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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Rad: 06-047666-00002-0000

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Tra 11 PATENTERII

Ere: 379 FASENACIONALI

Act 444 RESPUESTAREQUE Folios: 73

Señora Jefe de la

DIVISION DE NUEVAS CREACIONES

Superintendencia de Industria y Comercio

E. S. D.

Trámite : 011

Evento : 379

Actuación: 444

Referencia : Expediente No. 06047666
Asunto : Solicitud de patente para ANTAGONISTAS DEL
RECEPTOR B1 DE BRADIQUININA
Solicitante : AMGEN INC.

CONTESTACION OFICIO No. 8787

1. Yo, Emilio FERRERO, en mi condición de apoderado de la sociedad solicitante, AMGEN INC., doy contestación al requerimiento efectuado por este Despacho mediante Oficio No. 8787 notificado por fijación en lista el 11 de agosto de 2006, para lo cual presento los siguientes documentos:

1.1. Copia del Reporte de Examen Preliminar Internacional, el cual no contiene anexos.

A este respecto me permito informar a este Despacho que el listado de secuencias de la invención, anexo al Reporte de Examen Preliminar Internacional, fue presentado conjuntamente con la solicitud.

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1.2. Documento en que consta la cesión del derecho a la patente efectuado por los inventores en favor de la sociedad AMGEN INC.

Se presenta este documento en copia certificada del documento original que fue presentado en el trámite de la fase internacional, debidamente legalizado por Apostille y acompañado de su correspondiente traducción oficial al español.

1.3. Poder otorgado por AMGEN INC. a los doctores Emilio FERRERO, Gonzalo PERDOMO, Luz Clemencia de PÁEZ y Daniel PEÑA, junto con el certificado que acredita la existencia y representación legal de la compañía y que hace parte integral del poder.

Se presenta este documento en fotocopia auténtica del original que fue debidamente legalizado por Apostille y traducido oficialmente al español.

2. De acuerdo con lo anterior, comedidamente solicito a Usted proseguir con el trámite de este asunto y ordenar la publicación de la solicitud de la patente identificada en la referencia.

Señora Jefe,



EMILIO FERRERO

T.P.A. No. 31.929

PCT

WIPO

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference A-836B		FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/US2004/034976		International filing date (day/month/year) 22.10.2004		Priority date (day/month/year) 22.10.2003
International Patent Classification (IPC) or national classification and IPC INV. A61K47/48 C07K7/18 A61P29/00				
Applicant AMGEN INC. et al.				
1. This report is the International preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 10 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☒ sent to the applicant and to the International Bureau a total of 1-31 sheets, as follows: ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the International application as filed, as indicated in Item 4 of Box No. I and the Supplemental Box. b. ☐ (sent to the International Bureau only) a total of (Indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).				
4. This report contains indications relating to the following items: ☒ 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				
Date of submission of the demand 24.02.2006		Date of completion of this report 27.03.2006		
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80289 Munich Tel. +49 89 2399 - 0 Tlx 523856 epmu d Fax: +49 89 2399 - 4485		Authorized officer Lopez García, F Telephone No. +49 89 2399-2171 		

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the elements* of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-109 as originally filed

Sequence listings part of the description, Pages

1-31 received on 05.08.2005 with letter of 05.08.2005

Claims, Numbers

1-49 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-49 (partially)

because:

☒ the said international application, or the said claims Nos. 15-18, 36, 37, 46, 47 (all partially) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-49 (all partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

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Box No V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement

1 Statement

Novelty (N)	Yes	Claims	1 49 (all partially)
	No	Claims	
Inventive step (IS)	Yes	Claims	
	No	Claims	1 49 (all partially)
Industrial applicability (IA)	Yes	Claims	1 14, 19 26, 38 45, 48 49 (all partially)
	No	Claims	15 18 36 37 46 47 (all partially)

2 Citations and explanations (Rule 70 7)

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

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Supplemental Box relating to Sequence Listing

Continuation of Box I, Item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report 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:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☒ received by this Authority as an amendment on 05.08.2005
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) 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 observations, if necessary:

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Re Item I

Basle of the report

1. The amendments filed under Art. 34 PCT with the demand (identical to those received on 05.08.2005) corresponding to substitute sequence listing (pages 1-31) meet the requirements of said article.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2. No opinion will be established for the subject-matter of inventions 2-45 as set by the ISA, since the applicant has not paid additional search fees after the invitation to pay additional search fees.

3. Claims 15-18, 36, 37, 46 and 47 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

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

This report relates exclusively to invention 1, which comprises the subject-matter of claims 1-49 insofar as SEQ. ID. No: 15 is concerned.

4. Reference is made to the following documents:

- D1: STEWART JOHN M ET AL: "Metabolism-resistant bradykinin antagonists: Development and applications" BIOLOGICAL CHEMISTRY, vol. 382, no. 1, January 2001 (2001-01), pages 37-41, XP009042832 ISSN: 1431-6730
- D2: US-A-5 834 431
- D3: RAYMOND P ET AL: "Quantification of des-Arg<9>-bradykinin using a

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chemiluminescence enzyme immunoassay: application to its kinetic profile during plasma activation" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 180, no. 2, 27 March 1995 (1995-03-27), pages 247-257, XP004021047 ISSN: 0022-1759

D4: US-A-5 849 863

D5: DE 24 35 642 A

D6: US-B1-6 407 207

D7: NEUGEBAUER WITOLD ET AL: "Kinin B1 receptor antagonists with multienzymatic resistance properties" CANADIAN JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY, vol. 80, no. 4, April 2002 (2002-04), pages 287-292, XP009042834 ISSN: 0008-4212

D8: US-A-6 075 120 (MARATHE MANOJ VINAYAK ET AL) 13 June 2000 (2000-06-13)

D9: DATABASE UniProt [Online] 1 November 1996 (1996-11-01), "Rat T-kininogen (T-KG)." XP002314946 retrieved from EBI accession no. UNIPROT:Q63581 Database accession no. Q63581

D10: EP-A-0 885 899 (SEIKO INSTR INC) 23 December 1998 (1998-12-23)

D11: MORPURGO M ET AL: "SELECTIVE ALKYLATION AND ACYLATION OF ALPHA AND EPSILON AMINO GROUPS WITH PEG N A SOMATOSTATIN ANALOGUE: TAILORED CHEMISTRY FOR OPTIMIZED BIOCONJUGATES" BIOCONJUGATE CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 13, 2002, pages 1238-1243, XP008040597 ISSN: 1043-1802

D12: ZALIPSKY S ET AL: "Use ethylene glycol) chemistry of Functionalized Poly(Ethylene Glycol)s for Modification of Polypeptides" POLY(ETHYLENE GLYCOL) CHEMISTRY: BIOTECHNICAL AND BIOMEDICAL APPLICATIONS, XX, XX, 1992, pages 347-370, XP002972803

D13: EP-A-0 318 162

D14: US-A-5 252 714

D15: WO 01/62827 A2

5. Novelty (Art. 33(2) PCT)

None of the document cited in the SR discloses the present peptide of sequence SEQ. ID.

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No.: 15.

Therefore, the present subject-matter is novel.

6. Inventive step (Art. 33(3) PCT)

The present subject-matter relates to the peptide of SEQ. ID. NO.: 15 and its conjugates.

The present peptide shares with the peptides of D1, D2 and D4 the sequence Arg-Pro-Hyp-Gly-Cpg-Ser-Dtic-Cpg and only differs in the replacement of D-Arg by D-Orn-Lys.

The technical problem is the provision of alternative peptidic Bradykinin B1 receptor antagonists.

The solution proposed does not seem to involve any inventive activity, since the present peptide maintains the core of the sequences known to antagonize the Bradykinin B1 receptor. The replacement of D-Arg for D-Orn-Lys or any other equivalent seems to be obvious skilled person wishing to provide alternatives, since the fragment D-Arg-Arg-Pro-Hyp-Gly-Cpg-Ser-Dtic-Cpg is already a Bradykinin B1 receptor antagonist. This replacement could only be considered inventive if an advantage is obtained over the known antagonist.

On the other hand, the provision of conjugates of non-inventive peptides does not seem to involve any inventive merit. Moreover, the vehicle as disclosed in the claims has not any special feature that could render said conjugates inventive.

Furthermore, the provision of conjugates of peptidic bradykinin antagonists is suggested in D1 when combining the compounds BKA-X (col. 5, l. 65) and the linkers X mentioned in col. 4, l. 19-20.

Moreover, the provision of bioconjugates, in particular, PEG-modified peptides, seems to be obvious to the skilled person as evident from the disclosure of D11-D15. It is well known in the art the advantages of administering pegylated active compounds.

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7. Industrial applicability (Art. 33(4) PCT).

For the assessment of the present claims 15-18, 36, 37, 46 and 47 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

8. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D3, D5, D6, D8, D9, D10, D13 and D15 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

9. Claim 1, 2 and 20 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempts to define the subject-matter in terms of the result to be achieved, namely that P1 and P2 are peptidic Bradykinin B1 receptor antagonists, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result (structural information regarding said antagonists).

Furthermore, it would be an undue burden to isolate and characterize the antagonists against Bradykinin B1 receptor and therefore to know the scope of said claims without any clue to their chemical structure or to test each and every known peptide and future compounds whether they fall within the scope of the claim.

10. Claims 1, 2, 20, 26 and 27 are not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description. The reasons therefor are

the following: only few examples of peptidic Bradykinin B1 receptor antagonists have been disclosed.

11. No unified criteria exist in the PCT as to the acceptance of documents "incorporated by reference" in an application. The EPO for example request these references to be deleted from the description in case such publication (and other material) are not essential for carrying out the invention. If, however, it turns out that said publications and other materials are in fact essential for carrying the invention, the EPO requests them/it to be expressly incorporated into the description. Such incorporation is, however, subject to the restrictions as listed in the decision T666/90, OJ 10/93, 616, of the EPO's Technical Board of Appeal.

12. Claims 21 and 37 have a wrong dependency upon claims 2 and 35, respectively. They should be dependent upon claims 20 and 36, respectively.

13. The vague and imprecise statement in the description on page 1, l. 3-7, p. 79, l. 24-28 and page 109, l. 14-17 implies 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.

14. Although claims 1, 2, 20, 26 and 27 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 and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

15. Claims 1, 2, 20, 26 and 27 have been drafted as separate independent claims. The provision of Article 84 in combination with Rule 29(2) EPC in that an application may contain more than one independent claim in a particular category only if the subject matter claimed falls within one or more of the exceptional situations set out in paragraphs (a), (b) or (c) of Rule 29(2) EPC, should be taken into account when entering the regional phase.

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Xaa Xaa

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2

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385

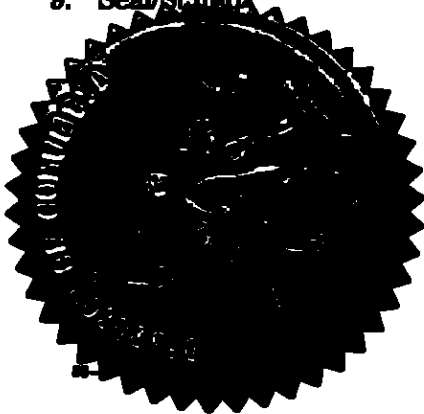
Apostille

(Convention de La Haye du 5 octobre 1961)

1. *District of Columbia*
United States of America
2. This public document has been signed by ALBERT L. THEMES
3. acting in the capacity of NOTARY PUBLIC IN AND FOR THE DISTRICT OF COLUMBIA
ALBERT L. THEMES, NOTARY PUBLIC IN AND FOR THE
4. bears the seal/stamp of DISTRICT OF COLUMBIA

CERTIFIED

5. at Washington, D.C.
22 JUNE 2006
6. the _____ day of _____
7. by Secretary of the District of Columbia
8. No. 158186
9. Seal/Stamp

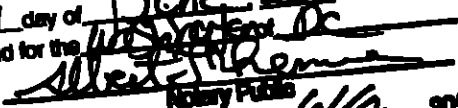


10. Signature
PATRICIA ELWOOD

Patricia Elwood

326

I hereby certify that the attached are true copies
of the original documents.


Subscribed and sworn to before me, in my presence, this
21 day of June, 2008, a Notary Public
in and for the District of Columbia

Notary Public
My commission expires 6/14, 2009

ALBERT L. THEMES
NOTARY PUBLIC DISTRICT OF COLUMBIA
My Commission Expires June 14, 2009

387

ASSIGNMENT

Whereas, we, Gordon Ng, 1733 BLUE CANYON, NEWBURY PARK, CALIFORNIA 91320, US

Yue-Sheng Li, 3025 SHADOW HILL CIRCLE, THOUSAND OAKS, CALIFORNIA 91360 US

Colin V. Gegg, 487 DELWOOD COURT, NEWBURY PARK, CALIFORNIA 91320, US

Benny C. Askaw, Jr., 515 HAVENSIDE AVENUE, NEWBURY PARK, CALIFORNIA 91320, US

Thomas Storz, 1724 BLUE CANYON STREET, THOUSAND OAKS, CALIFORNIA 91320 US

Yuelie Lu, 2479 RIDGEBROOK PLACE, THOUSAND OAKS, CALIFORNIA 91360 US

Derin C. D'Amico, 4571 CALLE NORTE, NEWBURY PARK, CALIFORNIA 91320, US

have made an invention which is the subject of an application for Letters Patent of the United States ("Application") entitled

Antagonists of the Bradykinin B1 Receptor

which is found in:

- ☐ (a) the US Patent Application executed on even date herewith;
- ☐ (b) the US Patent Application executed on _____ [which claims the benefit of U.S. Provisional Application No. _____ filed _____.]
- ☒ (c) US Application Serial No.: 10/972,236 filed on October 21, 2004, which claims the benefit of U.S. Provisional Application No. 60/513,913 filed 22 October 2003 and U.S. Provisional Application No: 60/538,929 filed 24 January 2004.
- ☐ (d) US Patent No.: _____

Whereas AMGEN INC., a Delaware corporation having its principal place of business at One Amgen Center Drive, Thousand Oaks, California 91320-1799, wishes to acquire the entire interest in all inventions disclosed in such Application:

Now, therefore, in consideration of the sum of one dollar (\$1.00) and other good and valuable consideration, the receipt of which is hereby acknowledged, we hereby sell, assign, transfer and set over unto AMGEN INC., its successors and assigns (collectively "AMGEN") our entire right, title and interest in, to and under the Application, and any provisional application(s) from which Application is derived, and all priority rights to which the Application may be entitled, including all priority rights for other countries arising therefrom, all inventions therein disclosed, and any and all Letters Patent of the United States and of all other countries which may be granted for such inventions, or any of them, including divisional, continuation, and/or continuation-in-part applications based on the above-identified Application, all such inventions and all rights in such Application and Letters Patent to be held and enjoyed by AMGEN for its own use and enjoyment to the full end of the term or terms for which such Letters Patent may be granted as fully and entirely as the same would have been held and enjoyed by us had this assignment and sale not been made.

Further, we hereby sell, assign, transfer, and set over unto AMGEN our entire right, title and interest in or to the right to refer to, to access, and to control microorganism(s) or other biological material(s) related to the Application and which are deposited by us or at our direction or deposited on our behalf by Amgen, its affiliates, employees or employees of its affiliates. The transfer of such right, title and interest includes, without limitation, our unreserved and irrevocable consent and authorization to AMGEN to refer to the deposited microorganisms(s) or other biological materials(s) in the Application and the right to make available to the public the deposited material in accordance with the laws, treaties, statutes, rules, regulations and the like of the United States, all other countries, and any patent granting authority or organization.

We authorize and request the Commissioner of Patents and Trademarks of the United States to issue any such Letters Patent which may be granted on the Application to AMGEN as assignee of the entire right, title and interest therein and thereto.

For ourselves and for our legal representatives, we covenant and agree with AMGEN that we have not granted to any others any license to make, use or sell any of such inventions, that our right title and interest in such inventions has not been encumbered, that we have good right and title to sell and assign the same, and that we will not execute any instrument in conflict herewith.

For ourselves and for our heirs, successors and legal representatives, we further covenant and agree with AMGEN that upon request we and they will: (i) execute continuing, divisional or reissue applications, amended specifications, or rightful declarations or oaths; (ii) communicate to AMGEN any facts known to us or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings or litigations; (iv) execute and deliver any application papers, assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for AMGEN, may be necessary or desirable to secure the grant of Letters Patent to AMGEN or its nominees, in the United States and in all other countries where AMGEN may desire to have such

inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for AMGEN and to vest and confirm in AMGEN or its nominees, the full and complete legal and equitable title to all such Letters Patent, without further consideration than that now paid but at the expense of AMGEN.

389

In Witness Whereof I have executed this assignment on the 4 day of November 20 04

Gordon Ng
(Name of Inventor)

Gordon Ng
(Signature of Inventor)

UNITED STATES OF AMERICA

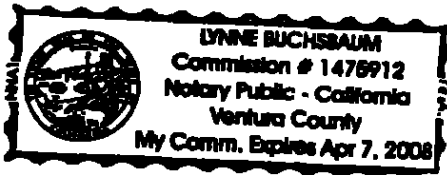
State of California }
County of Ventura } ss:

November 4 20 04

Before me, a Notary Public for Ventura County, State of California, personally appeared _____

Gordon Ng

☒ personally known to me - OR - ☐ proved to me on the basis of satisfactory evidence to be the person whose name is subscribed to the within Instrument and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.



WITNESS my hand and official seal.

Lynne Buchsbaum
Notary Public

My commission expires

April 7 20 08

390

In Witness Whereof I have executed this assignment on the 11 day of November 20 04

Yue-Sheng Li
(Name of Inventor)

[Signature]
(Signature of Inventor)

UNITED STATES OF AMERICA

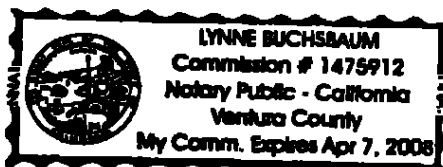
State of California }
County of Ventura } ss:

November 11 20 04

Before me, a Notary Public for Ventura County, State of California, personally appeared _____

Yue-Sheng Li

☐ personally known to me - OR - ☒ proved to me on the basis of satisfactory evidence to be the person whose name is subscribed to the within instrument and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.



WITNESS my hand and official seal.

Lynne Buchsbaum
Notary Public

My commission expires

April 7 20 04

In Witness Whereof I have executed this assignment on the 3 day of November 20 04 391

Colin V. Gegg
(Name of Inventor)

Colin V. Gegg
(Signature of Inventor)

UNITED STATES OF AMERICA

State of California }
County of Ventura } ss:

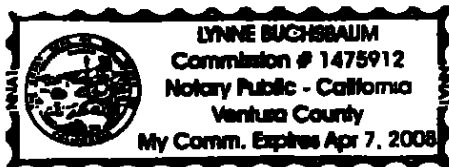
November 3 20 04

Before me, a Notary Public for Ventura County, State of California, personally appeared _____

Colin Gegg

☒ personally known to me - OR - ☐

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



WITNESS my hand and official seal.

Lynne Buchsbaum
Notary Public

My commission expires

April 7 20 08

392

In Witness Whereof I have executed this assignment on the 10 day of November 20 04Benny C. Askew, Jr.
(Name of Inventor)
(Signature of Inventor)

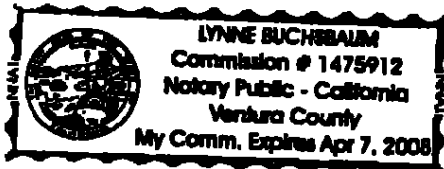
UNITED STATES OF AMERICA

State of California }
County of Ventura } ss:November 10 20 04

Before me, a Notary Public for Ventura County, State of California, personally appeared _____

Benny C. Askew, Jr.☒ personally known to me - OR - ☐ proved to me on the basis of satisfactory evidence to be the person whose name is subscribed to the within instrument and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.

WITNESS my hand and official seal.


Notary Public

My commission expires

April 7 20 04

In Witness Whereof I have executed this assignment on the 08 day of November 2004

Thomas Storz
(Name of Inventor)

Th Storz
(Signature of Inventor)

393

UNITED STATES OF AMERICA

State of California }
County of Ventura } ss:

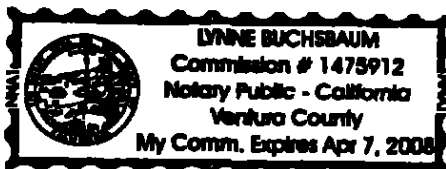
November 8 2004

Before me, a Notary Public for Ventura County, State of California, personally appeared _____

Thomas Storz

☒ personally known to me - OR - ☐ proved to me on the basis of satisfactory evidence to be the person whose name is subscribed to the within instrument and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.

WITNESS my hand and official seal.



Lynne Buchsbaum
Notary Public

My commission expires

April 7 2008

In Witness Whereof I have executed this assignment on the 03 day of Nov. 20 04

Yuelie Lu
(Name of Inventor)

[Signature]
(Signature of Inventor)

394

UNITED STATES OF AMERICA

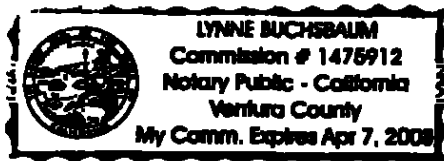
State of California }
County of Ventura } ss:

November 3 20 04

Before me, a Notary Public for Ventura County, State of California, personally appeared _____

Yuelie Lu

☒ personally known to me - OR - ☐ proved to me on the basis of satisfactory evidence to be the person whose name is subscribed to the within Instrument and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.



WITNESS my hand and official seal.

[Signature]
Notary Public

My commission expires

April 7 20 08

In Witness Whereof I have executed this assignment on the

4th day of November 2004

Derin C. D'Amico
(Name of Inventor)

Derin C. D'Amico
(Signature of Inventor)

395

UNITED STATES OF AMERICA

State of California }
County of Ventura }

ss:

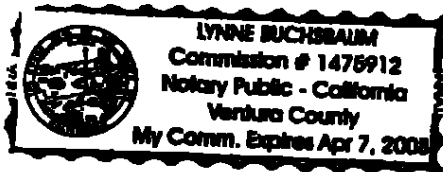
November 4 2004

Before me, a Notary Public for Ventura County, State of California, personally appeared _____

Derin C. D'Amico

☐ personally known to me - OR - ☒ proved to me on the basis of satisfactory evidence to be the person whose name is subscribed to the within instrument and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.

WITNESS my hand and official seal.



Lynne Buchsbaum
Notary Public

My commission expires

April 7 2008

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TRADUCCIÓN OFICIAL No. 07.07/06a realizada por Diego Vargas, Traductor
Oficial, Resolución No. 0001 de 1999 del Ministerio de Justicia y
registrado ante el Ministerio de Relaciones Exteriores de Colombia.

Referencia No.:A-836B

CESIÓN

Considerando que nosotros Gordon Ng, 1733 BLUE CANYON, NEWBURY
PARK, CALIFORNIA 91320, ESTADOS UNIDOS DE AMÉRICA

Yue-Sheng Li, 3025 SHADOW HILL CIRCLE, THOUSAND OAKS,
CALIFORNIA 91360, ESTADOS UNIDOS DE AMÉRICA

Colin V. Gegg, 487 DELWOOD COURT, NEWBURY PARK, CALIFORNIA
91320, ESTADOS UNIDOS DE AMÉRICA

Benny C. Askew, Jr., 515 HAVENSIDE AVENUE, NEWBURY PARK,
CALIFORNIA 91320, ESTADOS UNIDOS DE AMÉRICA

Thomas Storz, 1724 BLUE CANYON STREET, THOUSAND OAKS,
CALIFORNIA 91320, ESTADOS UNIDOS DE AMÉRICA

Yuelie Lu, 2479 RIDGEBROOK PLACE, THOUSAND OAKS, CALIFORNIA
91360, ESTADOS UNIDOS DE AMÉRICA

Derin C. D'Amico, 4571 CALLE NORTE, NEWBURY PARK, CALIFORNIA
91320, ESTADOS UNIDOS DE AMÉRICA

hemos realizado un invención la cual es el objeto de una solicitud
de Patente de Invención de los Estados Unidos ("Solicitud")
titulada:

Antagonistas Del Receptor B1 De Bradiquinina

la cual se encuentra en:

☐ (a) la Solicitud de Patente de los Estados Unidos suscrita en
la misma fecha del presente:

☐ (b) la Solicitud de Patente de los Estados Unidos suscrita el
_____ [la cual reivindica el beneficio de la Solicitud
Provisional de los Estados Unidos

No. _____ presentada _____].

397

☐ (c) la Solicitud de Patente de los Estados Unidos No. de Serie 10/972,236 presentada el 21 de octubre de 2004 la cual reivindica el beneficio de la Solicitud Provisional de los Estados Unidos No. 60/513,913 presentada el 22 de octubre de 2003 y de la Solicitud Provisional de los Estados Unidos No.: 60/538,929 presentada el 24 de enero de 2004.

☐ (d) la Patente de los Estados Unidos No. _____

Considerando que AMGEN INC., una sociedad de Delaware, domiciliada en One Amgen Center Drive, Thousand Oaks, California 91320-1799, desea adquirir todo el interés en las invenciones reveladas en dicha solicitud:

Por consiguiente, por contraprestación de la suma de un dólar (\$1.00) y de otras contraprestaciones válidas y legales, el recibo de las cuales se reconoce por el presente, por el presente nosotros vendemos, cedemos, transferimos y traspasamos a AMGEN INC., sus sucesores y cesionarios (colectivamente "AMGEN") todo nuestro derecho, título e interés en, para y sobre la Solicitud y todas las solicitudes provisionales de las cuales se derivan la Solicitud y todos los derechos de prioridad a los cuales pueda tener derecho la Solicitud, incluyendo todos los derechos de prioridad para otros países que surjan de esta, todas las invenciones reveladas en ellas y cualquier y todas las Patentes de Invención de los Estados Unidos y de todos los demás países que puedan ser otorgadas a dichas invenciones o a cualquiera de ellas, incluyendo solicitudes divisionales, de continuación y/o continuación en parte con fundamento en la Solicitud de la referencia, para que dichas invenciones y todos los derechos en dicha Solicitud y Patentes de Invención sean tenidos y usufructuados por AMGEN para su propio uso y usufructo hasta la conclusión del término o términos para los

cuales se lleguen a otorgar dichas Patentes de Invención tan plena y completamente como si los mismos hubiesen sido tenidos y 398 usufructuados por nosotros si esta cesión y venta no se hubiese efectuado.

Adicionalmente, por el presente vendemos, cedemos, transferimos y traspasamos a AMGEN todo nuestro derecho, título e interés en o a el derecho a hacer referencia, o tener acceso o control de microorganismo(s) u otro(s) material(es) biológico(s) relativos a la Solicitud y los cuales has sido depositados por nosotros o bajo nuestra dirección o depositaos a nuestro nombre por parte de Amgen, sus afiliadas, empleados o empleados de sus afiliados. La transferencia de dicho derecho, título e interés incluye, sin limitación, nuestro consentimiento y autorización irrevocable y completa para que AMGEN haga referencia a el(los) microorganismo(s) depositado(s) o a otro(s) material(es) biológico(s) en la Solicitud y el derecho de poner a disposición del público el material depositado de conformidad con las leyes, tratados, estatutos, reglas, regulaciones y similares de los Estados Unidos, de todos los demás países y de cualquier autoridad u organización otorgante de patentes.

Nosotros autorizamos y le solicitamos al Comisionado de Marcas y Patentes de los Estados Unidos que expida cualquier Patente de Invención que le llegue a ser otorgada a la Solicitud a nombre de AMGEN como cesionario de todo el derecho, título e interés a y en la misma.

Para nosotros mismos y para nuestros representantes legales, garantizamos y nos comprometemos con AMGEN que no hemos otorgado a nadie más licencia alguna para hacer, usar o vender dichas invenciones, que nuestro derecho, título e interés en dichas invención no ha sido afectado, que tenemos pleno derecho y título

para vender y ceder la misma y que no suscribiremos ningún documento que esté en conflicto con el presente.

399

Para nosotros y para nuestro herederos, sucesores y representantes legales, adicionalmente garantizamos y nos comprometemos con AMGEN que por petición nosotros (i) suscribiremos solicitudes de continuación, divisionales o de nueva publicación, corregiremos especificaciones o declaraciones o juramentos verdaderos; (ii) le comunicaremos a AMGEN todos los hechos que sean de nuestro o de su conocimiento relativos a dichas invenciones o la historia de las mismas; (iii) suscribiremos declaraciones preliminares y testificaremos en cualquier proceso de interferencia o litigio; (iv) suscribiremos y entregaremos todos los documentos de solicitudes, cesiones u otros instrumentos; y (v) realizaremos todas las demás acciones que en opinión del asesor legal de AMGEN puedan ser necesarios o convenientes para asegurar la obtención de Patentes de Invención a AMGEN o sus nominatarios en los Estados Unidos y en todos los países en donde AMGEN desee hacer que dicha invención o cualquier de ellas sean patentadas, con especificaciones y reivindicaciones de la forma tal que sea aprobada por el asesor legal de AMGEN y para invertir y confirmar en AMGEN o sus nominatarios el pleno y completo título legal y en equidad a dichas Patentes de Invención sin contraprestación adicional a la que ahora ha sido pagada pero por cuenta de AMGEN.

En testimonio de lo cual, he suscrito esta cesión hoy 4 de Noviembre de 2004

Gordon Ng
(Nombre del Inventor)

Firma Ilegible
(Firma del Inventor)

ESTADOS UNIDOS DE AMÉRICA

Estado de California
Condado de Ventura

}

Declaración Juramentada

4 de Noviembre de 2004

400

Ante mí, un Notario Público del Condado de Ventura, compareció personalmente Gordon Ng

☒ a quien conozco personalmente - Ó - ☐ probó ante mí con evidencia satisfactoria ser la persona cuyo nombre está suscrito en el documento y reconoció ante mí que él suscribió el mismo en su calidad autorizada y que por medio de su firma en el documento la persona o la entidad a nombre de la cual dicha persona actuó, ejecutó el documento.

LYNNE BUCHSBAUM
Comisión # 1475912
Notario Público - California
Condado de Ventura
Comisión vence Abr. 7 de 2008

TESTIFICA mí firma y sello oficial.

Firma Ilegible

Notario Público

Mí comisión vence

7 de abril de 2008

En testimonio de lo cual, he suscrito esta cesión hoy 11 de Noviembre de 2004

Yue-Sheng Li
(Nombre del Inventor)

Firma Ilegible
(Firma del Inventor)

ESTADOS UNIDOS DE AMÉRICA

Estado de California
Condado de Ventura

}

Declaración Juramentada

11 de Noviembre de 2004

Ante mí, un Notario Público del Condado de Ventura, compareció personalmente Yue-Sheng Li

☐ a quien conozco personalmente - Ó - ☒ probó ante mí con evidencia satisfactoria ser la persona cuyo nombre está suscrito en el documento y reconoció ante mí que él suscribió el mismo en su calidad autorizada y que por medio de su firma en el documento

LYNNE BUCHSBAUM
Comisión # 1475912
Notario Público - California
Condado de Ventura
Comisión vence Abr. 7 de 2008

la persona o la entidad a nombre de la cual
dicha persona actuó, ejecutó el documento.

401

TESTIFICA mí firma y sello oficial.

Firma Ilegible

Notario Público

Mí comisión vence

7 de abril de 2004

En testimonio de lo cual, he suscrito esta cesión hoy 3 de
Noviembre de 2004

Colin V. Gegg
(Nombre del Inventor)

Firma Ilegible
(Firma del Inventor)

ESTADOS UNIDOS DE AMÉRICA

Estado de California
Condado de Ventura

}

Declaración Juramentada

3 de Noviembre de 2004

Ante mí, un Notario Público del Condado de Ventura, compareció
personalmente Colin Gegg

☒ a quien conozco personalmente - Ó - ☐ probó ante mí con evidencia
satisfactoria ser la persona cuyo nombre está
suscrito en el documento y reconoció ante mí
que él suscribió el mismo en su calidad autorizada
y que por medio de su firma en el documento
la persona o la entidad a nombre de la cual
dicha persona actuó, ejecutó el documento.

LYNNE BUCHSBAUM
Comisión # 1475912
Notario Público - California
Condado de Ventura
Comisión vence Abr. 7 de 2008

TESTIFICA mí firma y sello oficial.

Firma Ilegible

Notario Público

Mí comisión vence

7 de abril de 2008

En testimonio de lo cual, he suscrito esta cesión hoy 10 de Noviembre de 2004

402

Benny C. Askew, Jr.
(Nombre del Inventor)

Firma Ilegible
(Firma del Inventor)

ESTADOS UNIDOS DE AMÉRICA

Estado de California
Condado de Ventura

}

Declaración Juramentada

10 de Noviembre de 2004

Ante mí, un Notario Público del Condado de Ventura, compareció personalmente Benny C. Askew, Jr.

☒ a quien conozco personalmente - Ó - ☐ probó ante mí con evidencia satisfactoria ser la persona cuyo nombre está suscrito en el documento y reconoció ante mí que él suscribió el mismo en su calidad autorizada y que por medio de su firma en el documento la persona o la entidad a nombre de la cual dicha persona actuó, ejecutó el documento.

LYNNE BUCHSBAUM
Comisión # 1475912
Notario Público - California
Condado de Ventura
Comisión vence Abr. 7 de 2008

TESTIFICA mí firma y sello oficial.

Firma Ilegible
Notario Público

Mí comisión vence

7 de abril de 2004

En testimonio de lo cual, he suscrito esta cesión hoy 8 de Noviembre de 2004

Thomas Storz
(Nombre del Inventor)

Firma Ilegible
(Firma del Inventor)

ESTADOS UNIDOS DE AMÉRICA

Estado de California
Condado de Ventura

}

Declaración Juramentada

8 de Noviembre de 2004

Ante mí, un Notario Público del Condado de Ventura, compareció personalmente Thomas Storz 403

☒ a quien conozco personalmente - Ó - ☐ probó ante mí con evidencia satisfactoria ser la persona cuyo nombre está suscrito en el documento y reconoció ante mí que él suscribió el mismo en su calidad autorizada y que por medio de su firma en el documento la persona o la entidad a nombre de la cual dicha persona actuó, ejecutó el documento.

LYNNE BUCHSBAUM
Comisión # 1475912
Notario Público - California
Condado de Ventura
Comisión vence Abr. 7 de 2008

TESTIFICA mí firma y sello oficial.

Firma Ilegible

Notario Público

Mí comisión vence

7 de abril de 2008

En testimonio de lo cual, he suscrito esta cesión hoy 3 de Noviembre de 2004

Yuelie Lu
(Nombre del Inventor)

Firma Ilegible
(Firma del Inventor)

ESTADOS UNIDOS DE AMÉRICA

Estado de California
Condado de Ventura

} Declaración Juramentada

3 de Noviembre de 2004

Ante mí, un Notario Público del Condado de Ventura, compareció personalmente Yuelie Lu

☒ a quien conozco personalmente - Ó - ☐ probó ante mí con evidencia satisfactoria ser la persona cuyo nombre está suscrito en el documento y reconoció ante mí que él suscribió el mismo en su calidad autorizada y que por medio de su firma en el documento la persona o la entidad a nombre de la cual

LYNNE BUCHSBAUM
Comisión # 1475912

Notario Público - California
Condado de Ventura
Comisión vence Abr. 7 de 2008

dicha persona actuó, ejecutó el documento.

404

TESTIFICA mi firma y sello oficial.

Firma Ilegible
Notario Público

Mi comisión vence

7 de abril de 2008

En testimonio de lo cual, he suscrito esta cesión hoy 4 de Noviembre de 2004

Derin C. D'Amico
(Nombre del Inventor)

Firma Ilegible
(Firma del Inventor)

ESTADOS UNIDOS DE AMÉRICA

Estado de California
Condado de Ventura

}

Declaración Juramentada

4 de Noviembre de 2004

Ante mí, un Notario Público del Condado de Ventura, compareció personalmente Derin C. D'Amico

☒ a quien conozco personalmente - Ó - ☐ probó ante mí con evidencia satisfactoria ser la persona cuyo nombre está suscrito en el documento y reconoció ante mí que él suscribió el mismo en su calidad autorizada y que por medio de su firma en el documento la persona o la entidad a nombre de la cual dicha persona actuó, ejecutó el documento.

LYNNE BUCHSBAUM
Comisión # 1475912
Notario Público - California
Condado de Ventura
Comisión vence Abr. 7 de 2008

TESTIFICA mi firma y sello oficial.

Firma Ilegible
Notario Público

Mi comisión vence

7 de abril de 2008

Por el presente certifico que las adjuntas son copias fieles de los documentos originales.

Firma Ilegible

Suscrito y juramentado ante mí en mi presencia, hoy

21 de Junio de 2006, Notario Público en y para

Washington D.C.

Firma Ilegible

Notario Público

MI comisión vence 6/14/ de 2009

ALBERT L. THEMES

NOTARIO PÚBLICO DISTRITO DE COLUMBIA

MI Comisión Vence Junio 14 de 2009

APOSTILLA

(Convention de La Haye du 5 octobre 1961)

1. País: Estados Unidos de América

Este documento público

2. ha sido firmado por ALBERT L. THEMES

3. actuando en calidad de NOTARIO PÚBLICO EN Y PARA EL DISTRITO DE COLUMBIA

4. lleva el sello/estampilla de DISTRITO DE COLUMBIA

Certificado

5. en Washington, D.C.

6. el 22 DE JUNIO DE 2006

7. por Funcionario Asistente de Autenticaciones, Departamento de Estado de los Estados Unidos

8. No. 158186

9. Sello/estampilla:

10. Firma:

Firma Ilegible

PATRICIA ELWOOD

Es traducción fiel y completa de la cual se deja copia en esta oficina para su confrontación.

DVZ/ID-7910/WPCL002G/COLO 15193-841-002-5

Diego F. Vargas
DIEGO F. VARGAS Z.
TRADUCTOR E INTERPRETE OFICIAL
ESPAÑOL - INGLÉS - INGLÉS - ESPAÑOL
RES. 0001 DE ENERO 4 DE 1999
MINISTERIO DE JUSTICIA

69

COMO NOTARIO SEXTO DEL CIRCULO DE SANTAFE DE
BOGOTA, HAGO CONSTAR QUE LA(S) FIRMAN(S) DE

Diego Felipe Vargas

CON LA FIRMA REGISTRADA POR
EL CIRCULO EN ESTA NOTARIA

11 JUL 2006



NO SE ASUME
RESPONSABILIDAD DEL TEXTO

2006 JUL 11 P 2:49

WCD
JEFE DE LEGALIZACIONES
SANTAFE DE BOGOTA D.C.

MINISTERIO DE RELACIONES
EXTERIORES

158242
Diego Vargas
CUYA FIRMA APARECE EN EL
DOCUMENTO RESEMPENA
LAS FUNCIONES INDICADAS

Representación, Ratificación y Poder con autenticación notarial y Apostille para patentes, modelos de utilidad diseños industriales, marcas de fábrica, nombres comerciales, enseñas, nombres de dominio, lemas comerciales, licencias.

406

Representation, ratification and Power-of-Attorney with notarial authentication and Apostille for patents, utility models, industrial designs, trademarks, commercial names, trade emblems, domain names, slogans, licenses.

REPRESENTACION, RATIFICACION Y PODER

REPRESENTATION, RATIFICATION AND POWER-OF-ATTORNEY

15143
12203

Yo (nosotros), abajo firmado (s)/I (we), the undersigned

AMGEN INC.

domiciliado (s) en/of

One Amgen Center Drive

Thousand Oaks, California 91320

United States of America

por el presente ratificamos las solicitudes de patente Nos. 06.014.624 y 06.047.666 presentadas por Emilio Ferrero

como agente oficioso ante Superintendencia de Industria y Comercio

en Bogotá

el 14 de febrero de 2006 y el 18 de mayo de 2006 respectivamente

por el presente nombramos a EMILIO FERRERO, tpa. 31929; GONZALO PERDOMO, tpa. 831; LUZ CLEMENCIA DE PAEZ, tpa. 23555 y DANIEL PEÑA, tpa. 65620 domiciliados en la Carrera 4° N° 72-35, Bogotá, Colombia, en obediencia a lo dispuesto en el parágrafo 1o del Artículo 543 del Código de Comercio, el primero como principal y los demás como suplentes, en su orden, como mis (nuestros) representantes en todos los asuntos de propiedad industrial con facultad para recibir notificaciones y nombrar apoderados judiciales o extrajudiciales. El primer representante suplente reemplazará al principal en caso de ausencia o impedimento temporal o definitivo de aquél. La misma regla se aplicará cuando el segundo representante suplente haya de reemplazar al primero, o el tercero al segundo. En tales casos, el representante principal, o el primero, o segundo suplente, en su caso, o ambos, declararán su intención de no ejercer la representación mediante declaración autenticada por Notario Público en Colombia, o por Notario u otro Funcionario Público, o Cónsul de Colombia, en el extranjero; y si se tratare de impedimento, con el certificado respectivo. Si alguno de los nombrados faltare definitivamente, el siguiente tomará su lugar. Cuando cesare la ausencia o impedimento del representante principal, o de su primero o segundo suplentes, en su caso, podrán ejercer la representación, en su orden, uno u otros según el caso, asumiéndola por el solo hecho de ejercerla, cesando en ese momento el ejercicio de la representación por el primero, segundo o tercer suplente en su caso.

Además, confiero (conferimos) poder a los abogados arriba nombrados, para obtener la protección de mi (nuestra) propiedad industrial y contra la competencia desleal, a cuyo efecto autorizo (amos) a los dichos

Hereby ratify the Patent Applications Nos. 06.014.624 and 06.047.666

filed without a Power of Attorney by Emilio Ferrero

before Patent Office

in Bogotá

on February 14, 2006 and May 18, 2006 respectively

and do hereby appoint EMILIO FERRERO, tpa. 31929; GONZALO PERDOMO, tpa. 831; LUZ CLEMENCIA DE PAEZ, tpa. 23555 and DANIEL PEÑA, tpa. 65620, domiciled at Carrera 4° N° 72-35, Bogotá, Colombia, in due compliance with the terms of Paragraph 1st. of Article 543 of the Commercial Code, the first as principal and the others as alternates, in the order of their appointment, as our representatives for all industrial property matters with faculty to receive notifications and to appoint attorneys in and out of Court. The first alternate shall replace the principal in case of his absence or of temporal or definitive impediment. The same rule will apply when the second alternate representative is to replace the first one, or when the third is to replace the first or second alternates in their turn, or both by the second. In such cases, the principal representative, or the shall state their intention not to act as representatives through a declaration given before a Notary Public in Colombia, or before a Notary or another Public Official or a Colombian Consul abroad; and in case of impediment, the appropriate certificate shall suffice. If any of the appointees were to be definitely absent, the following alternate shall take his place. When the absence or impediment of the principal representative, or of the first or second alternate in their turn ceases, the representation can be taken again in their sequence, by the principal, the first or second alternate depending on case, and the mere fact or its exercise will suffice. The exercise of the representation by the first, second or third alternates in their turn shall end at such time.

In addition, we grant a Power of Attorney in favor of the above-named attorneys-at-law so that they may obtain the protection of my (our) industrial property and against the unfair competition, for which purpose

apoderados para que me (nos) representen ante cualesquiera entidades o personas, ejerzan o no jurisdicción, especialmente ante las del orden administrativo, contencioso-administrativo y judicial, así como los tribunales de arbitramento, en todo lo concerniente a los siguientes asuntos: a) Obtención de patentes de invención, modelos de utilidad y diseños industriales; el registro de marcas de fábrica, colectivas, defensivas, de servicio, lemas comerciales, nombres comerciales, enseñas, nombres de dominio, variedades vegetales y denominaciones de origen; su renovación, traspaso, cambio de nombre o domicilio, cancelación voluntaria; y el registro de licencias de uso de esos derechos; b) Las acciones de competencia desleal, protección del consumidor, oposiciones u observaciones, cancelación administrativa o judicial, nulidad, medidas cautelares, concesión de licencias, la tutela, la protección de secretos industriales, y en general los juicios civiles, penales, administrativos o contencioso-administrativos relacionados con estos derechos; acciones y procesos que promovamos o se nos promuevan. Y para que en todos los asuntos arriba determinados, puedan sustituir este mandato, transigir, conciliar, admitir los hechos del proceso, desistir, cancelar, recibir, renunciar, y ratificar los actos de agentes oficiosos.

407
(we) authorize the said attorneys to represent me (us) before any authorities or persons, with or without jurisdiction, specially those administrative, administrative contentious and judicial, as well as before Arbitration Court, in all matters concerning the following: a) Obtainment of patents, utility models and industrial designs; the registration of trademarks, collective, defensive and service marks, slogans, commercial names, trade emblems, domain names, vegetal varieties and denominations of origin; its renewal, assignment, change of name or domicile, voluntary cancellation; and the registration of licenses of use of the above rights; b) Actions of unfair competition, protection to the consumer, oppositions or observations, administrative or Court cancellation, nullity, infringement, granting of licenses, the action for writ mandamus, the protection of trade secrets, and in general the civil, penal, and administrative suits relating to those rights; actions and suits instituted by me (us) or against me (us). And that in all the above matters they may substitute this Power of Attorney, compromise, conciliate, admit the facts of the case, desist, cancel, receive, resign, and ratify acts done by representatives without a power of attorney.

RE: Patent Application
PCTUS2004/022876

Dado y firmado hoy Given and signed this 24 February 2006

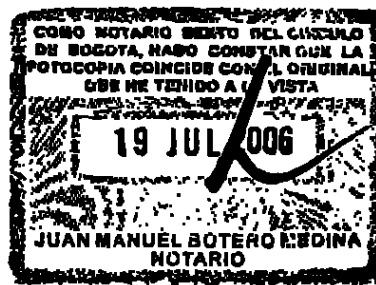
en/in

por/by Stuart L. Watt Vice President Law

Signed in Thousand Oaks, Ventura County, CA, US

Firma

Signature



A-860 (C0)

408

State of California

SECRETARY OF STATE

APOSTILLE

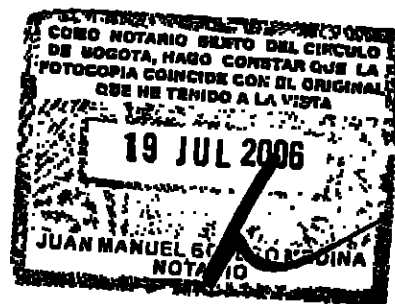
(Convention de La Haye du 5 octobre 1961)

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

CERTIFIED

5. *At Sacramento, California*
6. *the 8th day of April 2006*
7. *by Deputy Secretary of State, State of California*
8. *No. 281687*
9. *Seal/Stamp:*

10. *Signature*



[Signature]

Secretary of State

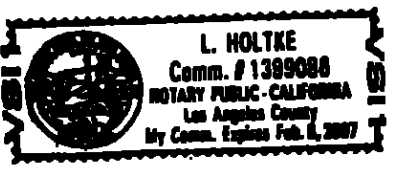
409

CALIFORNIA ALL-PURPOSE ACKNOWLEDGMENT

State of California }
County of VENTURA } ss.

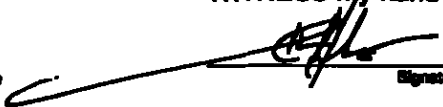
on 21 February 2006, before me, L. Holtke,
Name and Title of Officer (e.g., "Jane Doe, Notary Public")
personally appeared STUART L. WATTS,
Name(s) of Signer(s)

☒ personally known to me
☐ 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.

WITNESS my hand and official seal.

Place Notary Seal Above  Signature of Notary Public

OPTIONAL

Though the information below is not required by law, it may prove valuable to persons relying on the document and could prevent fraudulent removal and reattachment of this form to another document.

Description of Attached Document

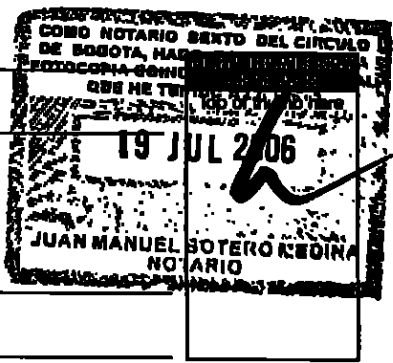
Title or Type of Document: REPRESENTATION, RATIFICATION + POWER OF ATTORNEY

Document Date: _____ Number of Pages: 2

Signer(s) Other Than Named Above: _____

Capacity(ies) Claimed by Signer

Signer's Name: STUART L. WATTS
☐ Individual
☒ Corporate Officer — Title(s) Vice President, Law
☐ Partner — ☐ Limited ☐ General
☐ Attorney in Fact
☐ Trustee
☐ Guardian or Conservator
☐ Other: _____



Signer is Representing: AUGER INC.

A-860C (0)

CORPORATE CERTIFICATE

State of California)
)
County of Ventura) SS:

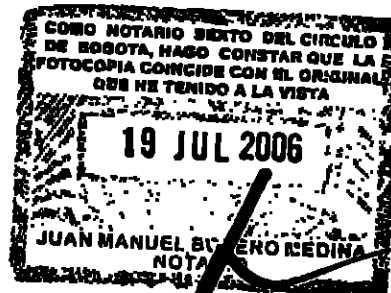
I, Stuart L. Watt, am the person who signed the foregoing instrument as Vice President, Law, of Amgen Inc., and I hereby certify the following:

1. That Amgen is a corporation duly organized and legally existing under the laws of the State of Delaware and is domiciled at One Amgen Center Drive, Thousand Oaks, California 91320-1799 USA.
2. That I am its legitimate Vice President in accordance with the appointment issued in the City of Los Angeles, California on June 27, 2000, by the Board of Directors of said corporation, which was duly elected by the General Meeting of Stockholders held in Los Angeles, California on May 11, 2000, as evidenced by the minutes, which I have seen, and I have the competence of representing same, including faculties to grant powers.
3. That I am duly authorized to sign the foregoing instrument in the name of said corporation in accordance with my above-mentioned position and/or with a resolution of the Board of Directors of said corporation, which I have seen, taken on June 27, 2000, in the City of Los Angeles, California.
4. That the purposes for which said instrument is granted are within the scope of the objects or activities of said corporation, in accordance with the Act of Incorporation issued in the City of Dover, Delaware and dated October 31, 1986, and/or the Amended and Restated By-Laws issued in the City of Thousand Oaks, California and dated April 11, 1996, both of which I have seen.

Karen Podgorny
Witness (Karen Podgorny)

Stuart L. Watt
Stuart L. Watt
Vice President, Law

Debbie Merrill
Witness (Debbie Merrill)

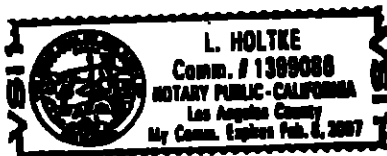


State of California)
)
County of Ventura) SS:

On this 22 day of February, 2006, before me, L. Holtke, Notary Public, personally appeared Stuart L. Watt, Vice President, Law, and Associate General Counsel, personally known to me to be the person, whose name is subscribed to the within instrument and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the instrument the person, or the entity upon behalf of which the person acted, executed the instrument.

Witness my hand and seal.

L. Holtke
Notary Public



A-860 (CO)

411

TRADUCCIÓN OFICIAL 161/2006 DE UN DOCUMENTO ESCRITO EN INGLÉS Y EN ESPAÑOL DE ACUERDO CON EL CUAL AMGEN INC., EMPRESA DOMICILIADA EN ONE AMGEN CENTER DRIVE THOUSAND OAKS, CALIFORNIA 91320 ESTADOS UNIDOS DE AMÉRICA RATIFICAN LAS SOLICITUDES DE PATENTE NOS. 06.014.624 Y 06.047.666 PRESENTADAS POR EMILIO FERRERO EL 14 DE FEBRERO DE 2006 Y EL 18 DE MAYO DE 2006 RESPECTIVAMENTE, COMO AGENTE OFICIOSO ANTE LA SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO EN BOGOTÁ Y OTORGA PODER A EMILIO FERRERO, TPA 31929, GONZALO PERDOMO, TPA 831; LUZ CLEMENCIA DE PAEZ, TPA 23555 Y A DANIEL PEÑA, TPA 65620.

EXPEDIDO Y FIRMADO HOY 24 DE FEBRERO DE 2006 POR STUART L. WATT, VICEPRESIDENTE ASUNTOS JURÍDICOS. FIRMADO EN THOUSAND OAKS, VENTURA COUNTY, CA, US.

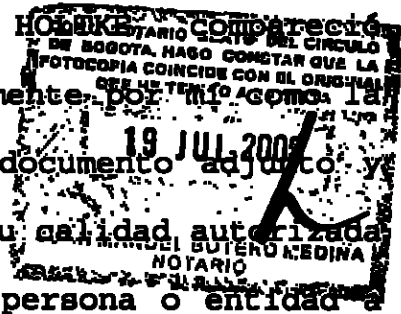
RE: SOLICITUD DE PATENTE PCTUS2004/022876

RECONOCIMIENTO MULTIPROPÓSITO DE CALIFORNIA

ESTADO DE CALIFORNIA

CONDADO DE VENTURA

DECLARACIÓN JURADA

El 24 de febrero de 2006, ante mi L.  comparecí personalmente STUART WATT, conocido personalmente por mí como la persona cuyo nombre aparece firmado en el documento adjunto, y reconoció ante mi haber firmado el mismo en su calidad autorizada y que mediante su firma en el documento la persona o entidad a nombre de la cual la persona actuaba, firmó el documento.

Atestiguo mediante mi firma y sello oficial

Firma ilegible

DESCRIPCIÓN DEL DOCUMENTO ADJUNTO:

Tipo de documento o título: REPRESENTACIÓN, RATIFICACIÓN Y PODER.

CALIDAD RECLAMADA POR EL FIRMANTE:

NOMBRE DEL FIRMANTE:

STUART L. WATT, VICEPRESIDENTE ASUNTOS JURÍDICOS

EL FIRMANTE REPRESENTA A AMGEN, INC.

412

CERTIFICADO SOCIETARIO

ESTADO DE CALIFORNIA, CONDADO DE VENTURA

DECLARACIÓN JURAMENTADA

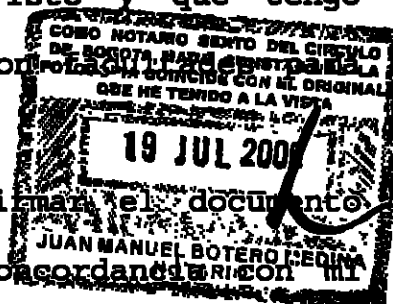
Yo, Stuart L. Watt, soy la persona que firmó el documento precedente en mi calidad de vicepresidente de asuntos jurídicos de Amgen Inc. y por la presente verifico lo siguiente:

1. Que Amgen es una sociedad debidamente constituida y legalmente existente de acuerdo con las leyes del estado de Delaware y se encuentra domiciliada en ONE AMGEN CENTER DRIVE, THOUSAND OAKS, CALIFORNIA 91320-1799, USA (Estados Unidos de América).

2. Que soy su vicepresidente legítimo de acuerdo con el nombramiento realizado en la ciudad de Los Angeles, California el 27 de junio de 2000 por la junta directiva de dicha empresa, que fue debidamente elegida por la reunión general de accionistas realizada en Los Angeles, California el 11 de mayo de 2000, tal como se evidencia por las actas que he visto y que tengo competencia para representarla, incluyendo con el poder otorgar poderes.

3. Que estoy debidamente autorizado para firmar el documento precedente a nombre de dicha sociedad en concordancia con el cargo arriba mencionado y/con una resolución de la junta directiva de dicha sociedad, que he visto, tomada el 27 de junio de 2000 en la ciudad de Los Angeles, California.

4. Que los objetos por los cuales se otorga dicho instrumento están bajo el alcance del objeto social de dicha empresa, en concordancia con el acta de constitución expedida en la ciudad de



Dover, Delaware y de fecha 31 de octubre de 1986 y con los estatutos reformados y reestructurados emitidos en la ciudad de Thousand Oaks, California y de fecha 11 de abril de 1986, los cuales ambos he visto. 413

FIRMADO: STUART L. WATT, vicepresidente asuntos jurídicos.

Firmado: dos testigos, Karen Podgorny y Debbie Merrill

ESTADO DE CALIFORNIA

CONDADO DE VENTURA

DECLARACION JURADA

Hoy 22 de febrero de 2006, ante mí, L HOLTKE, notario público, compareció personalmente STUART L. WATT, vicepresidente asuntos jurídicos, y abogado general asociado, de quien me consta es la persona cuyo nombre aparece escrito en el documento adjunto y reconoció ante mí haber firmado el mismo en su calidad autorizada, y que mediante su firma en el documento la persona o la entidad a nombre de la cual actuaba la persona, firmó el documento.

Atestiguo mediante mi firma y sello.

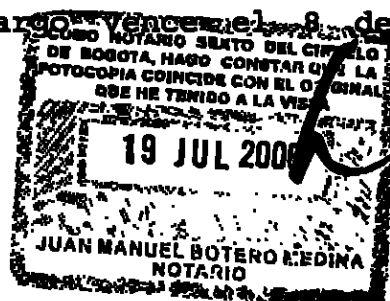
Firmado: (ilegible) notario público

SELLO: L HOLTKE, Nombramiento #139086, notario público, California. Condado de Los Angeles. Mi cargo vence el 8 de febrero de 2007.

ESTADO DE CALIFORNIA

SECRETARÍA DE ESTADO

APOSTILLA



(CONVENCIÓN DE LA HAYA DEL 5 DE OCTUBRE DE 1961)

1. PAIS: ESTADOS UNIDOS DE AMÉRICA

Este documento público

2. ha sido firmado por L. HOLTKE

3. quien actúa en su calidad de NOTARIO PÚBLICO, ESTADO DE CALIFORNIA

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4. y lleva el sello/estampilla de L. HOLTKE, notario público, estado de California.

CERTIFICADO

5. en Sacramento, California 6. el 8 de abril de 2006

7. por el Secretario de estado suplente del estado de California

8. Certificado número 281687

9. Sello: EL GRAN SELLO DEL ESTADO DE CALIFORNIA

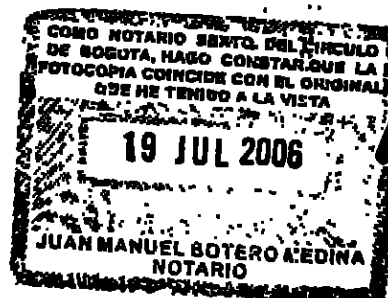
10. Firma: (ILEGIBLE)

COLO- 15193-841-001-7

WPCL002G ID 7879

Bogotá, 22 de junio de 2006.

Eduardo Calado
Eduardo Calado Noguera
"TRADUCTOR OFICIAL"
ESPAÑOL - ESPAÑOL
Dec. 31: Febrero de 1999



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COMO NOTARIO SEXTO DEL CIRCULO DE SANTAFE DE BOGOTA, HAGO CONSTAR QUE LA(S) FIRMA(S) DE Eduardo Calado Riquenza

CONCORDA CON LA FIRMA REGISTRADA POR EL CIRCULO EN ESTA FECHA 23 JUN 2006

SANTAFE DE BOGOTA



NO SE ASUME
RESPONSABILIDAD DEL TEXTO

2006 JUN 23 P 2:32

luc

JEFE DE LEGALIZACIONES
SANTAFE DE BOGOTA D.C.

MINISTERIO DE RELACIONES
EXTERIORES

071192

Eduardo Calado

ESTA FIRMA APARECE EN EL
DOCUMENTO DESEMPENA
LAS FUNCIONES INDICADAS

COMO NOTARIO SEXTO DEL CIRCULO DE BOGOTA, HAGO CONSTAR QUE LA FOTOCOPIA COINCIDE CON EL ORIGINAL QUE HE TENIDO A LA VISTA

19 JUL 2006

JUAN CARLOS MEDINA
NOTARIO