



No. 16-032714- -00005-0000

Fecha: 2016-05-11 16:11:39 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 444 RESPUESTAREQUE Folios: 18

As. 135598

Señor

**DIRECTOR DIVISIÓN DE NUEVAS CREACIONES
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO**

E.

S.

D.

A.S

REF: Expediente No. **16.032714**

RESPUESTA A EXAMEN DE FORMA

JUAN PABLO CADENA SARMIENTO, portador de la tarjeta profesional No. 57.492 del C.S.J., obrando como apoderado de la sociedad solicitante me permito dar respuesta al Oficio No. 430 notificado por fijación en lista el 5 de enero de 2016.

Poder y cesión

Adjuntamos poder y cesión respectivos.

Excepciones de patentabilidad

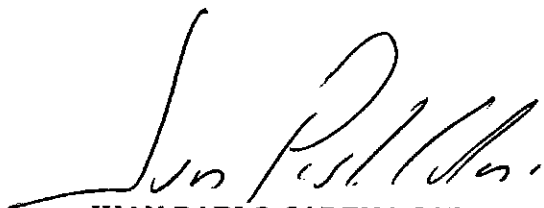
Las reivindicaciones 8-18 han sido eliminadas de pliego reivindicatorio.

Claridad

Consideramos que el alcance de las reivindicaciones es una justa generalización de los compuestos que han sido sintetizados por los inventores y que ha demostrado tener cierta actividad biológica. No obstante dicha justa generalización, el solicitante ha decidido incluir definiciones adicionales para los anillos A y B tal como puede corroborar su despacho en el pliego reivindicatorio adjunto. Adicionalmente, deseamos resaltar que los ejemplos en una solicitud de patentes deben considerarse como ilustrativos de la materia reivindicada pero en ningún momento deben considerarse limitativos de la misma.

En vista de lo anteriormente expuesto, respetuosamente solicito el retiro de las objeciones de la presente solicitud ya que en opinión del solicitante cumple con todos los requisitos establecidos en la Decisión 486.

Atentamente,



JUAN PABLO CADENA SARMIENTO

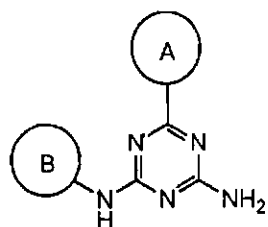
T.P. No. 57.492 del C.S.J.

C.C. 80.410.337 de Usaquén

Calle 70 A No. 4 - 41

REIVINDICACIONES

1. Un compuesto caracterizado porque tiene la Fórmula I o una sal o hidrato farmacéuticamente aceptable de la misma:



(I)

en donde:

el anillo A es un arilo monocíclico o heteroarilo monocíclico de 5-6 miembros opcionalmente sustituidos en donde los sustituyentes sobre al anillo A, cuando están presentes, se seleccionan de halo, alquilo C₁-C₄, haloalquilo C₁-C₄ ; hidroxialquilo C₁-C₄, -NH-S(O)₂-(alquilo C₁-C₄), -S(O)₂NH (alquilo C₁-C₄), -CN, -S(O)₂-(alquilo C₁-C₄), -NH(alquilo C₁-C₄), -OH, -OCF₃, -NH₂, -C(O)NH₂, -C(O)NH (alquilo C₁-C₄), -C(O)-N(alquilo C₁-C₄), y ciclopropilo opcionalmente sustituido con -OH; y

el anillo B es un arilo monocíclico o heteroarilo monocíclico de 5-6 miembros opcionalmente sustituidos; en donde los sustituyentes sobre al anillo B, cuando están presentes, se seleccionan de halo, alquilo -C₁-C₄, alquinilo C₂-C₄, haloalquilo C₁-C₄, hidroxialquilo C₁-C₄, cicloalquilo C₃-C₆, (alquileno C₀-C₂)-O-alquilo C₁-C₄, -O-(alquileno C₁-C₄)-cicloalquilo (C₃-C₆), -NH-S(O)₂-(alquililo C₁-C₄), -S(O)₂NH (alquilo C₁-C₄), -S(O)₂-NH-(cicloalquilo C₁-C₄), -S(O)₂-(heterociclil saturado), -CN, -S(O)₂-(alquilo C₁-C₄), -NH (alquilo C₁-C₄), N (alquilo C₁-C₄)₂, -OH, C(O)-O-(alquilo C₁-C₄), heterociclil saturado, y -NH₂ y en donde

a. el anillo A y el anillo B no son ambos un anillo monocíclico de 6 miembros opcionalmente sustituidos;

b. cuando el anillo A es piridilo no sustituido, entonces el anillo B no es fenilo opcionalmente sustituido con uno a tres grupos seleccionados independientemente de metilo, etilo, t-butilo, metoxi, CH(OH)CH₃, Cl, Br, SH, y CF₃;

c. cuando el anillo A es un heteroarilo de 5 miembros, entonces el anillo B no es fenilo opcionalmente sustituido con uno a dos grupos seleccionados independientemente de F, Cl, SO₂CH₃, C(O)OCH₃, metilo, etilo, t-butilo, metoxi, etoxi, O- fenilo, CF₃, OH, y NO₂;

d. cuando el anillo A es un 5-tiazolilo 2,4-disustituido, entonces el anillo B no es fenilo sustituido;

e. el compuesto no es:

(1) N²-2-piridinil-6-(3-piridinil)-1,3,5-triazin-2,4-diamina;

(2) 6-(6-metoxi-3-piridinil)-N²-(4-metilfenil)-1,3,5-triazin-2,4-diamina;

(3) 6-(2-metoxi-3-piridinil)-N²-(4-metilfenil)-1,3,5-triazin-2,4-diamina;

(4) N²-(3-clorofenil)-6-(2-cloro-4-piridinil)-1,3,5-triazin-2,4-diamina;

(5) 3-{[4-[4-amino-6-[(3-clorofenil)amino]-1,3,5-triazin-2-il]-2-piridinil]amino}-1-propanol;

(6) N-[3-{[4-amino-6-(2-metil-4-pirimidinil)-1,3,5-triazin-2-il]amino}-4-metilfenil]-N'-[4-cloro-3-(trifluorometil)fenil]-urea;

(7) N⁴,N^{4'}-difenil-[2,2'-bi-1,3,5-triazin]-4,4',6,6'-tetramina;

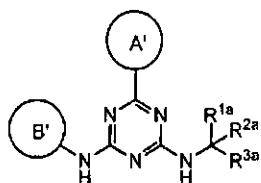
(8) 6,6'-(2,6-piridindiil)bis[N-fenil-1,3,5-triazin-2,4-diamina]; o

(9) 6,6'-(2,3-piridazindiil)bis[N-fenil-1,3,5-triazin-2,4-diamina.

2. El compuesto de conformidad con la reivindicación 1, caracterizado porque el anillo A se selecciona de fenilo, pirazolilo, oxazolilo, isoxazolilo, piridinilo, pirimidinilo, pirazinilo, y tiazolilo, en donde el anillo A se sustituye opcionalmente con hasta dos sustituyentes seleccionados independientemente de halo, -alquilo de C₁-C₄, -haloalquilo de C₁-C₄, hidroxialquilo de C₁-C₄, -NH-S(O)₂-(alquilo de C₁-C₄), -S(O)₂NH(alquilo de C₁-C₄), -CN, -S(O)₂-(alquilo de C₁-C₄), alcoxi de C₁-C₄, -NH(ALQUILO DE C₁-C₄), -OH, -CN, y -NH₂.

3. El compuesto de conformidad con la reivindicación 1, caracterizado porque el anillo B se selecciona de fenilo, pirazolilo, oxazolilo, isoxazolilo, tiazolilo, piridinilo, pirimidinilo, piridazinilo, y pirazinilo, en donde el anillo B se sustituye opcionalmente con hasta dos sustituyentes seleccionados independientemente de halo, -alquilo de C₁-C₄, -alquinilo de C₂-C₄, -haloalquilo de C₁-C₄, hidroxialquilo de C₁-C₄, cicloalquilo de C₃-C₆, -(alquilenos de C₀-C₂)-O-alquilo de C₁-C₄, -O-(alquilenos de C₁-C₄)cicloalquilo de C₃-C₆, -NH-S(O)₂-(ALQUILO DE C₁-C₄), -S(O)₂NH(alquilo de C₁-C₄), -S(O)₂-NH-(cicloalquilo de C₃-C₆), -S(O)₂-(heterociclilo saturado), -CN, -S(O)₂-(alquilo de C₁-C₄), -NH(ALQUILO DE C₁-C₄), -N(ALQUILO DE C₁-C₄)₂, -OH, C(O)-O-(alquilo de C₁-C₄), heterociclilo saturado, y -NH₂.

4. Un compuesto caracterizado porque tiene la Fórmula Estructural II:



(II), o una sal farmacéuticamente aceptable del mismo, en donde:

el anillo A' se selecciona de fenilo y piridin-2-ilo, en donde el anillo A' se sustituye opcionalmente con

uno o dos sustituyentes seleccionados independientemente de cloro, flúor, $-\text{CF}_3$, $-\text{CHF}_2$, $-\text{CH}_3$, $-\text{CH}_2\text{CH}_3$, $-\text{CF}_2\text{CH}_3$, $-\text{OH}$, $-\text{OCH}_3$, $-\text{OCH}_2\text{CH}_3$, $-\text{NH}_2$, $-\text{NH}(\text{CH}_3)$, y $-\text{N}(\text{CH}_3)_2$;

el anillo B' se selecciona de piridin-3-ilo, piridin-4-ilo, isoxazol-4-ilo, isoxazol-3-ilo, tiazol-5-ilo, pirimidin-5-ilo y pirazol-4-ilo, en donde el anillo B' se sustituye opcionalmente con uno a dos sustituyentes seleccionados independientemente de halo; $-\text{CN}$; $-\text{OH}$; alquilo de C_1 - C_4 opcionalmente sustituidos con halo, CN o $-\text{OH}$; $-\text{S}(\text{O})_2$ -alquilo de C_1 - C_4 ; $-\text{S}(\text{O})$ -alquilo de C_1 - C_4 ; $-\text{S}(\text{O})_2$ -NH-ALQUILO DE C_1 - C_4 ; $-\text{S}(\text{O})_2$ -N(alquilo de C_1 - C_4) $_2$; $-\text{S}(\text{O})_2$ -azetidin-1-ilo; $-\text{O}$ -alquilo de C_1 - C_4 ; $-\text{CH}_2$ - O - CH_3 , morfolin-4-ilo, ciclopropilo, $-\text{S}(\text{O})_2$ -NH-ciclopropilo; $-\text{C}(\text{O})$ - O - CH_3 ; y

$-\text{C}(\text{R}^{1a})(\text{R}^{2a})(\text{R}^{3a})$ se selecciona de alquilo de C_1 - C_6 opcionalmente sustituido con halo o $-\text{OH}$; $-(\text{alquilenos de } \text{C}_0\text{-}\text{C}_1)\text{-cicloalquilo}$, en donde el alquileno se sustituye opcionalmente con metilo y el cicloalquilo se sustituye opcionalmente con halo, $-\text{OCH}_3$ o metilo; heterocicliclo saturado opcionalmente sustituido con halo o metilo; $-\text{C}(\text{O})$ - O -alquilo de C_1 - C_6 ; $-\text{C}(\text{O})$ -(alquilenos de $\text{C}_0\text{-}\text{C}_1$)-ciclopropilo; y $\text{C}(\text{O})$ -bencilo.

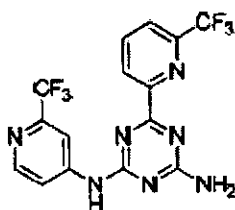
5. El compuesto de conformidad con la reivindicación 4, caracterizado porque el anillo A' se selecciona de 2-clorofenilo, 2-fluorofenilo, 2-metoxifenilo, 3-hidroxifenilo, 6-aminopiridin-2-ilo, 6-cloropiridin-2-ilo, 6-trifluorometilpiridin-2-ilo, y fenilo.

6. El compuesto de conformidad con la reivindicación 4, caracterizado porque el anillo B' se selecciona de 2-(morfolin-4-il)piridin-4-ilo, 2-dimetilaminopiridin-4-ilo, 3-(2-metoxietil)fenilo, 3,5-difluorofenilo, 3-clorofenilo, 3-cianometilfenilo, 3-cianofenilo, 3-ciclopropilaminosulfonilfenilo, 3-dimetilaminosulfonilfenilo, 3-etilsulfonilfenilo, 3-fluorofenilo, 3-metilsulfonilfenilo,

4-fluorofenilo, 5-cloropiridin-3-ilo, 5-cianopiridin-3-ilo,
5- cianopiridin-3-ilo, 5-cianopiridin-4-ilo, 5-fluoropiridin-3-ilo,
5-trifluorometilpiridin-3-ilo, 6-cloropiridin-4-ilo, 6-cianopiridin-
4-ilo, 6-ciclopropilpiridin-4-ilo, 6-etoxipiridin-4-ilo,
6-fluoropiridin-3-ilo, 6-fluoropiridin-4-ilo, 6-metilpiridin-4-ilo,
6-trifluorometilpiridin-4-ilo, isoxazol-4-ilo, fenilo,
piridin-4-ilo, y tiazol-5-ilo.

7. Una composición farmacéutica caracterizada porque comprende un compuesto de conformidad con la reivindicación 1, y un portador farmacéuticamente aceptable.

8. El compuesto de la reivindicación 1 en donde el compuesto es



The Commonwealth of Massachusetts

William Francis Galvin
Secretary of the Commonwealth

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: United States of America

This public document

2. has been signed by: Katerina Belvin

3. acting in the capacity of: Notary Public

4. bears the seal/stamp of: Katerina Belvin
whose commission expires on: April 15, 2022

Certified

5. at: Boston, Massachusetts

6. the: 4 February, 2016

7. by: the Secretary of the Commonwealth

8. No.: 1870759

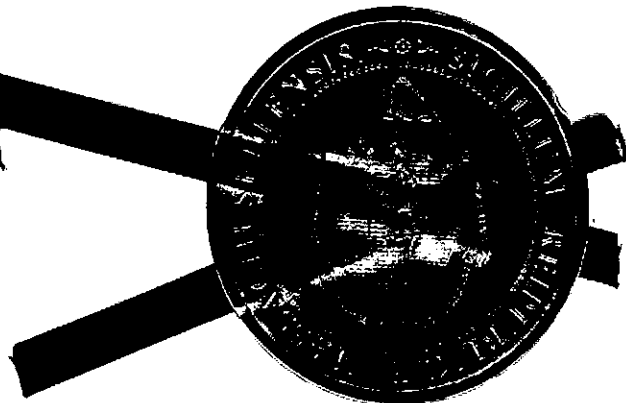
9. Seal/stamp:

Great Seal of the Commonwealth

10. Signature:



William Francis Galvin
Secretary of the Commonwealth



Brigard & Castro

BOGOTÁ - COLOMBIA

12827-842-026

PODER

POWER OF ATTORNEY

Yo (nosotros), **AGIOS PHARMACEUTICALS, INC.**

I (We), **AGIOS PHARMACEUTICALS, INC.**

domiciliado(s) en 88 Sidney Street, Cambridge, MA 02139, US.

domiciled in 88 Sidney Street, Cambridge, MA 02139, US.

For PCT/US2014/046204 entitled N,6-BIS(ARYL OR HETEROARYL)-1,3,5-TRIAZINE-2,4-DIAMINE COMPOUNDS AS IDH2 MUTANTS INHIBITORS FOR THE TREATMENT OF CANCER

For PCT/US2014/046204 entitled N,6-BIS(ARYL OR HETEROARYL)-1,3,5-TRIAZINE-2,4-DIAMINE COMPOUNDS AS IDH2 MUTANTS INHIBITORS FOR THE TREATMENT OF CANCER

Nombro(amos) a: **JUAN PABLO CADENA SARMIENTO** y/o **MARTIN E. TORRES CARDOZO**, de Bogotá, Colombia, apoderados verdaderos y legales con poder especial, amplio y suficiente, para recabar de las oficinas y autoridades colombianas administrativas, judiciales y de policía, en cualquier instancia o recurso, la obtención de patentes de invención, registros de marcas, diseños industriales, modelos de utilidad, depósitos de nombres comerciales y enseñas, lemas comerciales, nombres comerciales, registros de derechos de autor y contratos sobre los mismos, obtención de certificados de obtentor de variedades vegetales, así como sus prórrogas, renovaciones, anotaciones de traspaso, cambios de nombre y/o domicilio y/o dirección; elaborar, tramitar y registrar contratos de licencia y licencias de cualesquiera clases; intervenir como demandante o como demandado en cualquier instancia y recurso ante cualquier juez, corporación, funcionario público o autoridad en acciones judiciales, administrativas y de policía tales como: oposiciones al registro de marcas; acciones de caducidad, cancelación y nulidad; acciones reivindicatorias, acciones derivadas de la obtención o explotación de licencias; acciones de competencia desleal; demandas penales; acciones de indemnización de perjuicios, reclamos y observaciones a solicitudes de patentes, diseños industriales, modelos de utilidad, en el ejercicio de medidas cautelares y en otras acciones o medidas similares.

Hereby appoints **JUAN PABLO CADENA SARMIENTO** and/or **MARTIN E. TORRES CARDOZO**, of Bogotá, Colombia, my (our) true and lawful attorneys with special, ample and sufficient power to obtain from the Colombian administrative, judicial and police offices and authorities, in any instance, privileges of patents of invention, registration of trademarks, industrial designs and utility models; registration of commercial names, slogans and emblems, registration of copyright and contracts related thereto, certificates of obtainers of vegetables varieties, as well as extensions, renewals and recordal of assignments and changes of name, domicile and address related to the above; to prepare, prosecute and register licenses of any kind; to act as plaintiff or defendant in any instance or recourse, and before any judge, corporation, public official or authority in judicial, administrative and police actions, such as: oppositions to the registration of trademarks; caducity, cancellation and nullity actions; claim actions derived from the obtaining or exploitation of licenses, action of unfair competition; criminal proceedings, actions for payment of damages: claims or observations on patent applications, models, industrial designs and utility models; in the exercise of preventive measures and in other actions or similar proceedings.

A este efecto, lo(s) faculto(amos) para elevar solicitudes, formular descripciones, enmiendas, protestas, declaraciones, oposiciones, cancelaciones, nulidades, apelaciones y reclamos; pagar impuestos, cuotas y gravámenes prescritos por la ley; renunciar o desistir a derechos concedidos o en curso de concesión; recibir toda clase de documentos y valores, dando el descargo respectivo, y, en general, para dar ante dichas autoridades todos los pasos necesarios al efecto indicado y tomar todas las medidas que creyeren conducentes al resguardo de mis

To that effect they hereby empowered to file applications, formulate descriptions, amendments, protests, declarations, oppositions, cancellations, nullities, appeals and claims; to pay taxes, quotas and assessments prescribed by law, renounce or waive the rights granted or in the process of granting; to receive all kinds of documents and values, giving the respective release of receipt, and, in general, to take before said authorities the necessary steps to such effect, and any measures that they may deem pertinent to the safeguard of my (our) interest(s) with all the other

COMMONWEALTH OF MASSACHUSETTS)

)

On this 20th day of January, 2016, before me, the undersigned Notary Public, personally appeared Min Wang, Ph.D., J.D., proved to me through satisfactory evidence of identification, which were was a drivers license to be the person whose name is signed on the preceding or attached document in my presence.

WITNESS my hand and notarial seal, this 20th day of January, 2016.

Katerina Belvin
Notary Public

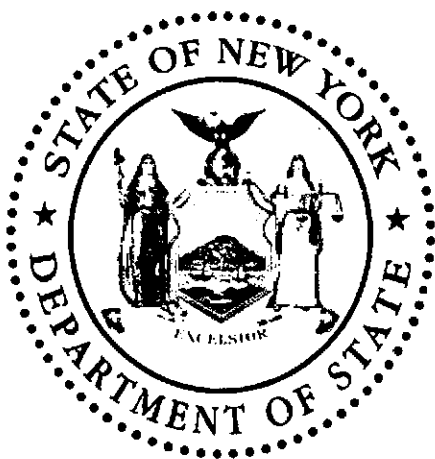
Apostille

(Convention de La Haye du 5 Octobre 1961)

1. Country: United States of America
This public document
2. has been signed by **Milton A. Tingling**
3. acting in the capacity of **County Clerk**
4. bears the seal/stamp of the **county of New York**

Certified

5. at New York City, New York
6. the 27th day of January 2016
7. by Special Deputy Secretary of State, State of New York
8. No. NYC-526155
9. Seal/Stamp
10. Signature



Whitney A. Clark

Whitney A. Clark
Special Deputy Secretary of State

State of New York }
County of New York } ss:

No. 181276

I, **Milton Adair Tingling**, Clerk of the County of New York, and Clerk of the Supreme Court in and for said county, the same being a court of record having a seal, **DO HEREBY CERTIFY THAT**

AMY LEWIS



whose name is subscribed to the annexed original instrument has been commissioned and qualified as a NOTARY PUBLIC.....
and has filed his/her original signature in this office and that he/she was at the time of taking such proof or acknowledgment or oath duly authorized by the laws of the State of New York to take the same: that he/she is well acquainted with the handwriting of such public officer or has compared the signature on the certificate of proof or acknowledgment or oath with the original signature filed in his/her office by such public officer and he/she believes that the signature on the original instrument is genuine.

IN WITNESS WHEREOF, I have hereunto set my hand and my official seal this
27th day of January, 2016

Milton Adair Tingling

County Clerk, New York County



12827-842-026

VERIFICATION

STATE OF NEW YORK)
) ss:
COUNTY OF NEW YORK)

I verify that the attached document identified as:

Assignment

is a copy of the document as executed on June 24, 2014 by Jeremy Travins and Luke Utley, to **AGIOS PHARMACEUTICALS, INC.** of United States and corresponding foreign rights in connection with U.S. Serial No. 61/845,352 filed July 11, 2013.

Corinne Zang
JONES DAY
International Patent
Applications Supervisor

Subscribed and sworn to before me this 12th day of
January, 2016.

Amy Lewis
Notary Public

AMY LEWIS
Notary Public, State of New York
No. 01LE6180070
Qualified in Kings County
Certificate Filed in New York County
Commission Expires Jan. 7, 2020

ASSIGNMENT

For good and valuable consideration, the sufficiency and receipt of which is hereby acknowledged, I, Jeremy Travins (Citizenship: United States), 14 Overlook Drive, Southborough, Massachusetts 01772, United States of America; Luke Utley (Citizenship: United States of America), 652 Rte. 13 S., Milford, New Hampshire 03055, United States of America hereby:

Sell, assign and transfer to Agios Pharmaceuticals, Inc., a Delaware corporation having a place of business at 38 Sidney Street, Cambridge, Massachusetts 02139, United States of America, its successors, assigns and legal representatives, all hereinafter referred to as said Assignee, the entire right, title and interest for the United States and all foreign countries, in and to any and all inventions which are disclosed in the International Application for Patent filed with the State Intellectual Property Office of the People's Republic of China as Receiving Office of the World Intellectual Property Organization in accordance with the Patent Cooperation Treaty (PCT) on

Filed _____

under International Application Serial No. _____

and

entitled THERAPEUTICALLY ACTIVE COMPOUNDS AND THEIR METHODS OF USE,

and in and to said application and all continuing, divisional, continuation-in-part, substitute, renewal, reissue and all other applications for Letters Patent which have been or shall be filed in the United States and all foreign countries on said any and all inventions (including without limitation U.S. Provisional Application No. 61/845352, filed July 11, 2013, and entitled THERAPEUTICALLY ACTIVE COMPOUNDS AND THEIR METHODS OF USE); and in and to all original and reissued patents which have been or shall be issued in the United States and all foreign countries on said any and all inventions including the right to apply for patent rights in each foreign country and all rights to priority; and further including any right to sue for past infringement;

Appoint, authorize and request the attorneys appointed in said application to hereafter complete this assignment by inserting in the spaces provided above the filing date and serial number of said application when known;

Agree that said Assignee may apply for and receive Letters Patent for said any and all inventions in its own name; and when requested, without charge to but at the expense of said Assignee, I agree to carry out in good faith the intent and purpose of this assignment, by executing all divisional, continuing, substitute, renewal, reissue, and all other patent applications on said any and all inventions, by executing all rightful oaths, assignments, powers of attorney and other papers, by communicating to said Assignee all facts known to me relating to said any and all inventions and the history thereof, and generally by doing everything reasonably possible which said Assignee shall consider desirable for aiding in securing and maintaining proper patent

protection for said any and all inventions and for vesting title to said any and all inventions and all applications for patents and all patents on said inventions, in said Assignee;

Request the Honorable Commissioner of Patents and Trademarks to issue said Letters Patent to said Assignee; and

Covenant with said Assignee that no assignment, grant, mortgage, license or other agreement affecting the rights and property herein conveyed has been made to others by me and that full right to convey the same as herein expressed is possessed by me.

Said Assignee does hereby acknowledge and accept the above sale, assignment and transfer of all the rights, title and interest enumerated above, including but not limited to the right to priority and the right to sue for past infringement.

In the event that the execution date, filing date and/or Application No. are not entered or are incorrect at the time Assignor(s) executed this document, Assignor(s) hereby authorize and request an attorney of Assignee to insert the information or make the correction.

THE ASSIGNOR

Jeremy M. Travins
Jeremy Travins

Given and signed in Cambridge, MA this 14th day of June 2014.

State of Massachusetts

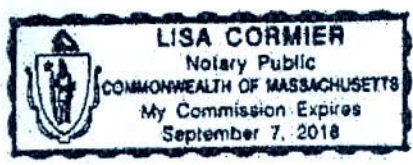
County of Middlesex

NOTARIAL CERTIFICATE

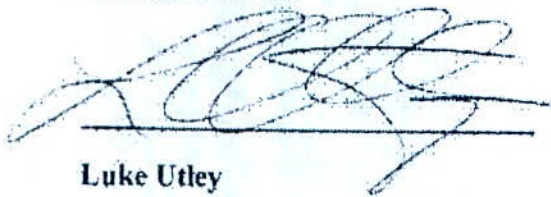
The foregoing instrument was acknowledged before me this 14th day of June, 2014, by **Jeremy Travins**. ✓ Personally known or Produced as identification.

Lisa Cormier
Notary Public

{Notary Seal}



THE ASSIGNOR



Luke Utley

Given and signed in Cambridge Ma this 24th day of June 2014.

State of Massachusetts

County of Middlesex

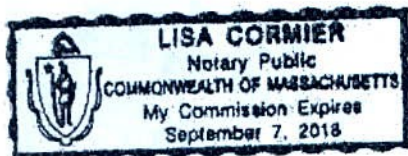
NOTARIAL CERTIFICATE

The foregoing instrument was acknowledged before me this 24th day of June, 2014, by **Luke Utley**. ✓ Personally known or
Produced _____ as identification.



Notary Public

{Notary Seal}



THE ASSIGNEE



Agiros Pharmaceutical, Inc.

Authorized Representative

By: **J. Duncan Higgons**

Title: **Chief Operating Officer**

Given and signed in Cambridge, MA this 24th day of June 2014.

NOTARIAL CERTIFICATE

On this 24th day of June of 2014, personally appeared before me J. Duncan Higgons, whose signature is authentic and was duly identified. Duly sworn he declared that he is the COO of Agiros Pharmaceuticals, Inc. I further certify that the person appearing before me is authorized to sign this document on behalf of this corporation, which according to the Charter and By Laws is a legally existing and duly organized corporation, as its duration term has not yet expired.



Notary Public

{Notary Seal}

