**Señor**

**SUPERINTENDENTE DE INDUSTRIA Y COMERCIO**

**E. S. D.**

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**REF:** **Expediente No. PCT/13-046124**

**TÍTULO SOLICITADO:** **"ANTICUERPO ANTI-VEGFR-3"**

**PUBLICACIÓN:** **Gaceta 669 del 17/06/2013, Nº de publicación 754.**

**SOLICITANTE:** **IMCLONE LLC.**

**APODERADO:** **CARLOS REINALDO OLARTE GARCÍA.**

**TRÁMITE:** **Recurso de Reposición y en subsidio el de apelación en contra de la Resolución 39054 de julio 30 de 2015 por la cual se concede una patente de invención tramitada bajo el número de expediente PCT/13-046124.**

**TITO NOÉ PARRA MURILLO**, mayor de edad, identificado como aparece al pie de mi firma, reconocido apoderado de la sociedad **LAFRANCOL S.A.S.** en el asunto de la referencia, de manera respetuosa, y dentro de los términos de ley, presento **Recurso de Reposición y en subsidio de apelación** contra la Resolución 39054 de julio 30 de 2015 por la cual se concedió a la solicitud PCT/13-046124 el privilegio de patente de invención.

## I. PETICIÓN

Sírvase, Señor Superintendente, reponer íntegramente la Resolución 39054 de julio 30 de 2015, por la cual se declaró infundada la oposición presentada y se otorgó el privilegio de patente solicitado en el expediente de la referencia, y en su remplazo emitir otra que, con

fundamento en los argumentos expuestos en el escrito de observación y en el presente escrito, declare fundada dicha oposición y niegue el privilegio de patente mencionado, procediendo luego al definitivo archivo del expediente en cuestión.

## II. ARGUMENTOS SOBRE LOS FUNDAMENTOS DE LA CONCESIÓN Y MOTIVOS DE INCONFORMIDAD

La Resolución 39054 de julio 30 de 2015, que concede el privilegio de patente de invención solicitado para el capítulo reivindicatorio del expediente 13-046124 del título de referencia, viola flagrantemente la Decisión 486 si se tiene en cuenta que existían motivos suficientes para afectar los requisitos de novedad y nivel inventivo de la solicitud en mención. Es evidente que el solicitante y la Resolución cometen un error cuando afirman que la oposición presentada por mi representada no muestra ningún tipo de argumento soportado técnicamente, ni desvirtúa la patentabilidad del objeto de estudio, declarándola infundada por cuanto, al momento de presentación del escrito de oposición se dejó en claro que para el presente caso nos encontramos frente a una combinación de compuestos, lo cual indudablemente afecta el requisito de nivel inventivo, éste mismo indispensable para acceder a cualquier beneficio patentario.

Así las cosas, me permito reiterar que la concesión de patente objeto del presente escrito se ve afectada por los documentos del estado del arte que fueron presentados inicialmente en el escrito de observación, por lo cual, basado en lo siguiente, solicito respetuosamente a ese Despacho dar análisis completo y a cabalidad sobre los siguientes documentos, los cuales sin lugar a dudas objetan la concesión en mención, toda vez que develan de manera expresa y sucinta lo que se pretende proteger en la presente solicitud.

También es necesario reiterar que la solicitud de la referencia pretende proteger mediante el derecho patentario objetos que no son considerados invenciones. Es claro que una invención es toda creación humana que permita transformar la materia o energía que existe en la naturaleza, para su aprovechamiento por los seres humanos y satisfacer sus necesidades concretas. De igual modo, como ya se mencionó, según los parámetros de la Decisión 486 y normas concordantes, serán patentables las invenciones que cumplan con los requisitos de novedad, nivel inventivo y aplicación industrial. No obstante, puede observarse que la solicitud en comento pretende reivindicar combinaciones, las cuales no se consideran invenciones. En este sentido, la mezcla (Combinaciones) de productos (Moléculas) conocidos y su variación, bien sea en uso, forma, dimensión o de materia, NO

se consideran invenciones por cuanto no son susceptibles de aplicación industrial, nivel inventivo y novedad, luego NO pueden acceder a beneficios patentarios. Por lo tanto, se suma una circunstancia más que imposibilita definitivamente la concesión de la solicitud en mención.

Y sobre el particular, es imprescindible señalar que un efecto sinérgico nuevo no se considera inventivo como tal, dado que puede ser obvio para una persona versada en la materia, cosa que sucede en el presente caso. En palabras del Doctor Carlos Correa, "*El efecto sinérgico entre dos o más drogas se puede considerar un "descubrimiento" y no una "invención", dado que la sinergia ocurre en el cuerpo y se descubre a través de ensayos clínicos. Asimismo, cabe destacar que, en algunos casos, las reivindicaciones de combinaciones pueden equivaler, en términos prácticos, a reivindicaciones sobre tratamientos médicos (cuya patentabilidad está excluida en la mayoría de los países), cuando sólo brindan un método para administrar una combinación de drogas conocidas. Asimismo, la combinación de drogas para evitar la resistencia particular a una de ellas es una práctica normal en el desarrollo farmacéutico y, por lo general, es evidente para el hombre del oficio de nivel medio*" (Pautas para el examen de patentes farmacéuticas, CEIDIE, Pág. 8). En estos términos, está claro que nos encontramos frente a un tema totalmente sensible que merece toda la evaluación por cuanto las combinaciones deben considerarse excluidas de beneficios de patente.

Y en caso que ese Despacho decidiere insistir en el cabal cumplimiento de los requisitos exigidos para acceder al beneficio de patente, me permito allegar copia del International Search Report y el respectivo Written Opinion Of The International Searching Authority, documentos en los cuales se resalta que la presente invención no cumple con los requisitos de novedad y nivel inventivo por cuanto existen documentos citados del estado del arte que afectan de manera definitiva tales exigencias. Lo anterior deja entrever, sin lugar a equívocos, que la presente solicitud no debió ser concedida, por lo cual es procedente la revocatoria de la Resolución objeto de este escrito.

En este sentido, reitero con el debido respeto la necesidad de analizar a profundidad los requisitos de novedad y nivel inventivo para así determinar si la presente solicitud es merecedora de concesión de privilegio de patente.

**ANEXOS**

International Search Report y el Written Opinion Of The International Searching Authority de la equivalente internacional WO 2012/033696

**En subsidio apelo.**

Señor Superintendente,

**TITO NOÉ PARRA MURILLO**
C.C. 79.579.680 de Bogotá
T.P. 71168 del C. S de la J.

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference<br>X18726 | **FOR FURTHER ACTION** | see Form PCT/ISA/220 as well as, where applicable, item 5 below. |
|---|---|---|
| International application No.<br>PCT/US2011/050131 | International filing date *(day/month/year)*<br>01/09/2011 | (Earliest) Priority Date *(day/month/year)*<br>07/09/2010 |
| Applicant<br>IMCLONE LLC | | |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] 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))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [X] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2011/050131

**Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. (means)

   [ ] on paper

   [X] in electronic form

   b. (time)

   [X] in the international application as filed

   [ ] together with the international application in electronic form

   [ ] subsequently to this Authority for the purpose of search

2. [ ] 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.

3. Additional comments:

# INTERNATIONAL SEARCH REPORT

International application No
PCT/US2011/050131

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, Sequence Search, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | K. PERSAUD: "Involvement of the VEGF receptor 3 in tubular morphogenesis demonstrated with a human anti-human VEGFR-3 monoclonal antibody that antagonizes receptor activation by VEGF-C", JOURNAL OF CELL SCIENCE, vol. 117, no. 13, 1 June 2004 (2004-06-01) , pages 2745-2756, XP55010516, ISSN: 0021-9533, DOI: 10.1242/jcs.01138 the whole document<br>-----<br>-/-- | 1-15 |

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 26 October 2011 | 08/11/2011 |

| Name and mailing address of the ISA/ | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016 | Aguilera, Miguel |

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## INTERNATIONAL SEARCH REPORT

International application No
PCT/US2011/050131

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | B. PYTOWSKI ET AL: "Complete and Specific Inhibition of Adult Lymphatic Regeneration by a Novel VEGFR-3 Neutralizing Antibody", JNCI JOURNAL OF THE NATIONAL CANCER INSTITUTE, vol. 97, no. 1, 4 January 2005 (2005-01-04), pages 14-21, XP55010514, ISSN: 0027-8874, DOI: 10.1093/jnci/dji003 the whole document<br>---- | 1-15 |
| A | WO 02/060950 A2 (LUDWIG INST CANCER RES [US]; LICENTIA LTD [FI]; ALITALO KARI [FI]; APR) 8 August 2002 (2002-08-08) examples 25-32<br>---- | 1-15 |

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2011/050131

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| WO 02060950 A2 | 08-08-2002 | AT 359300 T | 15-05-2007 |
| | | CA 2435503 A1 | 08-08-2002 |
| | | CN 1494552 A | 05-05-2004 |
| | | DE 60219419 T2 | 16-08-2007 |
| | | EP 1353952 A2 | 22-10-2003 |
| | | JP 4669984 B2 | 13-04-2011 |
| | | JP 2004532004 A | 21-10-2004 |
| | | JP 2010088433 A | 22-04-2010 |
| | | NO 20033285 A | 19-09-2003 |
| | | US 2006177901 A1 | 10-08-2006 |

# PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

# PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.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. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/US2011/050131 | 01.09.2011 | 07.09.2010 |

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

Applicant
IMCLONE 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 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

   If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(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: | Date of completion of this opinion | Authorized Officer |
|---|---|---|
| European Patent Office<br>P.B. 5818 Patentlaan 2<br>NL-2280 HV Rijswijk - Pays Bas<br>Tel. +31 70 340 - 2040<br>Fax: +31 70 340 - 3016 | see form PCT/ISA/210 | Aguilera, Miguel<br>Telephone No. +31 70 340-3897 |

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2011/050131

**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:

   a. (means)

      ☐ on paper

      ☒ in electronic form

   b. (time)

      ☒ in the international application as filed

      ☐ together with the international application in electronic form

      ☐ subsequently to this Authority for the purposes of search

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

**Box No. 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:

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2011/050131

**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 | 1-15 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-15 |
| Industrial applicability (IA) | Yes: | Claims | 1-15 |
| | No: | Claims | |

2. Citations and explanations

**see separate sheet**

**Box No. VIII Certain observations on the international application**

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

**see separate sheet**

## V. Reasoned statement (Continuation)

1 NOVELTY (Art. 33(2) PCT)

No antibodies were found in the prior art comprising the 6 CDR's listed in claim 1 (see also below, Clarity). Therefore, claims 1-15 are new.

2 INVENTIVE STEP (Art. 33(3) PCT)

2.1 Document D1 (Persaud et al., 2004) is considered to represent the most relevant state of the art and discloses a human antibody specifically binding to human VEGFR-3. The antibody, identified as 3C5, shows a number of properties and parameters *surprisingly identical* to the antibody of claim 1, for example:

- It strongly blocks the binding of a soluble form of the receptor, sR3-AP, to immobilized VEGF-C with an $IC_{50}$ of 2 nM for the Fab form and 1.3 nM for the IgG form (page 2749, column 1).
- It shows a Kd of 56 pM for sR3-AP (page 2749, column 1).
- It strongly inhibits the mitogenic response stimulated by VEGF-C in a cell system expressing a fusion of VEGFR-3 and cFMS, with an $IC_{50}$ of 5nm. (page 2749, column 2).

2.2 The subject-matter of claim 1 differs in that the antibody comprises the 6 CDR's defined by SEQ ID NOs: 1-3 and 6-8. Since no technical effect appears associated to this difference, the problem solved by the subject-matter of claim 1 is regarded as the provision of an alternative antibody having said properties and parameters. The solution would be the antibody comprising the 6 CDR's defined by SEQ ID NOs: 1-3 and 6-8.

2.3 This solution cannot however be considered as involving an inventive step because the provision of further antibodies for a known target is the inevitable result of routine screening methods known to the skilled person.

2.4 The same reasoning applies *mutatis mutandis* to the pharmaceutical compositions and medicaments of claims 11-13 (see also below, Clarity).

2.5 The medical use of said antibody in claim 14 does not introduce any inventive feature either, since anti-VEGFR-3 antibodies are well known anti-tumour drug candidates. All the documents cited in the search report are explicit in this sense.

2.6 Dependent claims do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step, because they either fall under the scope of routine experimental design and optimization (claims 2-4) or merely recite features which are implicit to the 6-CDR combination of the independent claim (claims 5-10).

2.7 Therefore, claims 1-15 do not involve an inventive step.

**VIII. Certain Observations** (Continuation)

1 Both LCDR1 and LCDR2 are identified in claim 1 by SEQ ID NO: 2. However, this does not make sense in biological terms and is not supported by the description (Article 84 EPC). Considering the logical consecutive numbering of CDR sequences and the passage on page 6, line 3, this seems to be a typographical error which should be corrected. For the purpose of this opinion, LCDR1 is considered to have SEQ ID NO: 1.

2 Since the treatment of a particular disease is not recited, claim 13 is interpreted as a mere product claim directed to an antibody having the six defined CDR's and being *suitable to be used as* a medicament, and not as a (medical) use claim.