this **9th** day of

Firma / signature





NOTARIAL CERTIFICATE
(When the applicant is a CORPORATION)

This 9th day of December, 2011
the undersigned Notary CERTIFIES that:

1. TAREK S. MANSOUR
(name of the person who signs the power of attorney)

of NEW CITY, NY, USA legal age and domiciled in NEW CITY, NY, USA set his hand on the foregoing document.

2. The grantor is to him personally known and that he/she has legal capacity to execute the document.

3. The grantor has executed the foregoing document in his capacity of OFFICER of the juridical person XENON PHARMACEUTICALS INC

y letra el documento que antecede.
2. Conoce al (a la) otorgante y que este (a) está legalmente capacitado para el otorgamiento.
3. El otorgante ha firmado el referido documento en su carácter de XENON PHARMACEUTICALS INC.

4. La citada persona jurídica con sede en 3650 Gilmore Way, Burnaby, British Columbia V5G 4W8, Canada., está legalmente constituida, que tiene actualmente existencia legal y que el acto para el cual se ha otorgado este poder está comprendido entre los que constituyen su objeto social.
5. El otorgante tiene efectivamente la representación que ostenta, que esta es legítima y que está facultado para otorgar este poder.
6. las anteriores certificaciones de los puntos 3, 4 y 5, me constan porque he tenido a la vista los documentos auténticos.

Notario Público

NOTA: A continuación de lo anterior, el Consúl de Colombia debe autenticar la firma del Notario Público.

CERTIFICADO NOTARIAL (Cuando el solicitante es INDIVIDUO)

A los días del mes de de , el Notario que suscribe DA FE de que:

1.
(nombre de la persona que firma el poder)

mayor de edad y domiciliado en firmó en su presencia

el documento que antecede, conoce al otorgante y que este está legalmente capacitado para el otorgamiento.

Notario Público

NOTA: A continuación de lo anterior, el Consúl de Colombia debe autenticar la firma del Notario Público.

Para todos los demás países el Señor Consúl de Colombia o ante quien se otorgue, debe expedir una certificación dejando constancia 1) de la existencia legal de la sociedad, 2) de que esta ejerce actualmente su objeto social, y 3) de que la persona o personas que otorgan el poder están facultadas para hacerlo, dejando constancia así mismo de que tuvo a la vista las pruebas que acrediten tales circunstancias.

LEGALIZACIÓN POR EL CONSUL DE COLOMBIA O POR APOSTILLA



NOTA: Then the Colombian Consul must legalize the signature of the Notary Public.

NOTARIAL CERTIFICATE (When the applicant is an INDIVIDUALS)

On this day of , the undersigned Notary CERTIFIES that:

1.
(name of the person who signs the Power of Attorney)

of legal age and domiciled at signed in his presence the foregoing document, the grantor is to him personally known and that he/she has legal capacity to execute the document.

Notary Public

NOTA: Then the Colombian Consul must legalize the signature of the Notary Public.

For all other countries the Colombian Consul or before who it is granted must issue a certification stating 1) the legal existence of the corporation, 2) that the corporate purposes are actually being accomplished, 3) that the person or persons who grant this Power of Attorney are empowered to do it. The Consul will certify also that the documents evidencing those circumstances were exhibited to him.

LEGALIZATION BY THE COLOMBIAN CONSUL OF OTTAWA BY APOSTILLA CONSULADO DE COLOMBIA

No. 016 En Ottawa, Canadá, a 9 de Febrero de 2012
se legaliza la firma de T. Wishak
quien en la fecha ejerce las funciones de Notario de legalizaciones
\$ 30=
Consul de Colombia

Colombia 027569-10



REPÚBLICA DE COLOMBIA
MINISTERIO DE RELACIONES EXTERIORES
LEGALIZACION

País: **REPUBLICA DE COLOMBIA**
(Country: - Pays:)

El presente documento público
(This public document - Le présent acte public)

Ha sido firmado por: **BELTRAN ESPITIA MONICA**
(Has been signed by: - A été signé par:)

Actuando en calidad de: **CONSUL GENERAL**
(Acting in the capacity of: - Agissant en qualité de:)

Lleva el sello/estampilla de: **MISIONES DE COLOMBIA EN EL EXTERIOR**
(Bears the seal/stamp of: - Est revêtu du sceau de / timbre de:)

Certificado
(Certified - Attesté)

En: **BOGOTA D.C**
(At: - À:)

El: **2/1/2012 11:58:29 a.m.**
(On: - Le:)

Por: **APOSTILLA Y LEGALIZACIÓN**
(By: The Ministry of Foreign Affairs of Colombia - Par: Ministère des Affaires Étrangères de la Colombie)

No: **LMCB115829792**
(Under Number: - Sous le numéro:)

Nombre del Titular: **TINA WISHAK**
(Name of the holder of document: - Nom du titulaire:)

Tipo de documento: **CERTIFICACION**
(Type of document: - Type du document:)

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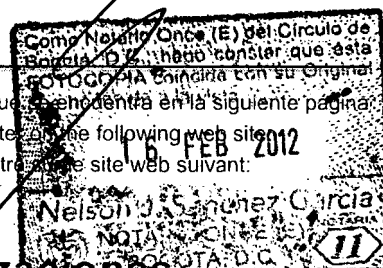
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(Number of pages: - Nombre de pages:)

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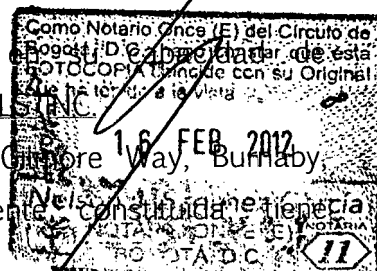
Firmado Digitalmente por: (Digitally Signed by:)
Ministerio de Relaciones Exteriores de Colombia
AMPARO DE LA CRUZ TAMAYO RODRIGUEZ
Reason: DOCUMENT AUTHENTICITY
BOGOTA - COLOMBIA

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www.cancilleria.gov.co/legalizaciones



12




JIMENA ESCOBAR URIBE
Traductor e Intérprete Oficial
Resolución No. 0369 Min. Justicia 1995

existencia legal vigente y los propósitos para los cuales se otorga el poder de abogado están dentro del ámbito de sus objetivos corporativos.

(Nota del traductor: El resto del documento se encuentra con idéntico texto en la parte izquierda del documento en idioma español, razón por la cual no se hace su traducción).

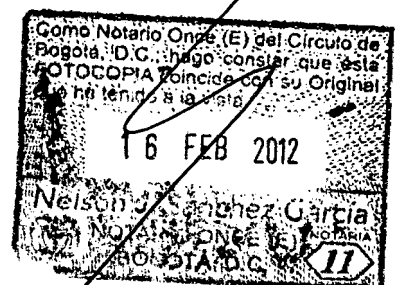
Documento legalizado mediante firma ilegible de notario público.

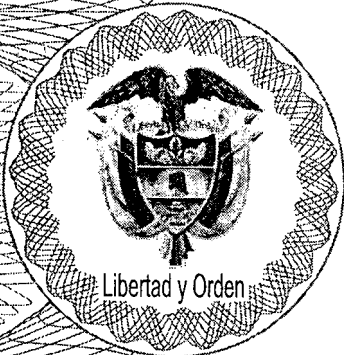
Sello: El Departamento de Asuntos Exteriores y Comercio Internacional de Canadá ha autenticado debidamente la firma anterior de: (ilegible).

Firma ilegible, Autenticado por el Viceministro de Asuntos Exteriores. Sello oficial.

Nota del Traductor: Documento legalizado por Consulado de Colombia en Ottawa, Canadá, bajo el número 016 de 9 de enero de 2012 y mediante Apostilla No. LMCB115829792 expedida por el Ministerio de Relaciones Exteriores de la República de Colombia el 2/1/2012, en español por lo que no se hace necesaria su traducción.


JIMENA ESCOBAR URIBE
Traductor e Intérprete Oficial
Resolución No. 0369 Min. Justicia 1995





REPÚBLICA DE COLOMBIA
MINISTERIO DE RELACIONES EXTERIORES
LEGALIZACION

País: REPUBLICA DE COLOMBIA
(Country: - Pays:)

El presente documento público
(This public document - Le présent acte public)

Ha sido firmado por: ESCOBAR URIBE JIMENA
(Has been signed by: - A été signé par:)

Actuando en calidad de: TRADUCTORA E INTERPRETE OFICIAL
(Acting in the capacity of: - Agissant en qualité de:)

Lleva el sello/estampilla de: TRADUCTOR E INTERPRETE OFICIAL
(Bears the seal/stamp of: - Est revêtu du sceau de / timbre de:)

Certificado
(Certified - Attesté)

En: BOGOTA D.C
(At: - À:)

El: 2/3/2012 13:26:45 p.m.
(On: - Le:)

Por: APOSTILLA Y LEGALIZACIÓN
(By: The Ministry of Foreign Affairs of Colombia - Par: Ministère des Affaires Étrangères de la Colombie)

No: LMCD132645970
(Under Number: - Sous le numéro:)

Nombre del Titular: TINA WISHAK
(Name of the holder of document: - Nom du titulaire:)

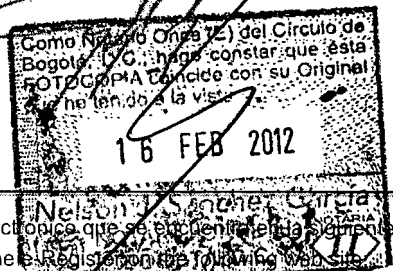
Tipo de documento: TRADUCCION CERTIFICACION
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 980057-472PC	FOR FURTHER ACTION See item 4 below	
International application No. PCT/US2010/040187	International filing date (<i>day/month/year</i>) 28 June 2010 (28.06.2010)	Priority date (<i>day/month/year</i>) 29 June 2009 (29.06.2009)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant XENON PHARMACEUTICALS INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a). 2. This REPORT consists of a total of 7 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3. This report contains indications relating to the following items: <table border="0"> <tr> <td>☒</td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td>☐</td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td>☐</td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td>☐</td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td>☒</td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td>☐</td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td>☐</td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td>☒</td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> 4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).	☒	Box No. I	Basis of the report	☐	Box No. II	Priority	☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	☐	Box No. IV	Lack of unity of invention	☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	☐	Box No. VI	Certain documents cited	☐	Box No. VII	Certain defects in the international application	☒	Box No. VIII	Certain observations on the international application
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☒	Box No. VIII	Certain observations on the international application																						

	Date of issuance of this report 04 January 2012 (04.01.2012)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Nora Lindner e-mail: pt03.pct@wipo.int

Form PCT/IB/373 (January 2004)

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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2010/040187

International filing date (day/month/year)
28.06.2010

Priority date (day/month/year)
29.06.2009

International Patent Classification (IPC) or both national classification and IPC
INV. C07D491/22 A61K31/404 A61P29/00

Applicant
XENON PHARMACEUTICALS INC.

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

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

2. FURTHER ACTION

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

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

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

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
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NL-2280 HV Rijswijk - Pays Bas
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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Menchaca, Roberto

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2010/040187

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
- ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:
- a. (means)
- ☐ on paper
 - ☐ in electronic form
- b. (time)
- ☐ in the international application as filed
 - ☐ together with the international application in electronic form
 - ☐ subsequently to this Authority for the purposes of search
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

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

1. Statement

Novelty (N)	Yes: Claims	<u>1-8</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-8</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-8</u>
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2010/040187

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Document

Reference is made to the following document:

D1 WO 2006/110917 A2 (2006-10-19) cited in the application

Rule 39 PCT

Claims 3-7 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 39(1)(iv) and Rule 67(1)(iv) PCT.

For the assessment of the present claims 3-7 on the question whether they are patentable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as patentable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claimsto a known compound for first or further use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Consequently, and even if no opinion should be formulated with respect to the subject-matter of said claims 3-7 (Article 34(4)(a)(I) PCT), this authority has decided to carry out and base the search and present opinion on the alleged effects of the compounds and/or compositions.

Novelty

No prior art document discloses the (S)-enantiomer of the compound of formula (I) as defined in present claim 1. The subject-matter of present claims 1-8, respectively disclosing the referred enantiomer, pharmaceutical compositions thereof and their therapeutic use for the treatment of diseases mediated by voltage-gated sodium channels, is therefore novel over the prior art in the sense of Article 33(2) PCT.

Inventive step

D1 is regarded as the closest prior art to the presently claimed subject-matter and discloses the compound of formula (I) in racemic form and a method for its preparation.

The present invention differs from D1 in that it discloses the (S)-enantiomer of the aforementioned compound.

The problem to be solved by the present invention may therefore be regarded as the provision of stereoisomers of the compound of formula (I). The applicant solves this problem by providing the (S)-enantiomer of the said compound.

The application as filed contains comparative data (see tables 2-3, pages 42 and 44), which demonstrate a significant higher (i.e. >1000-fold) inhibition potency and five times more affinity to the receptor of the (S)-enantiomer with respect to the corresponding (R)-enantiomer. These data demonstrate that the (S)-enantiomer is primarily responsible for the potency of the racemate (i.e. the compound of formula (I)).

There is no indication in the prior art for such an enhanced potency of the (S)-enantiomer. In the absence of such a hint in the art, the person skilled in the art would have no motivation to try and isolate the (S)-enantiomer of the compound of formula (I). Furthermore, he would certainly not expect the benefits associated to the latter.

In view of the above, the subject-matter of present claims 1-8 can therefore be regarded as involving an inventive step in the sense of Article 33(3) PCT.

Re Item VIII

Certain observations on the international application

Claims 1-3 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The expression "prodrug" given therein constitutes an attempt to define the subject-matter in terms of the result to be achieved since it encompasses a large number of compounds which are only defined by reference to a desired functional activity (compounds being a "prodrug"). This functional term does not give a specific technical guidance for the selection of the suitable derivatives, without proven general knowledge, to show which derivatives are suitable "prodrugs" in the particular case of the current problem. No test methods are known which allow to verify without undue burden if a compound is embraced by the claim or not. Such a claim would impose a severe and undue burden on those wishing to ascertain the scope of the exclusively right, which would be contrary to Article 6 PCT.

Furthermore, prodrugs of the presently claimed compounds may well represent a completely separate invention from that disclosed in the present application and as such, they are insufficiently supported and disclosed within the meaning of Articles 5-6 PCT. In such a situation, the invention cannot be carried out over the whole area claimed without imposing an undue burden and the skilled person would not be able to produce all these compounds without exercising an inventive step in accordance with Article 33(3) PCT.

The general expression "...incorporated herein by reference.." (see, for instance, pages 1, 8, 28 and 56) is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers. It may imply that the extent of the protection may be expanded in some vague and not precisely defined way (Article 5 PCT). The patent specification should, regarding to the features of the invention, be self-contained, i.e. capable of being understood without reference to any other document.