



No. 10-143959- -00016-0000

Fecha: 2013-06-28 14:38:12 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 412 REPOSPRESRECU Folios: 9

Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

E.

S.

D.

REF: Expediente No. PCT/10-143959

TÍTULO SOLICITADO: "DERIVADOS DEL ÁCIDO OLEANÓLICO CON
AMINO Y OTRAS MODIFICACIONES EN C-17,
COMO AGENTES ANTIOXIDANTES
MODULADORES DE LA INFLAMACIÓN"

PUBLICACIÓN: Gaceta 631 del 22/08/2011, N° de publicación 1071.

SOLICITANTE: REATA PHARMACEUTICALS INC.

APODERADO: DILIA MARÍA RODRÍGUEZ D'ALEMAN.

TRÁMITE: Recurso de Reposición y en subsidio el de apelación en
contra de la Resolución 27355 de mayo 10 de 2013 por la
cual se concede una patente de invención tramitada bajo
el número de expediente PCT/10-143959.

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 27355 de mayo 10 de 2013
por la cual se concedió a la solicitud PCT/10-143959 el privilegio de patente de invención.

I. PETICIÓN

Sírvase, Señor Superintendente, reponer íntegramente la Resolución 27355 de mayo 10 de
2013, 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 27355 de mayo 10 de 2013, que concede el privilegio de patente de invención solicitado para el capítulo reivindicatorio del expediente 10-143959 titulado **“Derivados del ácido oleanólico con amino y otras modificaciones en c-17, como agentes antioxidantes moduladores de la inflamación”**, 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.

Dicho así, me permito manifestar que agentes tales como Atorvastatina, Rosuvastatina, Imatinib, Cetuximab, Metropolol, entre otros, han sido ampliamente divulgados en el sector químico-farmacéutico, y concretamente se han develado materias muy similares, las cuales ruego a ese Despacho analizar, en los siguientes documentos:

- EP 409281
- US 5273995
- EP 521471
- US 5260440

- EP 564409
- US 5521184
- WO 9640210
- DE 2106209
- US 3998790

Así como resulta imprescindible manifestar que los anteriores documentos deben ser analizados a profundidad y cabalidad para así determinar finalmente si afectan o no la novedad y nivel inventivo de la presente solicitud, toda vez que en nuestra opinión se revelan materias muy similares, 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,

4

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 adicionalmente se encontró que la concesión que motivó el presente escrito también patenta métodos de tratamiento, los cuales están expresamente excluidos de las materias patentables.

Y en caso que ese Despacho decidiera 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

- 1- International Search Report y el Written Opinion Of The International Searching Authority de la equivalente internacional WO 2009/129546.

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

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

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

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

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

FOR FURTHER ACTION
See paragraph 2 below

International application No. PCT/US2009/041172	International filing date (day/month/year) 20.04.2009	Priority date (day/month/year) 18.04.2008
--	--	--

International Patent Classification (IPC) or both national classification and IPC
INV. A61K31/56 C07J63/00 A61P25/28 A61P35/00

Applicant
Reata Pharmaceuticals, Inc.

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

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step 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 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Tabanella, Stefania Telephone No. +31 70 340-9503 
---	---	---

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2009/041172

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/US2009/041172

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

1. Statement

Novelty (N)	Yes: Claims	<u>1-264</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-264</u>
Industrial applicability (IA)	Yes: Claims	<u>1-264</u>
	No: Claims	

2. Citations and explanations

see separate sheet

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

Box No. VIII Certain observations on the international application

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

see separate sheet

Re Item V.

- 1 Reference is made to the following document:
D1 : SUN, H. ET AL.: BOTANICAL STUDIES, vol. 47, 2006, pages 339-368,
XP008108435
- 2 The present application concerns oleanoic acid derivatives which are inhibitors of nitric oxide production and as such are active for the treatment of diseases associated with oxidative stress and inflammation.
- 3 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-264 does not involve an inventive step in the sense of Article 33(3) PCT.
 - 3.1 Document D1 is regarded as closest prior art. It also discloses oleanoic acid derivatives and their use as medicaments. The difference between D1 and the present application lies in the nature of the compounds disclosed. The effect associated with this difference is unknown. The remaining objective problem underlying the present application is therefore identified with the provision of alternative derivatives of oleanoic acid for the treatment of diseases associated with oxidative stress and inflammation. D1 reports the activity as NO inhibitors of a series of compounds and their use for the treatment of cancer. The most active one is compound 115 (Table 6). Such compound differs from the ones described in the present application in the nature of group Y which in compound 115 is (C=O)OMe whereas in the compounds of the application can be, among others, acyloxy, i.e. O(C=O)R. Clearly this structural difference is so small that the man skilled in the art would expect that the compounds of the application would possess the same activity of 115. Therefore no inventive step can be acknowledged for the subject-matter of claims 1-264. Moreover the applicant has claimed a very broad range of compounds whereas biological data have been provided for a limited number of molecules which share the same substitution pattern consisting of a carbonyl groups in position 3 and 12, double bonds between C₂-C₁ and C₉-C₁₁, methyl groups in position 4 and 20 and a bond between C₁₇ and nitrogen. Of all the compounds included in the definition of claim 1 activity is shown only for a very limited group. It is therefore doubtful that such activity is possessed over the entire claimed range.

- 4 Claims 175-257 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.

Re Item VII.

- 5 The vague and imprecise statements in the description such as on pp. 42 and 130 (spirit and scope) and on pp. 1, 2, 103 and 131 ('incorporated by reference') imply that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.
- 6 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1. is not mentioned in the description, nor is this document identified therein.

Re Item VIII.

- 7 The application does not meet the requirements of Article 6 PCT, because claims 1-10, 45, 46, 48, 50, 51, 54, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 126, 127, 134-136, 143, 144, 146, 148, 150, 152, 159, 161 are not clear.
- 7.1 The relative term 'substantially' used for example in claims 46, 48, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 135, 143, 146, 148, 150, 152 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear, Article 6 PCT.
- 7.2 Although claims 1, 126, 127, 136 and 144 have been drafted as separate

independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

- 7.3 Claims 1-10, 45 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. By using the expression 'convertible in vivo to hydrogen' and 'prodrug' the claims attempts to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.
- 7.4 Claims 1-10, 127, 136, 144, 159 and 161 do not meet the requirements of Article 6 PCT in that it is not specified to which group the 'ester' moiety should be attached.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference REAT: 029WO	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, Item 5 below.	
International application No. PCT/US2009/041172	International filing date (day/month/year) 20/04/2009	(Earliest) Priority Date (day/month/year) 18/04/2008
Applicant Reata Pharmaceuticals, Inc.		

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 3 sheets.

☒ 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:

- ☒ 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 43.6b/s(a)).

c. ☒ 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**,

- ☒ 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**,

- ☒ 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/US2009/041172

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b 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. 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 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/US2009/041172

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/56 C07J63/00 A61P25/28 A61P35/00

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)
C07J A61P A61K

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, BEILSTEIN Data, 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	SUN, H. ET AL.: BOTANICAL STUDIES, vol. 47, 2006, pages 339-368, XP008108435 the whole document	1-264
A	HONDA, T. ET AL.: BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 8, 1998, pages 2711-2714, XP002537196 cited in the application the whole document	

☐ Further documents are listed in the continuation of Box C.

☐ 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

16 July 2009

Date of mailing of the international search report

05/08/2009

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

Authorized officer

Tabanella, Stefania