

Respuesta a Requerimientos

1	Datos del Solicitante				
Nombre:	MARGARITA CASTELLANOS ABONDANO		Dirección Electrónica:	sic@castellanosyco.co	
Dirección:	CALLE 94A 7A 09		Domicilio/País de constitución:	COLOMBIA - BOGOTA D.C. - BOGOTA D.C.	
Identificación: ☒ CEDULA DE CIUDADANIA ☐ EMPRESA EXTRANJERA ☐ PASAPORTE ☐ CEDULA DE EXTRANJERIA ☐ NIT Número: 39779654-					
2	Dato de la Creación				
Identificación de la Creación		No. de Certificado	Vigencia	No. de Expediente	Tipo Trámite
INHIBIDORES DE BROMODOMINIOS		000000		15245450	PCT-PATENTE DE INVENCION CAPITULOS I Y II
3	Texto de la Comunicación		Se anexa memorial de respuesta al examen de fondo oficio 15227, así como un nuevo pliego reivindicatorio conformado por 2 reivindicaciones y la notificación de otorgamiento para la solicitud US 13/828,285 expedida por la Oficina de Patentes y Marcas de los Estados Unidos.		
4	Anexos				

☒ Anexos



Señor
Director de la Dirección de Nuevas Creaciones
Superintendencia de Industria y Comercio
Ministerio de Comercio, Industria y Turismo
E. S. D.

Re.: Expediente No. **15 245450**
Solicitud de Patente PCT Entrada en Fase Nacional, para:
“6-METIL-7-OXO-6,7-DIHIDRO-1H-PIRROLO[2,3-D]PIRIDAZINAS INHIBIDORAS DE BROMODOMINIO” (nuevo título)
Solicitante: **ABBVIE INC.**

RESPUESTA A EXAMEN DE FONDO

Yo, **MARGARITA CASTELLANOS ABONDANO**, mayor de edad, identificada y domiciliada como aparece al pie de mi firma, obrando en mi calidad de apoderada de la sociedad solicitante del asunto citado en la referencia, en atención a su oficio No. **15277** notificado el **22 de diciembre de 2015** y para el cual solicité oportunamente prórroga el día **11 de marzo de 2016**, atentamente me permito dar respuesta al mismo de la siguiente manera:

1. Título

Indica el examinador indica que debe asignársele un nuevo título a la presente solicitud. Dicho título debe tener la precisión necesaria para identificar el objeto de la solicitud.

A fin de superar dicha objeción, el título de la presente solicitud se ha modificado por:

“6-METIL-7-OXO-6,7-DIHIDRO-1H-PIRROLO[2,3-D]PIRIDAZINAS INHIBIDORAS DE BROMODOMINIO”

2. Modificación a las Reivindicaciones

De acuerdo con lo establecido en el Artículo 34 de la Decisión 486 y en vista de las observaciones realizadas por el examinador, se presenta en esta oportunidad un nuevo pliego reivindicatorio conformado por 2 reivindicaciones, en donde se han realizado las siguientes modificaciones:

- El Examinador objeta las antiguas reivindicaciones 1, 3-14, 17-18 alegando que las definiciones de X¹, X², A¹, A², A³, A⁴, L¹ y G1 son generales. A fin de superar esta objeción, en el nuevo pliego reivindicatorio que se presenta en esta oportunidad, se han limitado los valores de estos grupos de acuerdo con lo ejemplificado.
 - El grupo X² se ha limitado y “X² es CR^{x2}; donde R^{x2} es hidrogeno”

- Con respecto a X^1 , como en muchos de los compuestos ejemplificados este grupo es un grupo carboxilo o carboxamida, se ha modificado de acuerdo con lo siguiente:

“ X^1 es CR^{x1} donde R^{x1} es hidrógeno, $C(O)OR^{ax1}$, o $C(O)NR^{bx1}R^{cx1}$; R^{ax1} , R^{bx1} , y R^{cx1} , en cada caso, son en forma independiente entre sí hidrógeno o C_1-C_6 alquilo”

- En vista de las modificaciones realizadas, en esta oportunidad no se incluyen las antiguas reivindicaciones 3 a 19.
- En lo que respecta a los valores de los grupos A^1 , A^2 , A^3 , A^4 , L^1 y G^1 se informa que los mismos se han definido de la misma manera que se realizó en la solicitud parental y por lo tanto comprenden una generalización razonable de los sustituyentes probados. Se considera que con la limitación que se ha introducido se supera la objeción planteada por el examinador. Adicionalmente, se hace notar que en la solicitud parental, el examinador había realizado la misma objeción y la modificación que se introdujo fue aceptada y la patente fue concedida.

Teniendo en cuenta lo anterior, es posible determinar que el pliego reivindicatorio es claro y conciso, cumpliendo así con los requerimientos del Artículo 30 de la Decisión 486.

Se solicita atentamente tener en cuenta este nuevo pliego reivindicatorio para el análisis de patentabilidad, toda vez que no implica una ampliación de la materia inicialmente solicitada y además permite superar las objeciones comunicadas por el examinador.

3. Nivel inventivo

El examinador objetó la falta de actividad inventiva del pliego de reivindicaciones de la presente invención con base en los documentos D1: US20020099055, así como el documento D2: WO2004006836.

En este sentido, se hace notar que ni el documento D1 ni el documento D2 mencionan que los compuestos revelados **tengan actividad contra bromodominios**. Es más, dichos documentos se alejan de las enseñanzas de la presente invención si se analiza el tema de la actividad biológica.

En primer lugar, sería imposible estimar la actividad de cada uno de los compuestos de D1 porque éste documento no aporta datos biológicos sino solo una afirmación general acerca de que:

“se encontró que los compuestos de los Ejemplos 1 a 57 exhibían un valor de AI_{50} de menos de $1 \times 10^{-6}M$ en la prueba anterior”.

Tampoco se alega que exista una conexión entre la inhibición de bromodominios y la inhibición de MLR (Human Mixed Lymphocyte Reaction), el mecanismo de acción que alega D1.

En segundo lugar, se alega que los compuestos de D2, con ciertas excepciones que muestran baja actividad inhibitoria, inhiben la unión a gabapentina a un nivel de 10 micromolar (es decir $1 \times 10^{-5}M$), o menos.

En forma similar los documentos D1 y D2 no contienen ninguna afirmación que indique que la inhibición de la unión a gabapentina tenga alguna conexión con la inhibición de bromodominios.

Además, aún si los documentos D1 y D2 pudieran de alguna manera extenderse para abarcar la divulgación de la presente invención, ya que ninguna de estas referencias divulga el problema técnico resuelto por las presentes reivindicaciones, es decir, el tratamiento del cáncer mediante la inhibición de bromodominios. Vale mencionar que la Guía para el Examen de Solicitudes de Patente de Invención y Modelo de Utilidad en su página 132:

“El estado de la técnica cercano es un documento que se encuentra en el mismo campo técnico que la invención o trata de solucionar el mismo problema o uno semejante. Suele ser el que tiene más características en común con la invención o presenta leves modificaciones de estructura e indica la misma función, propósito”.

[subrayado fuera del texto]

En vista de lo anterior se puede concluir que hay escasa evidencia en D1 y D2 que pueda llevar a una persona versada en la materia a:

(1) elegir un compuesto que tenga una estructura similar a la de los compuestos inventivos de la presente solicitud, dada la casi total falta de guía que dan D1 y D2 en este sentido, y

(2) modificar cualquiera de dichos compuestos para arribar a los compuestos inventivos de la presente solicitud teniendo en cuenta la falta de guía debido a la ausencia de datos de pruebas biológicas y la falta de conexión entre la inhibición de bromodominios y los distintos mecanismos de acción de los compuestos de D1 y D2.

Por todas estas razones, se considera que los compuestos que se reivindican son inventivos frente a la combinación de D1 y D2

Por último, aunque se comprende que existe un principio de soberanía según el cual cada oficina, dependiendo de su jurisdicción, puede otorgar o denegar solicitudes de patente, sí se considera que las patentes otorgadas en otros países y más aún en aquellos con los cuales Colombia ha firmado programas de PPH, constituyen un antecedente importante que demuestra el nivel inventivo de una solicitud.

Así, se llama la atención del Examinador sobre la solicitud Estadounidense equivalente No. US 13/828,285, la cual fue aceptada por la Oficina de Patentes y Marcas de los Estados Unidos con reivindicaciones esencialmente similares a las reivindicaciones que fueron presentadas originalmente en la solicitud PCT de la cual se basa la presente solicitud colombiana. Se acompaña una copia de la notificación de aceptación de dicha solicitud US para mejor referencia.

4. No pago del nuevo examen

De acuerdo con la Resolución 3719 de 2016 y teniendo en cuenta ésta es una solicitud divisional cuya mamá fue publicada en gaceta el 11 de agosto de 2014, los 18 meses para el pago y solicitud de un nuevo examen de patentabilidad ya han caducado. Por lo tanto, no se realiza el pago por un nuevo examen de patentabilidad. No obstante lo anterior, se solicita atentamente el estudio del nuevo pliego reivindicatorio, toda vez que este es una limitación del pliego presentado originalmente.

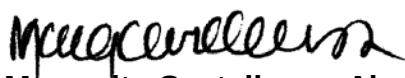
5. Conclusión

Teniendo en cuenta las modificaciones introducidas en esta oportunidad y los argumentos que se presentan, es posible establecer que las reivindicaciones cumplen con los requerimientos de la Decisión 486.

6. Anexos

- Nuevo pliego reivindicatorio conformado por dos (2) reivindicaciones.
- Notificación de otorgamiento para la solicitud US 13/828,285 expedida por la Oficina de Patentes y Marcas de los Estados Unidos.

Señor Director,



Margarita Castellanos Abondano

C.C. No. **39.779.654** de Bogotá

T.P.A. No. **70.819** del C.S.J.

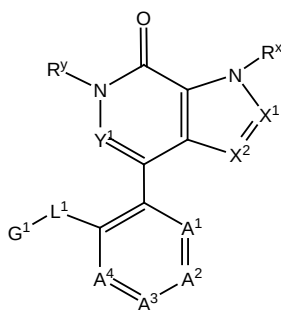
Calle 94A No. 7A-09 - Bogotá, D.C.

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Bogotá, D.C.
MCA/lt
P4225
RESPUESTA EXAMEN DE FONDO

REIVINDICACIONES MODIFICADAS CON LA RESPUESTA AL EXAMEN DE
FONDO OFICIO 15277 – EXPEDIENTE NO. 15 245450

1. Un compuesto CARACTERIZADO PORQUE es de fórmula (I) o una sal farmacéuticamente aceptable del mismo



(I)

donde

R^x es hidrógeno o C₁-C₃ alquilo;

R^y es metilo;

X^1 es CR^{x1} donde

R^{x1} es hidrógeno, -C(O)OR^{ax1}, o -C(O)NR^{bx1}R^{cx1};

R^{ax1} , R^{bx1} , y R^{cx1} , en cada caso, son en forma independiente entre sí hidrógeno o C₁-C₆ alquilo;

X^2 es CR^{x2}; donde

R^{x2} es hidrógeno;

Y^1 es N; y

A^1 es CR¹, A^2 es CR², A^3 es CR³; y A^4 es CR⁴; o uno de A^1 , A^2 , A^3 , y

A^4 es N;

R^1 , R^3 , y R^4 son en forma independiente entre sí hidrógeno, C₁-C₆ alquilo,

C₂-C₆ alqueno, C₂-C₆ alquino, halógeno, C₁-C₆ haloalquilo, CN, o NO₂;

R^2 es -S(O)₂R^{2d}, -S(O)₂NR^{2b}R^{2c}, -N(R^{2e})S(O)₂R^{2d}, o -N(R^{2e})S(O)₂NR^{2b}R^{2c};

R^{2b} , R^{2c} , y R^{2e} , en cada caso, son en forma independiente entre sí

hidrógeno, C₂-C₆ alqueno, C₂-C₆ alquino, C₁-C₆ haloalquilo, G^{2b}, o C₁-C₆ alquilo donde el C₁-C₆ alquilo no está sustituido o está sustituido con un sustituyente seleccionado entre el grupo que consiste en -OR^{z1}, NR^{z1}R^{z2}, -C(O)OR^{z1}, -C(O)NR^{z1}R^{z2}, -S(O)₂R^{z1}, -S(O)₂NR^{z1}R^{z2}, y G^{2b}; R^{2d}, en cada caso, es en forma independiente C₂-C₆ alqueno, C₂-C₆ alquino, C₁-C₆ haloalquilo, G^{2b}, o C₁-C₆ alquilo donde el C₁-C₆ alquilo no está sustituido o está sustituido con un sustituyente seleccionado entre el grupo que consiste en -OR^{z1}, NR^{z1}R^{z2}, -C(O)OR^{z1}, -C(O)NR^{z1}R^{z2}, -S(O)₂R^{z1}, -S(O)₂NR^{z1}R^{z2}, y G^{2b}; R^{z1} y R^{z2}, en cada caso, son en forma independiente entre sí hidrógeno, C₁-C₆ alquilo, o C₁-C₆ haloalquilo; G^{x1}, G^{x2}, G^a, G^b, G^{2a}, y G^{2b}, en cada caso, son en forma independiente entre sí C₆-C₁₄ arilo, heteroarilo, heterociclo, C₃-C₁₆ cicloalquilo, o C₄-C₁₆ cicloalqueno, y cada uno de los mismos no está sustituido o está sustituido en forma independiente con 1, 2, 3, 4, o 5 de R^v; L¹ se encuentra ausente, o es CH₂, C(O), C(H)(OH), (CH₂)_mO, (CH₂)_mS(O)_n donde n es 0, 1, o 2; o (CH₂)_mN(R^z) donde R^z es hidrógeno, C₁-C₃ alquilo, C₁-C₃ haloalquilo, (C₂-C₃ alquilenil)-OH, o ciclopropilo no sustituido; m es 0 o 1; G¹ es C₁-C₆ alquilo, C₁-C₁₀ alcoxi C₁-C₁₀ alquilo, G^{1a} o -(C₁-C₆ alquilenil)-G^{1a}; donde cada G^{1a} es en forma independiente C₆-C₁₄ arilo, heteroarilo, heterociclo, C₃-C₁₆ cicloalquilo, o C₄-C₁₆ cicloalqueno, y cada G^{1a} no está sustituido o está sustituido en forma independiente con 1, 2, 3, 4, o 5 de R^w; R^v y R^w, en cada caso, son en forma independiente entre sí C₁-C₆ alquilo,

C₂-C₆ alqueniilo, C₂-C₆ alquiniilo, halógeno, C₁-C₆ haloalquilo, -CN, oxo, -OR^h, -OC(O)Rⁱ, -OC(O)NR^jR^k, -SR^h, -S(O)₂R^h, -S(O)₂NR^jR^k, -C(O)R^h, -C(O)-heterociclo monocíclico, -C(O)-heteroarilo monocíclico, -C(O)OR^h, -C(O)NR^jR^k, -NR^jR^k, -N(R^h)C(O)Rⁱ, -N(R^h)S(O)₂Rⁱ, -N(R^h)C(O)O(Rⁱ), -N(R^h)C(O)NR^jR^k, -(C₁-C₆ alquilenil)-OR^h, -(C₁-C₆ alquilenil)-OC(O)Rⁱ, -(C₁-C₆ alquilenil)-OC(O)NR^jR^k, -(C₁-C₆ alquilenil)-S(O)₂R^h, -(C₁-C₆ alquilenil)-S(O)₂NR^jR^k, -(C₁-C₆ alquilenil)-C(O)R^h, -(C₁-C₆ alquilenil)-C(O)OR^h, -(C₁-C₆ alquilenil)-C(O)NR^jR^k, -(C₁-C₆ alquilenil)-NR^jR^k, -(C₁-C₆ alquilenil)-N(R^h)C(O)Rⁱ, -(C₁-C₆ alquilenil)-N(R^h)S(O)₂Rⁱ, -(C₁-C₆ alquilenil)-N(R^h)C(O)O(Rⁱ), -(C₁-C₆ alquilenil)-N(R^h)C(O)NR^jR^k, o -(C₁-C₆ alquilenil)-CN;

R^h, Rⁱ, R^k, en cada caso, son en forma independiente entre sí hidrógeno,

C₁-C₆ alquilo, o C₁-C₆ haloalquilo; y

R^j, en cada caso, es en forma independiente C₁-C₆ alquilo o C₁-C₆

haloalquilo;

en donde cada heteroarilo contiene 1-13 átomos de carbono y al menos un heteroátomo seleccionado entre oxígeno, nitrógeno y azufre, y no contiene más de 4 átomos de nitrógeno o 2 átomos de oxígeno o azufre por anillo heteroarilo;

en donde cada heterociclo tiene 3-16 átomos de carbono y al menos un heteroátomo seleccionado entre oxígeno, nitrógeno y azufre, y no contiene más de 3 átomos de oxígeno, nitrógeno o azufre por anillo heterociclo;

en donde cada heterociclo monocíclico contiene 3-8 átomos de carbono y al menos un heteroátomo seleccionado entre O, N y S, y no contiene más de 3 átomos de oxígeno, nitrógeno o azufre por anillo; y

en donde cada heteroarilo monocíclico es un anillo de 5 o 6 miembros que contiene al menos un heteroátomo seleccionado entre O, N y S, y no contiene más que cuatro átomos de nitrógeno o dos átomos de oxígeno o azufre.

2. Un compuesto o una sal farmacéuticamente aceptable del mismo, CARACTERIZADO PORQUE el compuesto se selecciona entre el grupo que consiste en:

4-(5-amino-2-fenoxifenil)-6-metil-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-2-carboxilato de etilo;

4-[5-(etilamino)-2-fenoxifenil]-6-metil-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-2-carboxilato de etilo;

4-{5-[etil(metilsulfonil)amino]-2-fenoxifenil}-6-metil-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-2-carboxilato de etilo;

ácido 6-metil-4-{5-[(metilsulfonil)amino]-2-fenoxifenil}-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-2-carboxílico;

6-metil-4-{5-[(metilsulfonil)amino]-2-fenoxifenil}-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-2-carboxamida;

6-metil-N-[2-(4-metilpiperazin-1-il)etil]-4-{5-[(metilsulfonil)amino]-2-fenoxifenil}-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-2-carboxamida;

N-[3-(6-metil-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-4-il)-4-fenoxifenil]metansulfonamida;

N-etil-6-metil-4-{5-[(metilsulfonil)amino]-2-fenoxifenil}-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-2-carboxamida;

6-metil-4-(2-fenoxifenil)-1,6-dihidro-7H-pirrolo[2,3-d]piridazin-7-ona;

N-etil-N,6-dimetil-4-{5-[(metilsulfonil)amino]-2-fenoxifenil}-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-2-carboxamida;

4-[5-amino-2-(2,4-difluorofenoxi)fenil]-6-metil-1,6-dihidro-7H-pirrolo[2,3-d]piridazin-7-ona;

N-[4-(2,4-difluorofenoxi)-3-(6-metil-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-4-il)fenil]metansulfonamida;

N-[4-(2,4-difluorofenoxi)-3-(6-metil-7-oxo-6,7-dihidro-1H-pirrolo[2,3-d]piridazin-4-il)fenil]etansulfonamida; y

4-[2-(ciclopropilmetoxi)-5-(etilsulfonil)fenil]-6-metil-1,6-dihidro-7H-pirrolo[2,3-d]piridazin-7-ona.



UNITED STATES PATENT AND TRADEMARK OFFICE

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NOTICE OF ALLOWANCE AND FEE(S) DUE

111504 7590 10/08/2015
ABBVIE INC.
1 North Waukegan Road
Dept. V377
North Chicago, IL 60064

EXAMINER

SHIAO, YIH-HORNG

ART UNIT

PAPER NUMBER

1672

DATE MAILED: 10/08/2015

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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13/828,285

03/14/2013

Le WANG

11389USC2

9524

TITLE OF INVENTION: BROMODOMAIN INHIBITORS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
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nonprovisional

UNDISCOUNTED

\$960

\$0

\$0

\$960

01/08/2016

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
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P.O. Box 1450
Alexandria, Virginia 22313-1450
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

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111504 7590 10/08/2015
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1 North Waukegan Road
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I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

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

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/828,285	03/14/2013	Le WANG	11389USC2	9524

TITLE OF INVENTION: BROMODOMAIN INHIBITORS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$960	\$0	\$0	\$960	01/08/2016

EXAMINER	ART UNIT	CLASS-SUBCLASS
SHIAO, YIH-HORNG	1672	514-210210

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363). ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached. ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.	2. For printing on the patent front page, list (1) The names of up to 3 registered patent attorneys or agents OR, alternatively, 1 _____ (2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 _____ 3 _____
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3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

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

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

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

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

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

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

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

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

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

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____
 Typed or printed name _____ Registration No. _____



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/828,285	03/14/2013	Le WANG	11389USC2	9524
111504	7590	10/08/2015	EXAMINER	
ABBVIE INC.			SHIAO, YIH-HORNG	
1 North Waukegan Road			ART UNIT	PAPER NUMBER
Dept. V377			1672	
North Chicago, IL 60064			DATE MAILED: 10/08/2015	

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

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

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

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

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

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

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

Privacy Act Statement

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

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

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

Notice of Allowability	Application No. 13/828,285	Applicant(s) WANG ET AL.	
	Examiner YIH-HORNG SHIAO	Art Unit 1672	AIA (First Inventor to File) Status No

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

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

1. ☒ This communication is responsive to RCE and Applicants' Arguments/Remarks filed on September 10, 2015.
☐ 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 1-55 and 65-70. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

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

Certified copies:
a) ☐ All b) ☐ Some *c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

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

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

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

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

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date <u>09-10-2015</u> 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material 4. ☒ Interview Summary (PTO-413), Paper No./Mail Date <u>09-30-2015</u> .	5. ☒ Examiner's Amendment/Comment 6. ☒ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____.
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/Y. S./ Examiner, Art Unit 1672	/Mark Shibuya/ Supervisory Patent Examiner, Art Unit 1674
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DETAILED ACTION

The present application is being examined under the pre-AIA first to invent provisions. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 10, 2015 has been entered.

Claims 56-64 are cancelled after Examiner's amendment. Claims 1-55 and 65-70 are currently under examination and allowed in this Office Action.

Priority

This application is a CON of PCT/CN2012/086357 filed on December 11, 2012 and is a CIP of PCT/CN2011/002224 filed on December 30, 2011 (the date 12/11/2012 is incorrectly entered in Bib Data Sheet).

Information Disclosure Statement

The information disclosure statement (IDS) filed on September 10, 2015 has been considered.

Withdrawn Objections/Rejections

The objection of claims 5, 16-54, and 65-70 because these claims depend from rejected claim 1, as set forth on pages 2 and 3 of the Final Rejection mailed on June 10, 2015, is *withdrawn* in view of allowed claim 1 (see Examiner's response below).

The rejection of claims 1-4, 6-15, and 55 under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Gilligan et al., as set forth on pages 4-7 of the Final Rejection mailed on June 10, 2015, is *withdrawn* in view of Applicants' Arguments/Remarks (page 5, 2nd paragraph). Applicants argue "it did not provide reasons for modifying the lead compound in a particular manner that would result in one of compounds of present claims 1-4, 6-15, and 55. The Federal Circuit in another post-*KSR* decision held that "in cases involving new chemical compounds, it remains necessary to identify **some reason** that would have led a chemist to **modify a known compound in a particular manner** to establish prima facie obviousness of a new claimed compound." See *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007) (emphasis added). The present application is indeed a case involving new chemical compounds, given the fact that no novelty-defeating prior art has been identified and applied against the present claims. However, no reasoning at all to modify the compounds of Gilligan '380 was provided in the Office Action dated June 10, 2015; instead, the Office Action dated June 10, 2015 states that the skilled artisan is "motivated to do so because the disclosure of Gilligan '380 suggests a compound of formula (I)..." without any reasoning to modify the compounds of Gilligan '380 in a particular manner". In response, this Examiner realizes that the motivation based on top ranking of functional groups as set forth in the Final Rejection mailed on June 10, 2015 provides reason to try but does not

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have guidance or reasonable expectation of success to modify specific carbon on aryl ring, such as L¹-G¹ group on carbon-2, as required by this instant application, and therefore agrees with Applicants' arguments.

Examiner's Amendment

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.

Authorization for this examiner's amendment was given in a telephone interview with Glen Gesicki on September 30, 2015.

The amended claims are listed below.

Previously withdrawn **claims 56-64 are cancelled.**

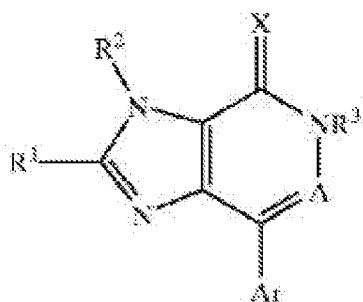
Allowable Subject Matter

The claims 1, 2, and 55 are allowed. Claims 3-54 and 65-70, depending from claim 1, are also allowed.

The following is an examiner's statement of reasons for allowance: The claims 1, 2, and 55, directed to a compound having the chemical structure of Formula I or a composition comprising the compound, are free of prior art rejection. The closest prior

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art is cited in the Final Rejection mailed on June 10, 2015, in which Gilligan et al. (US Patent No. 6,271,380, issued on August 07, 2001) disclosed a pharmaceutical composition comprising a compound of formula (1),



and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof, wherein:

X is O; A is N or CR⁹; Ar is phenyl, pyridyl, pyrimidinyl, or triazinyl, each Ar optionally substituted with 1 to 5 R⁴ groups and each Ar is attached via an unsaturated carbon atom; R¹ is independently H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₁-C₄ haloalkyl, or S(O)_nR¹²; R² is -H or -C₁-C₁₀ alkyl, R³ is C₁-C₄ alkyl or halo; R⁴ is independently C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl, NO₂, CN, C₁-C₄ haloalkyl, OR⁷; R⁷ is -C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, or C₃-C₆ cycloalkyl; R⁹ is independently H or C₁-C₄ alkyl; R¹² is C₁-C₄ alkyl or C₁-C₄ haloalkyl; and n is 2. The reference teaches “each Ar optionally substituted with 1 to 5 R⁴ groups” but did not teach or suggest specific modification on carbon-2 of aryl ring, as required in Formula I of this instant application. See also Applicants' arguments and Examiner's response in the **Withdrawn Objections/Rejections** section above.

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."

Conclusion

Claims 1-55 and 65-70 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to YIH-HORNG SHIAO whose telephone number is (571)272-7135. The examiner can normally be reached on Mon-Thur, 08:30 am to 07:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

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Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Y. S./

Examiner, Art Unit 1672

/Mark Shibuya/

Supervisory Patent Examiner, Art Unit 1674