

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 09-047482- -00005-0000

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Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIRECCION DE NUEVAS CREACIONES

E. _____ S. _____ D. _____

Ref.: Expediente No. 09-047.482

Solicitud de Patente de Invención titulada: "ANTICUERPOS AGONISTAS DEL
TRKB Y USOS DE LOS MISMOS"

Solicitante: IRM LLC

Nuestra Ref.: P2009/000077

RESPUESTA AL OFICIO N° 10548 NOTIFICADO

POR FIJACION EN LISTA No. 278, DE FECHA 11 DE SEPTIEMBRE DE 2009,

(EXAMEN DE FORMA)

CARLOS R. OLARTE, mayor de edad y vecino de Bogotá, identificado tal como aparece al pie de mi firma, en mi carácter de apoderado de las sociedades en referencia, me permito dar respuesta al auto proferido por ese Despacho, dentro del término legal previsto en el artículo 39 de la Decisión 486 en los siguientes términos:

1. En respuesta a la primera observación del Examinador, me permito aclarar que la presente solicitud entra en Fase Nacional Capítulo I y no Capítulo II como quedó señalado inicialmente, para tal efecto adjunto copia del Reporte Preliminar Internacional de Patentabilidad, el cual, valga la pena aclarar, no contiene anexos.

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2. En respuesta a la segunda observación del Examinador, me permito aportar junto al presente memorial dos (2) documentos de cesión debidamente legalizados, según los artículos 259 y 260 del CPC, en los que consta la cesión de tres (3) inventores al solicitante, junto con su correspondiente traducción, según lo previsto en el Art. 26-k de la Decisión 486.

Atentamente,



CARLOS R. OLARTE
CC. No. 79.782.747 de Bogotá
T.P. 74.295

Adjunto: Copia del Reporte Preliminar Internacional de Patentabilidad
Documentos de Cesión

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 P1275PC10	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2007/083774	International filing date (<i>day/month/year</i>) 06 November 2007 (06.11.2007)	Priority date (<i>day/month/year</i>) 09 November 2006 (09.11.2006)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant IRM LLC			

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 9 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 style="width: 100%; border: none;"> <tr> <td style="width: 10%; text-align: center;">☒</td> <td style="width: 30%;">Box No. I</td> <td style="width: 60%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;">☒</td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;">☐</td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;">☐</td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;">☒</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 style="text-align: center;">☒</td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;">☒</td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;">☐</td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	☒	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. VII	Certain defects in the international application																							
☐	Box No. VIII	Certain observations on the international application																							
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).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	<table style="width: 100%; border: none;"> <tr> <td style="width: 50%;">Date of issuance of this report 12 May 2009 (12.05.2009)</td> <td style="width: 50%;">Authorized officer Simin Baharlou</td> </tr> <tr> <td colspan="2">e-mail: pt09.pct@wipo.int</td> </tr> </table>	Date of issuance of this report 12 May 2009 (12.05.2009)	Authorized officer Simin Baharlou	e-mail: pt09.pct@wipo.int	
Date of issuance of this report 12 May 2009 (12.05.2009)	Authorized officer Simin Baharlou				
e-mail: pt09.pct@wipo.int					

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

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/US2007/083774

International filing date (day/month/year)
06.11.2007

Priority date (day/month/year)
09.11.2006

International Patent Classification (IPC) or both national classification and IPC
INV. C07K16/28 A61K39/395 A61P3/10

Applicant
IRM LLC

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 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

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 - P.B. 5818 Patentlaag 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Siaterli, Maria

Telephone No. +31 70 340-8922



WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2007/083774

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 and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ on paper
 - ☒ in electronic form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☒ furnished 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 and/or table relating thereto 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:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2007/083774

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:
see separate sheet

Box No. V Reasoned statement under Rule 43*bis*.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>6-9,12-14,16-25</u>
	No: Claims	<u>1-5,10-11,15</u>
Inventive step (IS)	Yes: Claims	<u>9,14</u>
	No: Claims	<u>1-8,10-13, 15-25</u>
Industrial applicability (IA)	Yes: Claims	<u>1-25</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)
and /or
2. Non-written disclosures (Rules 43*bis*.1 and 70.9)
see form 210

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2007/083774

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

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Re Item II Priority

The agonistic anti TrkB antibodies A10 & C20 were disclosed in the priority document. Thus, the priority is validly claimed and documents D5-D7 are not relevant to assess whether the claimed subject-matter satisfies the criteria of Art. 33 PCT.

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

1 REMARKS

1.1 Claims 18-25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv) / 67.1(iv) PCT. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

1.2 Reference is made to the following documents:

D1: Qian et al: "Novel agonist monoclonal antibodies activate TrkB receptors and demonstrate potent neurotrophic Activities" Journal of Neuroscience, vol. 26, no. 37, 2006-09-01, pages 9349-9403, XP009076184.

D2: Hanyu et al: "Brain-derived neurotrophic factor modulates glucagon secretion from pancreatic alpha cells: its contribution to glucose metabolism." Diabetes, Obesity & Metabolism, vol. 5, no. 1, 2003-01, pages 27-37, XP002487874.

D3: Tonra et al: "Brain-derived neurotrophic factor improves blood glucose control and alleviates fasting hyperglycemia in C57BLKS-Leprdb/leprdb mice" Diabetes, vol. 48, no. 3, 1999-03-01, pages 588-594, XP002210327.

D4: Ono et al: "Brain-derived neurotrophic factor reduces blood glucose level in obese diabetic mice but not in normal mice" Biochemical and Biophysical Research Communications, vol. 238, no. 2, 1997-01-01, pages 633-637, XP002933247.

2 NOVELTY

2.1 Document D1 describes agonistic anti TrkB monoclonal antibodies (results). The antibodies don't bind to TrkA or TrkC (§ bridging pages 9398-9399). Some were binding to LBD (page 9398, left-hand column, § 2). Thus, it anticipates the subject matter of claims 1-5, 10-11, 15 Article 33(2) PCT.

2.2 None of the available prior art discloses antibodies C20 and A10 neither the use of agonistic TrkB antibodies to reduce blood glucose levels and/or body weight. Thus, claims 6-9, 12-14, 16-25 are novel (Article 33(2) PCT).

3 INVENTIVE STEP

- 3.1 The document D2 disclosing the use of Brain derived neurotrophic factor (BDNF), a TrkB ligand in daily subcutaneous injections at 10mg/kg (page 30, left-hand column, § 1) to decrease fasting plasma glucose and to decrease food intake (page 33, right-hand column, § 2) is considered to the closest prior art.
- 3.2 The subject-matter of the claims differs from the disclosure of D2 in that anti TrkB agonistic antibodies are used instead of BDNF.
- 3.3 The problem to be solved by the present invention may therefore be regarded as the provision of alternative methods to reduce blood glucose level and/or body weight.
- 3.4 The solution proposed in the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:
- 3.5 Document D3 describes the use of Brain derived neurotrophic factor (BDNF), a TrkB ligand in daily subcutaneous injections to decrease fasting plasma glucose and to decrease food intake in a type II diabetic animal model (table 1).
- 3.6 Document D4 describes the use of Brain derived neurotrophic factor (BDNF), a TrkB ligand in daily subcutaneous injections to decrease fasting plasma glucose and to decrease food intake in a type II diabetic animal model. The administration of NT-3, another TrkB ligand has a similar effect to BDNF (figure 4A).
- 3.7 In the light of the disclosure of documents D2-D4, each one independently and aware of the agonistic anti TrkB antibodies of D1, the skilled person would consider to use alternative agonists of TrkB, namely anti TrkB agonistic antibodies without exerting inventive skills. Thus, claims 6, 16-24 are not inventive (Article 33(3) PCT).
- 3.8 Claims 7-8 & 12-13, 25 relate to antibodies which are structurally only defined by the CDRs. However, an antibody is structurally made of two light and two heavy chains and the combination of the heavy and light chain variable regions confers the antigen-binding specificity. Not only the CDRs, but also residues of the framework and the relative disposition of the CDRs determines the antigen-binding specificity (Article 6 PCT, see § 6-7). Hence, said claims are not solving the problem posed.
- 3.9 The combination of an anti TrkB agonistic antibody with a second agent effective in reducing blood glucose level and/or body weight (claims 20-23) is considered to be arbitrary since no unexpected effect is associated with the combined use.
- 3.10 However, in present application antibodies A10 (claim 14) & C20 (claim 9) are shown to reduce serum glucose concentration and increase body loss. Thus, although the prior art (D2-D4) teaches the use of TrkB agonists to reduce blood glucose level and/or body

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weight and anti TrkB agonistic antibodies were known (D1) the skilled person would not arrive to the specific antibodies A10 & C20 without exerting inventive skills. Thus, claims 9 & 14 are inventive in the sense of Article 33(3) PCT.

Re Item VI Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO2007088476 (D5)	09.08.2007	01.02.2007	02.02.2006
WO2007088479 (D6)	09.08.2007	29.01.2007	02.02.2006
WO2006133164 (D7)	14.12.2006	05.06.2006	06.06.2005

- 4 Although documents D5-D7 do not constitute prior art within the meaning of Rule 64.1(b) PCT, they appear to disclose all the features of claims 1-5, 15, 17-24. They might therefore be taken into consideration in the regional phase before EPO.

Re Item VII Certain defects in the international application

- 5 Claims 1-5, 10-11, do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The anti TrkB antibodies are defined in terms of function (agonist, binding/ not binding to..., competing or not with...). These functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated functions.
- 6 The present claims 7, 12, 16 & 25 relate to anti-TrkB antibodies which are structurally only defined by 2 CDRs (CDR 3 of VH and of VL). It is not sufficient to characterise an antibody with one of the CDR sequences since an antibody is structurally made of two light and two heavy chains and it needs at least 6 CDRs to confer antigen binding specificity. Unless the contrary is shown it is considered that 2 CDR's are neither equivalent to an antibody, nor sufficient to define the specificity of an antibody. Thus, claims 7, 12, 16 & 25 do not meet the requirement following from Art. 6 PCT taken in combination with Rule 6.3(b) PCT that the claims must contain all the technical features essential to the definition of the invention.
- 7 Claims 8 & 13 relate antibodies which are structurally only defined by the CDRs. However, an antibody is structurally made of two light and two heavy chains and the combination of the heavy and light chain variable regions confers the antigen-binding specificity. Not only the CDRs, but also residues of the framework and the relative disposition of the CDRs determines the antigen-binding specificity. Furthermore, the framework also influences the stability of the antibody. In general, simply combining the CDR sequences from one antibody with the framework sequence of a second one is not

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sufficient to retain antigen recognition. Thus, to define an antibody the full sequence of the heavy and light chain variable regions should be specified. Hence, claims 8 & 13 do not meet the requirements of Article 6 PCT.

09-077
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APOSTILLA

(Convención de La Haya del 5 de octubre de 1961)

1. País: ESTADOS UNIDOS DE AMERICA
2. Este documento público ha sido firmado por: **JOHN M. SHVETZ**
3. obrando en su condición de **Notario Público**
4. lleva el sello/estampilla de **JOHN M. SHVETZ** Notario Público Condado de MONTGOMERY, Estado de Pennsylvania

MINISTERIO DE
RELACIONES EXTERIORES
2009 AGO 14 9:24
JEFE DE LEGALIZACIONES
BOGOTA D.C.

CERTIFICADO

5. en Harrisburg, Pennsylvania
6. el **6 de mayo de 2009**
7. por: Pedro A. Cortés, Secretario de Estado, Estado de Pennsylvania.
8. No. **200920751**
9. Sello / Estampilla
[Sellado]
10. Firma: Pedro A. Cortés
[Firmado](por el Secretario de Estado).

NO SE ASUME
RESPONSABILIDAD
DEL LLANTO
949310
Noumea
Jefe de Legación
COSECHERÍA DE LA PENNA
ASFUNCIONES INDICADAS

Maurice Ur...
MAURICE UR
TRADUCTOR E INTERPRETE
INGLES - ESPAÑOL - ESPAÑOL - INGLÉS
RES. MINJUSTICIA 1780 - 1980

CESION**Los suscritos**

1. Yan WANG
2. Steven B. COHEN
3. Marc NASOFF

Domiciliado, respectivamente en

1. 844 Anbtoinette Lane, Apartment E, South San Francisco, California 94080 US
2. 4104 Via Candidiz No 89, San diego, Califronia 92130 US
3. PO. Box 1774, Rancho Sante Fe, California 92067 US

Por medio de la presente cedemos a

IRM LLC, Una sociedad organizada de conformidad con las leyes de Delaware, Estados Unidos de America, domiciliada en 131 Front Street, P.O. Box HM 2899, Hamilton, HM LX Bermuda, California, todos nuestros derechos, títulos e intereses sobre nuestro invento

ANTICUERPOS AGONISTAS TRKB Y SUS CONSECUENTES USOS

en lo que concierne a la República de Colombia.

Los cedentes y cesionarios firman este documento como prueba de la aceptación de la presente asignación.

FIRMA DE CEDENTES

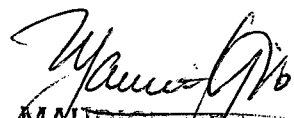
(Firma)

Yan WANG

29 de junio de 2009

FIRMA DE CEDENTE

Timothy L. Smith, J.D., Ph.D
Firma Autorizado
Y poder para IRM LLC
Fecha junio 30 de 2009


MAURICE DE
TRADUCTOR E INTERPRETE
INGLES - ESPAÑOL / ESPAÑOL - INGLÉS
RES. MINJUSTICIA 1790 - 1900

Estado de Pennsylvania

:SS

Condado de Montgomery:
Barrio de Lansdale

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El día 29 de Junio de 2009, ante mí, John M. Shevetz, el suscrito, compareció personalmente **YAN WANG** Pennsylvania Driver's Licencia No 29888667, quien (quien probó ante mí con evidencias satisfactorias) ser la persona cuyo nombre aparece suscrito en dicho documento.

ANTICUERPOS AGONISTAS TRKB Y SUS CONSECUENTES USOS

En constancia se firma y sella,

(firmado)

John M. Shvetz Notario Público
Barrio de Lansadle, Condado de Montgomery
Cuya comisión vence el 3 de febrero de 2013
(Sello)

CESION

Los suscritos

4. Yan WANG
5. Steven B. COHEN
6. Marc NASOFF

Domiciliado, respectivamente en

4. 844 Anbtoinette Lane, Apartment E, South San Francisco, California 94080 US
5. 4104 Via Candidiz No 89, San diego, California 92130 US
6. PO. Box 1774, Rancho Sante Fe, California 92067 US

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ANTICUERPOS AGONISTAS TRKB Y SUS CONSECUENTES USOS

en lo que concierne a la República de Colombia.

Yan Wang
MAJIDIC
TRADUCCION
INGLES - ESPAÑOL
C.R. MINJUSTICIA 1790 - 191

Mo

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

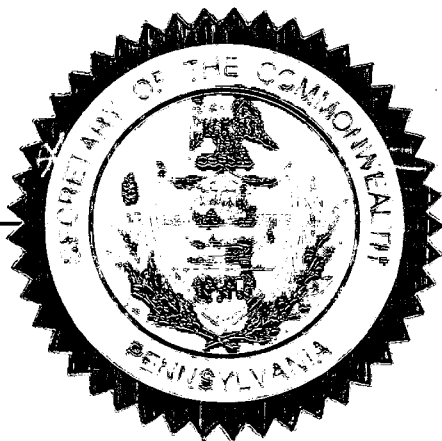
1. Country : United States of America
2. This public document has been signed by **JOHN M SHVETZ**
3. acting in the capacity of **NOTARY PUBLIC**
4. bears the seal/stamp **JOHN M SHVETZ , NOTARY PUBLIC, MONTGOMERY COUNTY, COMMONWEALTH OF PENNSYLVANIA**

Certified

5. at Harrisburg, Pennsylvania
6. The 6th day of July, 2009
7. by Pedro A. Cortés, Secretary of the Commonwealth of Pennsylvania
8. No: 200920751
9. Seal/Stamp
10. Signature

Pedro A. Cortés

Pedro A. Cortés



ASSIGNMENT DEED

The undersigned

1. Yan WANG
2. Steven B. COHEN
3. Marc NASOFF

domiciled, respectively, at

1. 844 Antoinette Lane, Apartment E, South San Francisco, California 94080 US
2. 4104 Via Candidiz #89, San Diego, California 92130 US
3. P.O. Box 1774, Rancho Santa Fe, California 92067 US

declare hereby that assign and transfer to

IRM LLC, organized under the laws of Delaware, United States of America, domiciled at 131 Front Street, P.O. Box HM 2899, Hamilton, HM LX Bermuda, all the rights which have or may have in and to patent application No. 09-044.589 filed on May 4, 2009 in so far as the Republic of Colombia is concerned.

The assignors and the assignee sign this document as proof of their acceptance of this assignment.

DOCUMENTO DE CESIÓN

Los suscritos, _____,
_____domiciliados, _____respectivamente, _____en
_____,

_____declaran por medio del presente documento que ceden y traspasan a la sociedad
_____, una compañía organizada bajo
las leyes de _____, domiciliada en
_____, todos y cada uno de los derechos que les
correspondan o puedan corresponderles sobre la solicitud de patente de invención
número _____presentada el _____,
en cuanto se refiere al territorio de la República de Colombia.

Los cedentes y la cesionaria firman este documento como prueba de la aceptación de esta cesión.

Signed at ~~San Diego, California, USA~~
Leansdale, Pennsylvania
on _____

Firmado en
_____el _____

SIGNATURE OF ASSIGNORS

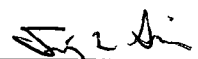
FIRMA DE LOS CEDENTES


Yan WANG Date 6/29/09

Steven B. COHEN Date

Marc NASOFF Date

SIGNATURE OF ASSIGNEE



Timothy L. Smith, J.D., Ph.D.
Authorized Signatory
and Power of Attorney for IRM LLC

Date: 6/30/09

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**Commonwealth of Pennsylvania }
County of Montgomery }
Borough of Lansdale }**

SS:

On this **29TH day of June 2009**, I, John M. Shvetz, before me, the undersigned officer, personally appeared **YAN WANG**, Pennsylvania driver's license # 29888667, who has satisfactorily proven to be the person named above, and who has admitted and agreed that she signed the attached documents relating to:

Agonist TRKB Antibodies and uses thereof P1275.

In witness whereof, I hereunto set my hand and official seal.





COMMONWEALTH OF PENNSYLVANIA
Notarial Seal
John M. Shvetz, Notary Public
Lansdale Boro, Montgomery County
My Commission Expires Feb. 3, 2013
Member, Pennsylvania Association of Notaries

Mh

3

09/77
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ESTADO DE CALIFORNIA
SECRETARIA DE ESTADO

Para usar en Colombia. Otros usos prohibidos

APOSTILLA

(Convención de La Haya del 5 de octubre de 1961)

1. País: ESTADOS UNIDOS DE AMERICA
2. Este documento público ha sido firmado por: **Jill R. Clarke**
3. obrando en su condición de **Notario Público Estado de California**
4. lleva el sello/estampilla de **Jill R. Clarke Notario Público Estado de California**

MINISTERIO DE
RELACIONES EXTERIORES
2009 AGO 11 A 9:24
JEFF D. REED
BOOIE D.C.

CERTIFICADO

5. en Sacramento California
 6. El **26 de junio de 2009**
 7. por: Deputy, Secretario de Estado, Estado de California
 8. No. **695431**
 9. Sello / Estampilla
 10. Firma:
- [Sellado] [Firmado](por el Secretario de Estado).

949311
Marcie Vinago
NOTARIO PUBLICO
ESTADO DE CALIFORNIA
ASISTENTE
DEL ESTADO
NO SE ASUME
RESPONSABILIDAD
DEL ESTADO

Estado de California :ss
Condado de San Diego:

El día 22 de junio de 2009, ante mí, Jill R, Clarke, el suscrito notario publico, compareció personalmente Steven B. COHEN y Marc NASOFF (quien probó ante mí con evidencias satisfactorias) ser la(s) persona(s) cuyo nombre(s) aparece suscrito en dicho documento y quien reconoció ante mí que suscribió el mismo en su condición autorizada, y que con su firma en el instrumento la persona o la entidad en cuyo nombre dicha persona actuó suscribió el instrumento.

[Signature]
Jill R. Clarke
Notario Público
Estado de California
1790 - 1966

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Yo certifico bajo la PENALIDAD DE PERJURIO y bajo las leyes del Estado de California que el párrafo anterior es verdadero y correcto.

En constancia se firma y sella,

(firmado) Gin R. Clarke
Comisión número 1847215
Notario Público, Estado de California
Condado de San Diego
Cuya comisión vence el 1 de mayo de 2013
(Sello)


MAURICE URREGO V.
DUCTOR E INTERPRETE OFICIAL
ESPAÑOL - ESPAÑOL - INGLÉS
INJUSTICIA 1790 - 1982

146

P12750010 21
09/77

ASSIGNMENT DEED

The undersigned

1. Yan WANG
2. Steven B. COHEN
3. Marc NASOFF

domiciled, respectively, at

1. 844 Antoinette Lane, Apartment E, South San Francisco, California 94080 US
2. 4104 Via Candidiz #89, San Diego, California 92130 US
3. P.O. Box 1774, Rancho Santa Fe, California 92067 US

declare hereby that assign and transfer to

IRM LLC, organized under the laws of Delaware, United States of America, domiciled at 131 Front Street, P.O. Box HM 2899, Hamilton, HM LX Bermuda, all the rights which have or may have in and to patent application No. 09-044.589 filed on May 4, 2009 in so far as the Republic of Colombia is concerned.

The assignors and the assignee sign this document as proof of their acceptance of this assignment.

DOCUMENTO DE CESIÓN

Los suscritos, _____,
_____domiciliados, _____respectivamente, _____en
_____,

_____declaran por medio del presente documento que ceden y traspasan a la sociedad
_____, una compañía organizada bajo
las leyes de _____, domiciliada en
_____, todos y cada uno de los derechos que les
correspondan o puedan corresponderles sobre la solicitud de patente de invención
número _____presentada el _____,
en cuanto se refiere al territorio de la República de Colombia.

Los cedentes y la cesionaria firman este documento como prueba de la aceptación de esta cesión.

Signed at San Diego, California, USA Firmado en

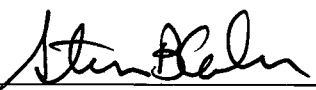
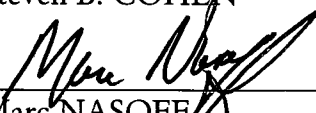
on el

148

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SIGNATURE OF ASSIGNORS

FIRMA DE LOS CEDENTES

Yan WANG	Date
	6-22-09
Steven B. COHEN	Date
	6/22/2009
Marc NASOFF	Date

SIGNATURE OF ASSIGNEE



Timothy L. Smith, J.D., Ph.D.
Authorized Signatory
and Power of Attorney for IRM LLC

Date: 6/22/09

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State of California

SECRETARY OF STATE

Requested for use in Colombia.

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APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: *United States of America*
This public document
2. *has been signed by Jill R. Clarke*
3. *acting in the capacity of Notary Public, State of California*
4. *bears the seal/stamp of Jill R. Clarke, Notary Public,*
State of California

CERTIFIED

5. *At Sacramento, California*
6. *the 26th day of June 2009*
7. *by Deputy Secretary of State, State of California*
8. *No. 695431*
9. *Seal/Stamp:*



10. Signature

Jeha Bowen
Secretary of State

BY

B. R.



CALIFORNIA ALL-PURPOSE ACKNOWLEDGMENT

State of California

County of San Diego

On June 22, 2009 before me, Jill R. Clarke, Notary Public

Date

Here Insert Name and Title of the Officer

personally appeared Steven B. Cohen and Mark Nasoff

Name(s) of Signer(s)



who proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within instrument and acknowledged to me that he/she/they executed the same in his/her/their authorized capacity(ies), and that by his/her/their signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the foregoing paragraph is true and correct.

WITNESS my hand and official seal.

Place Notary Seal Above

Signature Jill R. Clarke
Signature of Notary Public

OPTIONAL

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- ☐ Corporate Officer — Title(s): _____
- ☐ Partner — ☐ Limited ☐ General
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