Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

E. S. D.

REF: **Expediente No. PCT/12-116665**

TÍTULO SOLICITADO: **"ANTICUERPOS ANTAGONISTAS DE PCSK9"**

PUBLICACIÓN: **Gaceta 657 del 30/11/2012, N° de publicación 1828.**

SOLICITANTE: **IRM LLC.**

APODERADO: **CARLOS REINALDO OLARTE GARCÍA.**

TRÁMITE: **Recurso de Reposición y en subsidio el de apelación en contra de la Resolución 56417 de septiembre 23 de 2014 por la cual se concede una patente de invención tramitada bajo el número de expediente PCT/12-116665.**

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 56417 de septiembre 23 de 2014 por la cual se concedió a la solicitud PCT/12-116665 el privilegio de patente de invención.

I. PETICIÓN

Sírvase, Señor Superintendente, reponer íntegramente la Resolución 56417 de septiembre 23 de 2014, 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 56417 de septiembre 23 de 2014, que concede el privilegio de patente de invención solicitado para el capítulo reivindicatorio del expediente 12-116665 titulado "**Anticuerpos antagonistas de PCSK9**", 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, Simvastatina, Cerivastatina, Mevastatina, entre muchos 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 33538**
- **US 4444784**
- **EP 325130**

- **US 5006530**
- **US 5177080**
- **DE 2524355**
- **US 3983140**

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, 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 2011/072263.

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

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/US2010/059959	10.12.2010	11.12.2009

International Patent Classification (IPC) or both national classification and IPC
INV. C07K16/40 A61K39/395 A61P3/06

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 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 P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Luyten, Kattie Telephone No. +31 70 340-8924

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2010/059959

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/US2010/059959

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	4-28, 30-50
	No:	Claims	1-3, 29
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-50
Industrial applicability (IA)	Yes:	Claims	1-50
	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

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

SECTION V

1 PRIOR ART

1.1 Reference is made to the following documents:

D1 NI YAN G ET AL: "A PCSK9 C-terminal Domain Binding Fab Inhibits PCSK9 Internalization and Restores LDL-uptake", CIRCULATION, LIPPINCOTT WILLIAMS & WILKINS, US, vol. 120, no. 18, Suppl. 2, 1 November 2009 (2009-11-01), page S477, XP008121212, ISSN: 0009-7322

D2 WO 2008/057459 A2 (MERCK & CO INC [US]; SPARROW CARL P [US]; SITLANI AYESHA [US]; PANDIT) 15 May 2008 (2008-05-15)

D3 NI YAN G ET AL: "A proprotein convertase subtilisin-like/kexin type 9 (PCSK9) C-terminal domain antibody antigen-binding fragment inhibits PCSK9 internalization and restores low density lipoprotein uptake.", THE JOURNAL OF BIOLOGICAL CHEMISTRY 23 APR 2010 LNKD-PUBMED:20172854, vol. 285, no. 17, 23 April 2010 (2010-04-23), pages 12882-12891, ISSN: 1083-351X

D4 WO 2010/068526 A1 (MERCK SHARP & DOHME [US]; NI YAN [US]; SITLANI AYESHA [US]; PANDIT SHI) 17 June 2010 (2010-06-17)

D5 WO 2009/026558 A1 (AMGEN INC [US]; JACKSON SIMON MARK [US]; WALKER NIGEL PELHAM CLINTON [) 26 February 2009 (2009-02-26)

D6 WO 2009/100297 A1 (MERCK & CO INC [US]; ANGELETTI P IST RICHERCHE BIO [IT]; CONDRA JON H) 13 August 2009 (2009-08-13)

D7 LI HAI ET AL: "Recent patents on PCSK9: a new target for treating hypercholesterolemia.", RECENT PATENTS ON DNA & GENE SEQUENCES NOV 2009 LNKD-PUBMED:19601924, vol. 3, no. 3, November 2009 (2009-11), pages 201-212, ISSN: 1872-2156

1.2 Document D1 discloses that the human anti-PCSK9 Fab antibody 1G08 does not block PCSK9 binding to LDLR, but inhibits PCSK9-dependent effects on LDL uptake by HEK293 and HepG2 cells, and inhibits the internalization of PCSK9 in HEK293 cells, implying that the antibody inhibits PCSK9-mediated degradation of LDLR. Said antibody has an affinity for PCSK9 in the sub-nanomolar range and binds within the C-terminal domain of PCSK9 (whole document).

1.3 Document D2 discloses the production and characterization of the human anti-PCSK9 Fab antibody 1CX1G08 (the Examples). Said antibody shows a 53% inhibition of PCSK9-dependent inhibition of cellular LDL uptake (Figure 3 A and B) and a K_D of 550 ± 180 pM for human PCSK9 (measured using surface plasmon resonance, Biacore™) (Table 3).

1.4 Document D3 discloses the same as document D1 (see Abstract) and shows the corresponding experimental data (whole document).

1.5 Documents D1 to D4 have been published by MERCK. In document D4 an anti-PCSK9 antibody referred to as G08 or Eu-1G08 Fab has been used in the Examples. Document D4 states on page 4, lines 22-23 that "G08 is disclosed in WO2008057459". Hence, the anti-PCSK9 antibody from MERCK named either G08, 1G08 or 1CX1G08 in documents D1-D4, is considered to be one and the same antibody.

1.6 Document D5 discloses human anti-PCSK9 antibodies 31H4, 21B12 and 16F12. Said antibodies have a K_D of 190-470 pM for human PCSK9 and block PCSK9-dependent effects on LDL uptake by HepG2 cells. Anti-PCSK9 antibody 31H4 increases the LDLR level, lowers serum cholesterol by about 30%, and lowers serum LDL in an in vivo mouse model (Examples 1-7, 9, 11-17, 25-26; Table 7.1; Figures 8, 10-12, 14 and 28D). D5 furthermore refers to the use of said antibodies in the treatment of e.g. hypercholesterolemia (Examples 19-21), and the combined use of anti-PCSK9 antibodies with statins (Example 24).

1.7 Document D6 discloses human anti-PCSK9 Fab and IgG antibodies that inhibit PCSK9 internalization and restoration of LDL uptake, implying that they inhibit PCSK9-mediated degradation of LDLR. The Fab and IgG show, respectively, 20 and 34% reduction of serum LDL in an in vivo mouse model (Examples 1-14; Figures 5 and 15).

1.8 Document D7 reviews PCSK9 as target for treating hypercholesterolemia and refers to the use of neutralizing anti- PCSK9 antibodies (whole document, especially page 205, paragraph 2).

2 The patentability of claims 34-50 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 (claims 34-50), but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

Patentability, in particular novelty and inventive step, of claims 34-50 has been assessed on the basis of a purpose-limited product claim taking into account the alleged effects of the compound/composition.

3 NOVELTY (Art. 33(2) PCT)

3.1 The anti- PCSK9 antibody 1G08/1CX1G08 of D1 and D2 has the functional properties as defined in claim 1, see items 1.2, 1.3 and 1.5. Hence, claims 1 and 29 are not novel over D1 and D2.

3.2 Anti- PCSK9 antibody 1G08/1CX1G08 binds PCSK9 within the C- terminal domain. From the data in D1 and D3 it cannot be excluded that said antibody binds within amino acid residue positions 680-692. Hence, claim 2 is not novel over D1 and D2.

3.3 Taking into account the error margins when measuring a K_D value, the K_D of anti-PCSK9 antibody 1G08/1CX1G08 of 550 ± 180 pM for human PCSK9 falls within the expression "about 500 pM or less" as in claim 3. Hence, claim 3 is not novel over D1 and D2.

3.4 The antibody of D1 and D2 is an unlinked Fab, instead of a Fab' fragment, IgG or single chain antibody. Without a carrier a Fab fragment is considered to have an in vivo half-life of less than 7 days. D1 and D2 do not disclose a composition comprising antibody 1G08/1CX1G08 and a second agent that reduces LDL-C levels in an individual, nor the medical uses as in claims 34-50 Therefore, claims 4, 21-26 and 30-50 are novel over D1 and D2.

3.5 The cited prior art does not disclose any anti- PCSK9 antibody with a sequence as defined in claims 5 or 27. Hence, claims 5-20 and 27-28 are novel over the cited prior art.

3.6 Documents D5-D7 do not disclose an antibody which "does not block PCSK9 binding to LDLR". Hence, claims 1-50 are novel over D5-D7.

3.7 Thus, although claims 4-28 and 30-50 are novel, the present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-3 and 29 is not new in the sense of Article 33(2) PCT.

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

4.1 Document D2, disclosing the human anti-PCSK9 Fab antibody 1CX1G08, is regarded as being the closest prior art to the subject-matter of claims 4-28 and 30-50.

4.2 Claims 5-20 and 27-28 differ from document D2 with respect to the amino acid sequence of the antibody, claims 21-24 differ with respect to the antibody format, claims 25-26 differ with respect to linkage to a carrier protein, and claim 4 differs by means of the functional property "has an in vivo half-life of at least 7 days".

4.3 There is no particular effect associated with any of these differences. The problem to be solved by the present application may therefore be regarded as to provide an alternative anti-PCSK9 antibody that inhibits PCSK9-dependent inhibition of LDL uptake by liver cells, and that does not interfere with PCSK9 binding to the LDL-R.

4.4 The provision of a further antibody with the same functional properties as a prior art antibody falls within the routine skills of the skilled person. Hence, the present antibodies are mere arbitrary alternatives which without a surprising effect, do not involve an inventive step. The provision of a different antibody format or a fusion protein that results in an increased half-life, falls with routine procedures. Hence, the antibody claims 4-28 do not involve an inventive step.

4.5 A combination of two compounds which each individually are not inventive, does not involve an inventive step unless said combination results in a synergistic effect. No synergistic effect has been shown for the compositions as in claims 30-33. Hence, claims 30-33 lack an inventive step.

4.6 Document D2 suggests the therapeutic use of an PCSK9 antagonist in the treatment of disorders which would benefit from a reduction in the LDL-C serum level, e.g. hypercholesterolemia (page 3, lines 23-28). Moreover, the in vivo use of an anti-PCSK9 antibody for lowering serum LDL-C by inhibition of PCSK9-mediated degradation of LDLR, has been disclosed in e.g. documents D5, D6 and D7. Therefore, the therapeutic use of any further anti-PCSK9

antibody that inhibits PCSK9-mediated degradation of LDLR for the reduction of the LDL-C level in an individual, as in claims 34-50, does not involve an inventive step.

4.7 Thus, the present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 4-28 and 30-50 does not involve an inventive step in the sense of Article 33(3) PCT.

SECTION VI

Documents D3 and D4 have been cited in the ISR as P-documents. The examination has been based on the assumption that the claimed priority is valid for all claims, and that, therefore, D3 and D4 do not fall within the state of the art for assessing novelty and inventive step. However, if the priority is not valid, then D3 and D4 may become relevant for claims 1-50.

SECTION VIII

1 CLARITY AND SUPPORT (Art. 6 PCT)

1.1 The sequences of SEQ ID NOs 8, 11, 14, 22, 25, 28, 31 and 40-41 contain variants at certain amino acid positions. Though, those variants are not indicated in claims 6, 13, 15-17 and 27. The lack of said information is misleading and renders said claims unclear.

1.2 A "single chain antibody" is not limited to a single chain Fv, therefore the abbreviation "scFv" in claim 23 is inconsistent with the expression "single chain antibody". This inconsistency renders claim 23 unclear.

1.3 Thus, the application does not meet the requirements of Article 6 PCT, because claims 6, 13, 15-17, 23 and 27 are not clear.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
53967-WO-PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2010/059959	10/12/2010	11/12/2009
Applicant		
IRM 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 6 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,**
   [ ] the text is approved as submitted by the applicant
   [X] 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. [X] none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2010/059959

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. (means)

   - [ ] on paper
   - [X] in electronic form

   b. (time)

   - [ ] in the international application as filed
   - [X] 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/US2010/059959

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present disclosure provides antibody antagonists against proprotein convertase subtilisin/kexin type 9a ("PCSK9") and methods of using such antibodies.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/059959

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/40 A61K39/395 A61P3/06
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 A61K A61P

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, EMBASE, WPI Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NI YAN G ET AL: "A PCSK9 C-terminal Domain Binding Fab Inhibits PCSK9 Internalization and Restores LDL-uptake", CIRCULATION, LIPPINCOTT WILLIAMS & WILKINS, US, vol. 120, no. 18, Suppl. 2, 1 November 2009 (2009-11-01), page S477, XP008121212, ISSN: 0009-7322	1-33
Y	the whole document	34-50

X	WO 2008/057459 A2 (MERCK & CO INC [US]; SPARROW CARL P [US]; SITLANI AYESHA [US]; PANDIT) 15 May 2008 (2008-05-15)	1-33
Y	page 3, lines 23-28; figures 3A, 3B; examples; table 3	34-50

	-/--	

[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
28 January 2011	10/02/2011

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