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AS: 102.976

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-012628-00002-0000

Señores

SUPERINTENDENCIA DE INDUST.

DIVISION DE NUEVAS CREACIONES

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Fecha: 2007-05-07 16:16:29 Dep. 2020 NUECREACIONE
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Act 444 RESPUESTAREQUE Folios: 44

RESPUESTA A OFICIO 3274 DEL 09 DE MARZO, 2007

REF: Expediente No. 07 012.528 - Solicitud de Patente FASE NACIONAL

Corresp. a la Solicitud Internacional PCT/US2005/027626

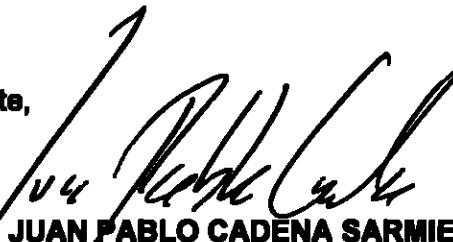
a favor de GENENTECH, INC.

Titulada: ANTAGONISTAS HUMANIZADOS ANTI-CMET

JUAN PABLO CADENA SARMIENTO, vecino de Bogotá, portador de la tarjeta profesional No. 57492, obrando como apoderado de la sociedad GENENTECH, INC., según lo acredita el documento de poder presentado en esa División, para dar cumplimiento al requerimiento notificado por fijación en lista el 09 de Marzo de 2007, y de acuerdo con los Artículos 38 y 39 de la Decisión 486 de la Comisión de la Comunidad Andina, Artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la SIC, me permito allegar:

1. Dos (2) documentos donde consta la cesión del derecho a la Patente otorgado por los inventores al solicitante, debidamente apostillados, junto con sus correspondientes traducciones al castellano.
2. Reporte Preliminar Internacional sobre Patentabilidad (Formas PCT/IB/373 y PCT/ISA/237).
3. Extracto para publicación y Tarjeta de Archivo Temático.

De la señora jefe atentamente,


JUAN PABLO CADENA SARMIENTO
C.C. No. 80.410.337 de Usaquén
Cra 7 No. 71-21 TORRE B - Piso 4

Bogotá, 07 de mayo de 2007
CHP/MEV/har.

(21) N° de solicitud: 07 012.528 (22) Fecha de solicitud: 08-02-2007

(51) Clasificación internacional:

(71) Solicitante(s) GENENTECH, INC.

(72) Inventor(es) Mark S. Dennis, Karen Billeci, Yudy Young, Zhong Zheng

(74) Agente: JUAN PABLO CADENA SARMIENTO

(30) Prioridad	(31) No. Prioridad	(32) Fecha	(33) País
	60/598,991	05-08-2004	US

FIGURA CARACTERISTICA
6 x 6 cm

(85) Fecha inicio fase nacional: 05-03-2007

(86) Datos relativos a la presentación de la solíc. PCT

Fecha de presentación de la solicitud: 04-08-2005

No. de solicitud PCT/US2005/027628

(87) Publicación internacional:

Fecha: 09-02-2006

No. Publicación: WO/2006/015371 A3

(54) Título: ANTAGONISTAS HUMANIZADOS ANTI-CMET

(57) Reivindicación(es): 1. Un anticuerpo anti-c-met que comprende:

(a) por lo menos una secuencia HVR seleccionada entre el grupo conformado por:

CONTINUA AL RESPALDO ...

- (i) HVR-L1 que comprende la secuencia A1-A17, donde A1-A17 es KSSQSLLYTSSQKNYLA (SEQ ID No: 1)
- (ii) HVR-L2 que comprende la secuencia B 1-B7, donde B 1-B7 es WASTRES (SEQ ID No:2)
- (iii) HVR-L3 que comprende la secuencia C1-C9, donde C1-C9 es QQYYAYPWT (SEQ ID No:3)
- (iv) HVR-H1 que comprende la secuencia D1-D10, donde D1-D10 es GYTFTSYWLH (SEQ ID No:4)
- (v) HVR-H2 que comprende la secuencia E1-E18, donde E1-E18 es GMIDPSNSDTRFNP NFKD (SEQ ID No:5)
- (vi) HVR-H3 que comprende la secuencia F1-F11, donde F1-F11 es XYGSYVSPLDY (SEQ ID No:6) y X no es R; y

- (b) por lo menos una variante HVR, donde la variante HVR comprende la modificación de por lo menos un residuo de la secuencia representada en SEQ ID No: 1, 2, 3, 4, 5 o 6.

- 2. El anticuerpo de la reivindicación 1, donde F1 en una variante HVR-H3 es T o S, F3 es R o S y F7 es T.
- 3. El anticuerpo de la reivindicación 1, donde el anticuerpo es humanizado.

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 Industria y Comercio SUPERINTENDENCIA		SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO DIVISION DE NUEVAS CREACIONES EXTRACTO PARA PUBLICACIÓN SOLICITUD DE PATENTE DE INVENCION PCT	
(1) N° de solicitud: 07 012.528 22) Fecha de solicitud: 08-02-2007 (30) Prioridad (31) No. Prioridad (32) Fecha (33) Pais 60/598,991 05-08-2004 US		(51) Int Cl: (71) Solicitante(s): GENENTECH, INC. (72) Inventor(es): Mark S. Dennis, Karen Bileci, Yudy Young, Zhong Zheng (74) Agente: JUAN PABLO CADENA SARMIENTO	
(85) Fecha inicio fase nacional: 05-03-2007 (86) Datos relativos a la presentación de la solicitud PCT Fecha de presentación de la solicitud: 04-08-2005 No. de solicitud PCT/US2005/027628		(87) Publicación internacional Fecha: 09-02-2008 N° publicación: WO/2008/015371 A3	
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 - (vi) HVR-H3 que comprende la secuencia F1-F11, donde F1-F11 es XYGSYVSPLDY (SEQ ID No:6) y X no es R; y
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2. El anticuerpo de la reivindicación 1, donde F1 en una variante HVR-H3 es T o S, F3 es R o S y F7 es T.
 3. El anticuerpo de la reivindicación 1, donde el anticuerpo es humanizado.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference P2138R1	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2005/027826	International filing date (day/month/year) 04 August 2005 (04.08.2005)	Priority date (day/month/year) 05 August 2004 (05.08.2004)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant GENENTECH, INC.			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 14 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | |
|--|---|
| ☒ 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 |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Date of issuance of this report 08 February 2007 (08.02.2007)
	Authorized officer Yolaine Cussac e-mail: pt11.pct@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 29 MAY 2006

WIPO

PC

PCT

To:

see form PCT/ISA/220

PTU
AP

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

Date of mailing

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

Applicant's or agent's file reference

see form PCT/ISA/220

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US2005/027626

International filing date (day/month/year)

04.08.2005

Priority date (day/month/year)

05.08.2004

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

INV. C07K16/28 C07K16/48 A61K39/395 A61P35/00 C12N15/13 C12N1/21

Applicant

GENENTECH, INC.

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

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Tel. +31 70 340 - 2040 Tx: 31 651 apo nl
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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Luyten, K

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

516
International application No.
PCT/US2005/027626

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. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ on paper
 - ☒ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ 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.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/027626

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

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. 1-34 (all partially); 45 (partially) and 46-50 (all completely) with respect to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 45 (partially) and 46-50 (all completely) with respect to industrial applicability relate to the following subject matter which does not require an international search (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-34 (all partially) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☒ the claims, or said claims Nos. 1-34 (all partially) are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ no international search report has been established for the whole application or for said claims Nos.

- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

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

- ☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

8 518
International application No.
PCT/US2005/027626

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

1. Statement

Novelty (N)	Yes: Claims	1-14, 20-23, 36-37, 42-44 and 48
	No: Claims	15-19, 24-35, 38-41, 45-47 and 49-54
Inventive step (IS)	Yes: Claims	
	No: Claims	1-54
Industrial applicability (IA)	Yes: Claims	1-44, 51-54
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.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 III

- 1 The antibodies of claims 1-14 and 20-23 are defined by comprising "at least one variant HVR, wherein the variant HVR comprises modification of at least one residue", therefore claims 1-14 and 20-23 relate to an extremely large number of possible antibodies. However, the description does provide support and disclosure in the sense of Article 6 and 5 PCT for only a very small proportion of the antibodies claimed (Examples and Figure 4; see also Section VIII 1.1-1.2).

Claims 15-19 and 24-34 relate to a humanized anti-c-met antibody which has a given desired property or effect. Support and disclosure is given for only a few antibodies having said property or effect and it is not known to the person skilled in the art which humanized anti-c-met antibodies will have said properties (see Section VIII, 1.3).

The non-compliance with the substantive provisions is to such an extent, that the search of claims 1-34 was restricted to the specifically disclosed 5D5 variants which have a higher affinity than the monovalent affinity of murine 5D5 (8.3 nM; description page 97, last line; Figure 4), i.e. the 5D5 variants #92, #78 (=rhuOA-5D5.v2), #75 and #95 (the search was done based on the sequence information available for these variants).

- 2 Claims 45 (partially, as far as an in vivo method is concerned) and 46-50 (all completely) 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).

SECTION V

1 PRIOR ART

1.1 Reference is made to the following documents:

D1: WO 96/38557 A1 (GENENTECH, INC; Schwall, Ralph, H; Tabor, Kelly, Helen)

5 December 1996 (1996-12-05) cited in the application

- D2: Morton P A et al: "In vitro and In vivo activity of fully-human monoclonal antibodies to c-met protein tyrosine kinase" Proceedings of the Annual Meeting of the American Association for Cancer Research, New York, NY, US, vol. 44, July 2003 (2003-07), page 1116, XP001194900 ISSN: 0197-016X
- D3: WO 2004/016769 A (ABGENIX, INC; Gudas, Jean, M; Haak-Frendscho, Mary; Foord, Orit; Liang) 26 February 2004 (2004-02-26)
- D4: LEE C V et al: "High-affinity Human Antibodies from Phage-displayed Synthetic Fab Libraries with a Single Framework Scaffold" Journal of Molecular Biology, London, GB, vol. 340, no. 5, 23 July 2004 (2004-07-23), pages 1073-1093, XP004518119 ISSN: 0022-2836 cited in the application

- 1.2 Document D1 discloses the production and characterization of the murine anti-c-met antibody 5D5, and the DNA cloning, sequencing, expression (*E. coli*) and characterization of the 5D5 Fab (Examples 1-2 and 10-15). SEQ ID NO: 1-6, 183-185 and 191-192 of the present application are 100% identical to the HVRs of 5D5. D1 also discloses a method of inhibiting c-met activated cell proliferation, wherein BaF3 cells expressing human c-met are contacted with the 5D5 Fab and block cell proliferation in the presence of HGF (hepatocyte growth factor) (Example 9A). D1 suggests and claims the use of an c-met (HGF receptor) antagonist, e.g. an antibody, for treating cancer (whole document).
- 1.3 Document D2 discloses human anti-c-met antibodies (scFvs) that inhibit binding of hepatocyte growth factor to c-met with an IC50 of less than 50 nM. D2 also discloses fully-human anti-c-met IgG1 with an affinity for c-met in the range of 0.8 to 55 nM measured using a BIAcore assay. These antibodies compete with HGF for c-met binding at 0.45-2.9 mM. The anti-c-met IgGs of D2 stimulate c-met activity, and only inhibit c-met dependent cell proliferation at concentrations higher than 100 nM. D2 furthermore suggests the use of affinity-matured monovalent versions of fully-human c-met IgG to modulate c-met activity in human cancers (whole document).
- 1.4 Document D3 discloses an anti-MCP-1 antibody comprising a light chain variable domain, which comprises HVR2-LC/SEQ ID NO: 184, FR4-LC/SEQ ID NO: 182, and the CL1 sequence according to SEQ ID NO: 186 of the present application (D3, SEQ

ID NO: 92).

- 1.5 Document D4 discloses a method for the affinity maturation of human antibodies by using HVR (CDR) diversity libraries. This approach was used to select an anti-mVEGF antibody with sub-nanomolar affinity (0.016 nM) (whole document).

2 NOVELTY (Art. 33(2) PCT)

- 2.1 The anti-c-met antibody of D1 contains the six HVRs according to SEQ ID NO: 1 to 6, but does not contain a variant HVR. Therefore, claim 1 is novel over D1. No other document appears to disclose an anti-c-met antibody with a variant HVR-H3 according to the SEQ ID NO: 175 to 178 (5D5 variants #92, #78, #75 and #95). Thus, claims 1-14 and 20-23 appear, to be novel. Though, note that claim 1 has been searched only partially due to lack of clarity and support (see Sections III and VIII).

- 2.2 The humanized anti-c-met antibodies of independent claims 15, 16, 24, 27 and 30 are defined by the result to be achieved, whereby the desired functions, "monovalent affinity for human c-met", "inhibits binding human hepatocyte growth factor to its receptor", "inhibits human hepatocyte growth factor (HGF) receptor activation", or "inhibits c-met-dependent cell proliferation" are compared to a reference antibody. The human anti-c-met scFvs and IgGs of document D2 have not been tested in comparison with the same reference antibody as in the application, however, it appears that their affinity for human c-met and binding inhibition (IC50) fall within the same range as for the antibodies of the examples and the antibodies as claimed. Therefore, claims 15-19, 24-26 and 33-34 are not novel over D2. Although, the anti-c-met IgGs of D2 stimulate c-met activity, and only inhibit cell proliferation at concentrations higher than 100 nM, no data are provided in D2 with respect to the anti-c-met scFvs and their effect on c-met activation and c-met dependent cell proliferation. But, the anti-c-met scFvs might have the functional features of the antibodies of claims 27-32, and therefore D2 also anticipates the novelty of claims 27-32.

- 2.3 The 5D5 antibody of document D1 comprises a heavy chain variable domain comprising HVR1-HC and HVR2-HC (SEQ ID NO: 191 and 192) and a light chain

variable domain comprising HVR1-LC, HVR2-LC and HVR3-LC (SEQ ID NO: 183-185). Therefore, D1 anticipates the novelty of claims 35, 38 and 41. D1 does not comprise any of the framework (FR) or constant regions (CH1, Fc) of claims 36 and 37, therefore claims 36 and 37 appear to be novel over D1. The 5D5 antibodies of D1 are either monovalent (Fab) or comprise an Fc region (IgG1/Kappa), but D1 does not disclose an 5D5 antibody that is both monovalent and comprises an Fc region. Therefore, claims 42-44 are novel over D1. D1 also disclose the nucleic acid encoding a 5D5 antibody, a host cell carrying said nucleic acid and compositions containing a 5D5 antibody. Thus, claims 51-53 are not novel over D1. Since, the term "carrier" is very broad and also covers a buffer, D1 also anticipates the novelty of claim 54.

- 2.4 The anti-MCP-1 antibody of document D3 comprises a light chain variable domain, which comprises HVR2-LC/SEQ ID NO: 184, FR4-LC/SEQ ID NO: 182 and the CL1 sequence according to SEQ ID NO: 186, therefore D3 anticipates the novelty of claims 38-40.
- 2.5 The method of inhibiting c-met activated cell proliferation using the anti-c-met 5D5 Fab as in D1, anticipates the novelty of claim 45.
- 2.6 Due to the broad definition of the disease (disease associated with dysregulation of the HGF/c-met signaling axis (claim 46); proliferative disorder (claim 49)) and/or the antibodies, the use of an anti-c-met antibody as in documents D1 and D2 for treating cancer, anticipates the novelty of claims 46-47 and 49-50. Though, neither D1 nor D2 disclose the use of an anti-c-met antibody for treating lung cancer, brain cancer, kidney cancer, gastric cancer, colorectal cancer and/or pancreatic cancer. Therefore, claim 48 appears to be novel over D1 and D2.
- 2.7 Thus, claims 1-14, 20-23, 36-37, 42-44 and 48 appear to be novel. Though, the present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 15-19, 24-35, 38-41, 45-47 and 49-54 is not new in the sense of Article 33(2) PCT.

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

- 3.1 Document D1 is regarded as being the closest prior art to the subject-matter of claims 1-14, 20-23, 36-37, 42-44 and 48.
- 3.2 Said claims differ from document D1 in that the sequence of the (anti-c-met) antibody is different (claims 1, 36-37, 42-44) or that the cancer to be treated is lung cancer, brain cancer, kidney cancer, gastric cancer, colorectal cancer or pancreatic cancer (claim 48). The effect of these differences is not known. The problems to be solved by the present invention may therefore be regarded as providing an alternative anti-c-met antibody (claim 1), providing an alternative antibody (claims 36-37, 42-44) or selecting a cancer to be treated with an antibody (claim 48).
- 3.3 The solutions as in claims 1, 36-37 and 42-44 are not solving the problem posed, since the antigen-binding domain of the antibodies is not fully defined. Only antibodies of which the full heavy and light chain variable regions are defined can be considered to have the characteristics and properties of the antibodies exemplified in the application (see also Section VIII, 1.1-1.2). For the same reasons claims 2-14, 20-23 are not solving the problems posed.
- 3.4 The solution as in claim 48 is also not solving the problem posed, since there is no support in the description for the medical use of the broad range of antibodies of claim 48.
- 3.5 If a new independent claim would be provided that is limited to fully-defined antibodies with support in the description, i.e. humanized anti-c-met antibodies comprising a light chain variable domain and a heavy chain variable domain of one of the following 5D5 variants: #92, #78, #75 or #95 (see Figure 4), whereby the antibodies are defined by the full sequence of both the heavy and light chain variable domains by means of the relevant SEQ ID NOs, an inventive step would still be missing for the following reason:

Said claim would differ from document D1 in that the anti-c-met antibody contains a human framework and that the HVR-H3 differs in sequence. The effect of the different HVR-H3 sequence is that said antibodies have a higher affinity than the

murine 5D5 of D1. The problem to be solved by the present invention may therefore be regarded as providing a humanized anti-c-met antibody with a higher affinity than the murine 5D5 (8.3 nM). D2 already discloses human anti-c-met antibodies with an affinity of 0.8 nM. Moreover, methods for affinity maturation of antibodies are known to the person skilled in the art. For example in document D4 picomolar affinities, 0.016 nM, were obtained for an anti-mVEGF Fab. Thus, it would be a routine procedure for the person skilled in the art to produce, starting from the murine 5D5, a humanized anti-c-met antibody with a higher affinity than 5D5. Therefore, said antibodies do not involve an inventive step.

Though, if the antibodies of the present application would show a surprising effect in vivo, i.e. if they would be more efficient in an in vivo pancreatic tumor model than the murine 5D5, then the antibodies and the use of said antibodies for preparing a medicament would be inventive. However, the present application lacks comparative experimental data to support a surprising effect.

- 3.6 In view of the above, the present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 1-14, 20-23, 36-37, 42-44 and 48 does not involve an inventive step in the sense of Article 56 EPC.

4 INDUSTRIAL APPLICABILITY (Art. 33(4) PCT)

- 4.1 For the assessment of the present claims 45-50 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.

SECTION VI

WO 2005/016382 A (PFIZER PRODUCTS INC; ABGENIX, INC; Michaud, Neil R; Kajiji, Shama; Bor), 24 February 2005 (2005-02-24), Filing date: 4 August 2004,

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

14 525
International application No.

PCT/US2005/027626

Priority date: 4 August 2003.

WO 2004/072117 A (PHARMACIA CORPORATION; Morton, Phillip, A; Arbuckle, J.,
Alan; Evans, M), 26 August 2004 (2004-08-26), Filing date: 11 February 2004,
Priority date: 13 February 2003.

SECTION VIII

1 CLARITY AND SUPPORT (Art. 6 PCT)

- 1.1** An antibody is structurally made of two light and two heavy chains and the combination of the heavy and light chain variable regions confers the antigen-binding properties. As is shown in the present examples, changing just one amino acid residue in either one of the HVRs or in one of the framework sequences can drastically change the antigen-binding affinity or even abolish binding of the antibody. Therefore, to define an antibody by structural features, the sequence of the full heavy and light chain variable regions of the antibody should be specified. However, in claims 1-14, 20-23 and 35-44 the variable regions are only partially defined. Therefore the antibodies are not clearly defined and claims 1-14, 20-23 and 35-44 do not meet the requirements of Article 6 PCT.
- 1.2** Claims 1-14, 20-23 and 35-44 are not only unclear, they are also very broad due to the different possible variations as a result of expressions like e.g. "at least one HVR", "at least one variant HVR", "modifications of at least one residue", "at least a portion", "substitutions in any combination of the following positions", "variable domain comprising HVR1, HVR2, and/or HVR3" and "comprises one or more mutations". However, the antigen-binding properties of all these possible antibodies are not disclosed, affinity data are only provided for selected clones (see Figure 4). Therefore, claims 1-14, 20-23 and 35-44 lack support. Also claims 50-54 related to a nucleic acid, host cell or composition comprising an antibody of any of said claims are not supported.
- 1.3** Claims 15-19 and 24-34 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, "wherein monovalent affinity of the antibody to human c-met is substantially the same as/at least 3-fold greater than monovalent affinity of a reference antibody", "inhibits binding human hepatocyte growth factor to its receptor better than a reference antibody", "Inhibits human hepatocyte growth factor (HGF) receptor activation better than a reference antibody", or "inhibits c-met-dependent cell proliferation better than a reference

antibody" wherein the reference antibody comprises a light and heavy chain variable sequence according SEQ ID NO: 9 and 10. This merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result. Therefore, said claims lack clarity and support.

- 1.4 Claims 45-49 are not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description and drawings. The reasons therefore are the following: the description only provides support for a method of inhibiting c-met activated cell proliferation, comprising contacting a cell with antibody rhuOA-5D5.v2 (claim 45) and the use of antibody rhuOA-5D5.v2 for treating pancreatic cancer (claims 46-49).
- 1.5 In the medical use claims 46 and 49 the therapeutic application is functionally defined by a mechanism of action (disease associated with dysregulation of the HGF/c-met signaling axis; proliferative disorder) which does not allow any practical application in the form of a defined, real treatment of a pathological condition (disease). Therefore, said claims are unclear.
- 1.6 Claims 15-16, 24, 27, 30, 35-40 and 44 do not meet the requirements of Rule 6.2(a) PCT, since they contain references to the Figures, There is no reason to refer to the Figures, since the technical features can be defined by the SEQ ID NOs.
- 1.7 Since it is unclear whether features within parentheses in the claims are limiting or not, the use of brackets in the claims should be avoided.
- 1.8 The application does not meet the requirements of Article 6 PCT, because claims 1-54 are not clear and/or lack support.

DOCUMENT OF ASSIGNMENT OF
PATENT APPLICATION

ASSIGNMENT

The Undersigned
Karen BILLECI
Judy YOUNG
Zhong ZHENG

acting as inventors
of Colombian Patent Appln. No. 07012.528
Entitled: **HUMANIZED ANTI-CMET
ANTAGONISTS**

with domiciles in:
5247 Shelter Creek Lane
San Bruno, California 94066 USA

2833 Tramanto Drive
San Carlos, California 94070 USA

1175 Balclutha Drive
Foster City, California 94404 USA

hereby declare(s) that they(he) assigns all
rights of ownership as well as all rights and
privileges relating thereto without exception over
the following patent application in Colombia:

Colombian Patent Appln. No. 07012.528
Entitled: **HUMANIZED ANTI-CMET
ANTAGONISTS**

to GENENTECH, INC.

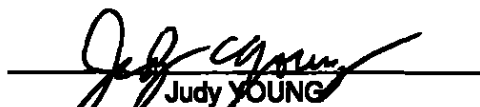
domiciled in 1DNA Way, South San Francisco,
CA 94080-4990., USA.

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

Given and signed on the 5th day of March of
2007

Signature of Assignors


Karen BILLECI


Judy YOUNG


Zhong ZHENG

Given and signed on the 5th day of March of
2007

Signature of Assignee


Timothy R. Schwartz
Associate General Counsel - Director
Genentech, Inc.
Authorized Corporate Signatory

DOCUMENTO DE TRASPASO DE
SOLICITUD DE PATENTE

CESION

Los Suacritos
Karen BILLECI
Judy YOUNG
Zhong ZHENG

en calidad de inventor
de la Sol. de Patente Colombiana No.
07012.528

Titulada: **HUMANIZED ANTI-CMET
ANTAGONISTS**

con domicilios en
5247 Shelter Creek Lane
San Bruno, California 94066 EUA

2833 Tramanto Drive
San Carlos, California 94070 EUA

1175 Balclutha Drive
Foster City, California 94404 EUA

declara por el presente documento que cede
todos los derechos de propiedad que le
correspondan, así como las prerrogativas, sin
excepción alguna, sobre la siguiente solicitud de
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Sol. de Patente Colombiana No. 07012.528
Titulada: **HUMANIZED ANTI-CMET
ANTAGONISTS**

a GENENTECH, INC.

domiciliada en 1 DNA Way, South San
Francisco, CA 94080-4990., EUA.

El cedente y el cesionario firman este
documento como prueba de su aceptación de la
cesión.

Dado y firmado a los días del mes de
de 2007

Firma del Cedente

Firma del Cesionario

(see attached California
All-Purpose acknowledgments)

19 524
State of California

SECRETARY OF STATE

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5. *At Sacramento, California*
6. *the 7th day of March 2007*
7. *by Deputy Secretary of State, State of California*
8. *No. 363160*
9. *Seal/Stamp:*

10. *Signature*



Jana Bowen
Secretary of State



70 530

ALIF RNIA ALL-PURPOSE ACKN WLEDGMENT

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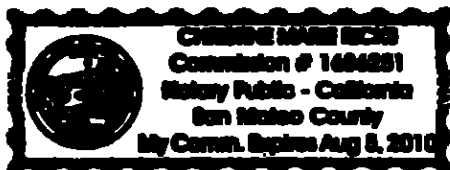
On March 5, 2007 before me, Christine Ricks, Notary Public
Date Name and Title of Officer (e.g., "Jane Doe, Notary Public")

personally appeared Karen Billeci
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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.



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Title or Type of Document: Assignment - Colombia

Document Date: March 5, 2007 Number of Pages: 1

Signer(s) Other Than Named Above: Judy Young, Zhang Zheng, Timothy R. Schwartz

Capacity(ies) Claimed by Signer(s)

Signer's Name: Karen Billeci

☒ Individual

☐ Corporate Officer — Title(s): _____

☐ Partner — ☐ Limited ☐ General

☐ Attorney In Fact

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Signer Is Representing: _____



Signer's Name: _____

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Jana Bowen
Secretary of State



22532

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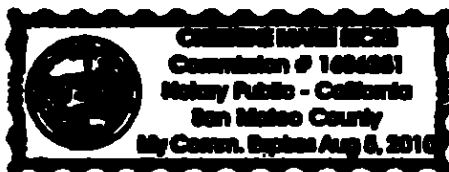
On March 5, 2007 before me, Christine Ricks, Notary Public

personally appeared Judy Young

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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.



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Signer's Name: Judy Young

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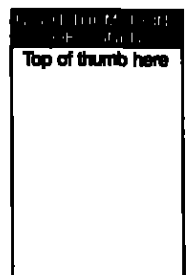
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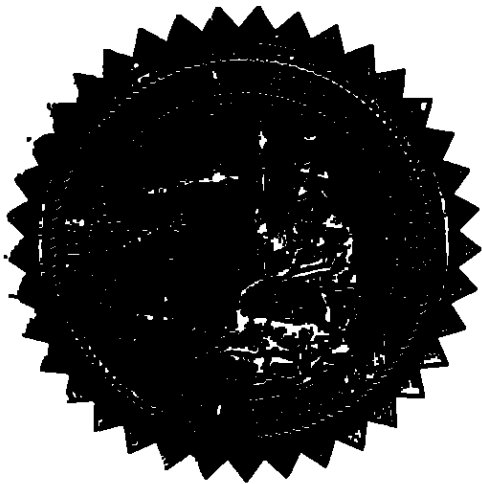
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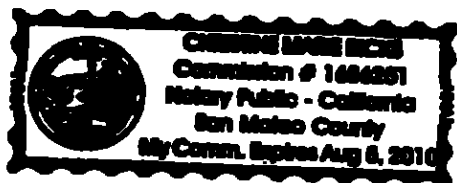
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☐ Partner — ☐ Limited ☐ General

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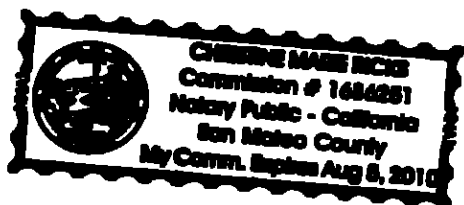
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Signer's Name: Timothy R. Schwartz
☐ Individual
☒ Corporate Officer — Title(s): Associate General Counsel, Director
☐ Partner — ☐ Limited ☐ General
☐ Attorney in Fact
☐ Trustee
☐ Guardian or Conservator
☐ Other: _____

Signer Is Representing: Genentech, Inc.



Signer's Name: _____
☐ Individual
☐ Corporate Officer — Title(s): _____
☐ Partner — ☐ Limited ☐ General
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☐ Trustee
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7A 537

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CERTIFICADO

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78 538

ACUERDO PARA TODO TIPO DE PROPÓSITOS DE CALIFORNIA

Estado de California)
) ss.
Condado de San Mateo)

El Marzo 5, 2007, ante mi Christine Ricks, Notario Público
Fecha Nombre y Título del Funcionario (ej. "Jane Doe, Notario Público")
se presentó Karen Billeci
Nombre(s) del Firmante(s)

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KIYOKO SHIMIZU
Comisión # 1527444
Notario Público – California
Condado de San Diego
Mi Comisión Vence Nov. 18, 2008

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Firmante(s) Además de los Nombrados Arriba: Judy Young, Zhong Zheng, Timothy R. Schwartz

Capacidad(es) Reclamada(s) por el Firmante(s)
Nombre del Firmante: Karen Billeci

☒ Individuo
☐ Funcionario Corporativo – Título(s): _____

☐ Socio - ☐ Limitado ☐ General
☐ Abogado de Hecho
☐ Fiado
☐ Tutor Legal o Conservador
☐ Otro: _____

El Firmante Representa a:

HUELLA DACTILAR
DERECHA DEL
FIRMANTE

Capacidad(es) Reclamada(s) por el
Nombre del Firmante: _____

☐ Individuo
☐ Funcionario Corporativo – Título(s): _____

☐ Socio - ☐ Limitado ☐ General
☐ Abogado de Hecho
☐ Fiado
☐ Tutor Legal o Conservador
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El Firmante Representa a:

HUELLA DACTILAR
DERECHA DEL
FIRMANTE

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ESTADO DE CALIFORNIA

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6. el 7mo día de Marzo de 2007
7. por el Secretario de Estado Encargado, Estado de California
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9. Sello/Timbre

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20 5401

ACUERDO PARA TODO TIPO DE PROPÓSITOS DE CALIFORNIA

Estado de California)
) ss.
Condado de San Mateo)

El Marzo 5, 2007, ante mi Christine Ricks, Notario Público
Fecha Nombre y Título del Funcionario (ej. "Jane Doe, Notario Público")
se presentó Judy Young
Nombre(s) del Firmante(s)

Hay un sello que dice:

KIYOKO SHIMIZU
Comisión # 1527444
Notario Público – California
Condado de San Diego
Mi Comisión Vence Nov. 18, 2008

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EN TESTIMONIO, mi firma y sello oficial.

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Capacidad(es) Reclamada(s) por el Firmante(s)
Nombre del Firmante: Judy Young

☒ Individuo
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☐ Fiado
☐ Tutor Legal o Conservador
☐ Otro: _____

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☐ Individuo
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Secretario de Estado

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ACUERDO PARA TODO TIPO DE PROPÓSITOS DE CALIFORNIA

Estado de California)
) ss.
Condado de San Mateo)

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Fecha Nombre y Título del Funcionario (e). "Jane Doe, Notario Público")
se presentó Zhong Zheng
Nombre(s) del Firmante(s)

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Comisión # 1527444
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Mi Comisión Vence Nov. 18, 2008

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Título o Tipo de Documento: Cesión - Colombia

Fecha del Documento: Marzo 5, 2007

Firmante(s) Además de los Nombrados Arriba: Judy Young, Zhong Zheng, Timothy R. Schwartz

Capacidad(es) Reclamada(s) por el Firmante(s)

Nombre del Firmante: Zhong Zheng

☒ Individuo

☐ Funcionario Corporativo - Título(s): _____

☐ Socio - ☐ Limitado ☐ General

☐ Abogado de Hecho

☐ Fido

☐ Tutor Legal o Conservador

☐ Otro: _____

El Firmante Representa a:

HUELLA DACTILAR
DERECHA DEL
FIRMANTE

Capacidad(es) Reclamada(s) por el

Nombre del Firmante: _____

☐ Individuo

☐ Funcionario Corporativo - Título(s): _____

☐ Socio - ☐ Limitado ☐ General

☐ Abogado de Hecho

☐ Fido

☐ Tutor Legal o Conservador

☐ Otro: _____

El Firmante Representa a:

HUELLA DACTILAR
DERECHA DEL
FIRMANTE

37 543
ESTADO DE CALIFORNIA

[Sello]

SECRETARIO DE ESTADO

APOSTILLA

(Convención de la Haya del 5 de Octubre 1961)

1. País: Estados Unidos de América
Este documento público
2. ha sido firmado por Christine Marie Ricks
3. actuando en capacidad de Notario Público, Estado de California
4. lleva el sello/timbre de Christine Marie Ricks, Notario Público
Estado de California

CERTIFICADO

5. En Sacramento, California
6. el 7mo día de Marzo de 2007
7. por el Secretario de Estado Encargado, Estado de California
8. No. 363163
9. Sello/Timbre

Hay un sello que dice:

10. Firma

**EL GRAN SELLO DE
EL ESTADO DE CALIFORNIA**

(firma)
Secretario de Estado

3F 544

ACUERDO PARA TODO TIPO DE PROPÓSITOS DE CALIFORNIA

Estado de California)
) ss.
Condado de San Mateo)

El Marzo 5, 2007, ante mi Christine Ricks, Notario Público,
Fecha Nombre y Título del Funcionario (e). "Jane Doe, Notario Público")
se presentó Timothy R. Schwartz, Ph.D.
Nombre(s) del Firmante(s)

Hay un sello que dice:

KIYOKO SHIMIZU
Comisión # 1527444
Notario Público - California
Condado de San Diego
Mi Comisión Vence Nov. 18, 2008

Colocar sello notarial arriba

☐ personalmente conocido por mi

☒ probado ante mi en base a evidencia satisfactoria que es la(s) persona(s) cuyo nombre(s) está(n) suscrito(s) al Instrumento presente y reconoció ante mi que el/ella/ellos ejecutaron la misma en su/sus capacidad(es) autorizada(s), y que por su/sus firma(s) en el instrumento las personas o la entidad en nombre de la cual la persona actuó ejecutó el Instrumento.

EN TESTIMONIO, mi firma y sello oficial.

(firma)

Firma del Notario Público

OPCIONAL

Aunque la información de abajo no es requerida por la ley, puede ser valiosa para personas que cuentan con el documento y podría evitar la remoción fraudulenta de este formato y su sujeción a otro documento

Descripción del Documento Anexo

Título o Tipo de Documento: Cesión - Colombia

Fecha del Documento: Marzo 5, 2007

Firmante(s) Además de los Nombrados Arriba: Judy Young, Zhong Zheng, Timothy R. Schwartz

Capacidad(es) Reclamada(s) por el Firmante(s)

Nombre del Firmante: Timothy R. Schwartz, Director

☒ Individuo Consejero General Asociado
☐ Funcionario Corporativo - Título(s): _____

☐ Socio - ☐ Limitado ☐ General
☐ Abogado de Hecho
☐ Fido
☐ Tutor Legal o Conservador
☐ Otro: _____

El Firmante Representa a:
Genentech, Inc.

HUELLA DACTILAR
DERECHA DEL
FIRMANTE

Capacidad(es) Reclamada(s) por el

Nombre del Firmante: _____

☐ Individuo
☐ Funcionario Corporativo - Título(s): _____

☐ Socio - ☐ Limitado ☐ General
☐ Abogado de Hecho
☐ Fido
☐ Tutor Legal o Conservador
☐ Otro: _____

El Firmante Representa a:

HUELLA DACTILAR
DERECHA DEL
FIRMANTE

36

545 (2/2)

APOSTILLE
(Convention de La Haye du 5 octobre 1961)

1. Country: United States of America

This public document
2. has been signed by E. Bornett

3. acting in the capacity of Certifying Officer

4. bears the seal/stamp of U.S. Patent and Trademark Office

Certified

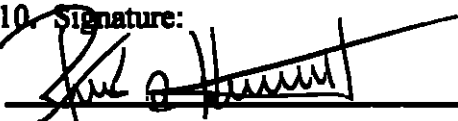
5. at Washington, D.C.

6. the thirteenth of March, 2007

7. by Assistant Authentication Officer, United States Department of State

8. No. 07016037-1

9. Seal/Stamp:

10. Signature:

Patrick O. Hatchett

77 546

A 7081388



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

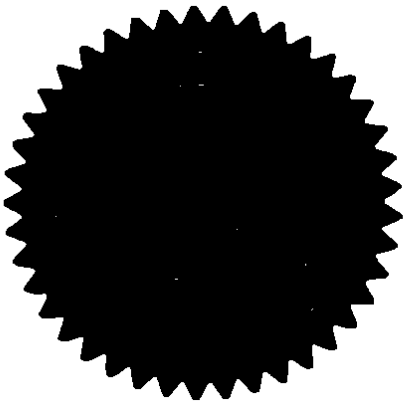
**UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office**

February 07, 2007

**THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE
RECORDS OF THIS OFFICE OF A DOCUMENT RECORDED ON
NOVEMBER 19, 2004.**

**By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office**


**E. BORNETT
Certifying Officer**



547

RECORDATION FORM COVER SHEET
PATENTS ONLYU.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

Any Dis No: PR2138

Assistant Commissioner of Patents: Please record the attached original document or copy thereof.

1. Name of conveying party(ies):

Mark S. Dennis

Additional name(s) of conveying party(ies) attached? ☐ Yes ☒ No

3. Nature of conveyance:

☒ Assignment

Merger

Security Agreement

Change of Name

Other:

Execution Date: Nov. 9, 2004

2. Name and address of receiving party(ies):

Name: GENENTECH, INC.

Internal Address:

Street Address: 1 DNA Way

City: South San Francisco State: California

ZIP: 94080-4990

Additional name(s) & address(es) attached? ☐ Yes ☒ No

4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of the application is:

A. Patent Application No.(s)

60/598,991

B. Patent No.(s)

Additional numbers attached? ☐ Yes ☒ No

5. Name and address of party to whom correspondence concerning document should be mailed:

Paul Naik, Ph.D.

GENENTECH, INC.

1 DNA Way

South San Francisco, CA 94080

6. Total number of applications and patents involved: 1

7. Total fee (37 CFR 3.41): \$ 40.00

☐ Enclosed☒ Authorized to be charged to deposit account

8. Deposit account number:

07-0630

DO NOT USE THIS SPACE

9. Statement and signature.

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

Paul Naik, Ph.D.
Name of Person Signing
Registration No. 49,075

Signature

November 10, 2004
Date

Total number of pages comprising cover sheet, attachments and document: 3

Revised (10/91,1400)

700132962

PATENT
REEL: 016395 FRAME: 0288

548

Docket No. PR2138

ASSIGNMENT

WHEREAS, Mark S. Dennis, a citizen of United States of America, residing at 120 Plymouth, San Carlos, California 94070 (hereinafter "ASSIGNOR"), has invented a new and useful invention in

HUMANIZED ANTI-CMET ANTAGONISTS

for which a provisional application Serial No. 60/598,991, if received (Docket No. PR2138) has been filed by him on 05 August 2004; and

WHEREAS, GENENTECH, INC., a corporation organized and existing under and by virtue of the laws of the State of Delaware, having a place of business at 1 DNA Way, South San Francisco, California 94080-4990, is desirous of acquiring an interest in and to said invention, and in and to the Letters Patents to be obtained therefor;

NOW, THEREFORE, be it known by all whom it may concern:

That for good and valuable consideration the receipt of which is hereby acknowledged, the said ASSIGNOR have and do hereby sell, assign, transfer and set over unto the said GENENTECH, INC., its successors and assigns, the full and exclusive right, title and interest including all rights under the Paris Convention for the Protection of Industrial Property, in and to said invention, and in and to any and all Letters Patents to be granted and issued therefor or any continuation, division, renewal, or substitute thereof, and as to Letters Patents any reissue or re-examination thereof, not only for, to, and in the United States of America, its territories and possessions, but for, to and in all other countries; and it has been and is hereby authorized and requested that the appropriate government agencies issue said Letters Patents to said GENENTECH, INC., in accordance with this Assignment.

Said ASSIGNOR covenants and agrees to cooperate with GENENTECH, INC., to enable said GENENTECH, INC. to enjoy to the fullest extent the right, title and interest herein conveyed in the United States and foreign countries. Such cooperation by said ASSIGNOR includes prompt production of pertinent facts and documents, giving of testimony, execution of petitions, oaths, specifications, declarations or other papers, and other assistance all to the extent deemed necessary or desirable by said GENENTECH, INC., (a) for perfecting the right, title and interest herein conveyed; (b) for prosecuting any of said applications; (c) for filing and prosecuting applications for reissuance of any of said patents; (d) for interference or other priority proceedings involving said invention; and (e) for legal proceedings involving said invention and any applications therefor and any patents granted thereon, including without limitation opposition proceedings, cancellation proceedings, priority contests, public use proceedings, infringement actions and court actions; provided, however, that the expense incurred by said ASSIGNOR in providing such cooperation shall be paid for by said GENENTECH, INC.

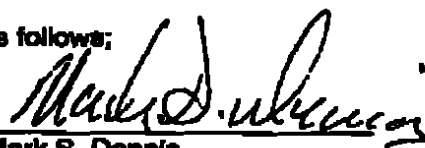
The terms and covenants of this assignment shall inure to the benefit of said GENENTECH, INC., its successors, assigns and other legal representatives, and shall be binding upon said ASSIGNOR, their respective heirs, legal representatives and assigns.

Said ASSIGNOR hereby warrants and represents that he has not entered and will not enter into any assignment, contract, or understanding in conflict herewith.

IN WITNESS WHEREOF I undersign as follows;

South San Francisco

Dated: 11-9-04


Mark S. Dennis

RECORDED: 11/19/2004

PATENT
REEL: 015395 FRAME: 0289

CH 549

TRADUCCION AL ESPAÑOL del Documento de Cesión a GENENTECH, INC.
firmado por el cedente y el cesionario.

APOSTILLA

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

1. País: Estados Unidos de América

Este documento público

2. ha sido firmado por E. Bonett

3. actuando en capacidad de Funcionario que Certifica

4. lleva el sello/timbre de la Oficina de marcas y patentes

Certificado

5. en Washington D.C.

6. el trece de Marzo de 2007

7. por el Funcionario de autenticación, Departamento de Estado de Estados Unidos

8. No. 07016037-1

9. Sello/timbre

10. Firma

(Firma)

Patrick O. Hatchett

[sello]

42 550

LOS ESTADOS UNIDOS DE AMÉRICA
A TODO AQUEL QUE PUEDA LLEGARLE LA PRESENTE:
DEPARTAMENTO DE COMERCIO DE ESTADOS UNIDOS
Oficina de Marcas y Patentes de Estados Unidos

Febrero 07 de 2007

**ESTE ES PARA CERTIFICAR QUE EL ANEXO ES UNA COPIA VERDADERA
DE LOS ARCHIVOS DE ESTA OFICINA DE UN DOCUMENTO ARCHIVADO EL
19 DE NOVIEMBRE DE 2004.**

Por autoridad del
Subsecretario de Comercio para la Propiedad Intelectual
y Director de la Oficina de Marcas y Patente de Estados Unidos

E. BORNETT
Funcionario que Certifica

Hay un sello que dice:
Oficina de Marcas y Patentes de Estados Unidos
Departamento de Comercio

Departamento de Comercio
Oficina de Marcas y Patentes
Expediente de abogado No. PR2138

Número total de páginas que comprenden portada, anexos y documento: 3

PATENTE
ROLLO: 015395 CUADR 0288

44 552

CESIÓN

CONSIDERANDO QUE, Mark S. Dennis, un ciudadano de los Estados Unidos de América, residente en 120 Plymouth, San Carlos, CA 94070 (en adelante referidos como "CEDENTE"), ha inventado una invención nueva y útil

ANTAGONISTAS HUMANIZADOS ANTI-CMET

para la cual se presentó la solicitud provisional No. 60/598,991 (Expediente No. PR2138) por ellos el 5 de Agosto de 2004; y

CONSIDERANDO QUE, GENENTECH, INC., una corporación organizada y existente bajo y por virtud de las leyes del Estado de Delaware, que tiene oficinas en 1 DNA Way, South San Francisco, California 94080-4990, está deseosa de adquirir un interés en y para dicha invención, y en y para las patentes que se obtendrán de la misma;

AHORA, POR LO TANTO, téngase por sabido por todo aquel que le concierna:

Que por una consideración buena y valiosa el recibo de la cual se reconoce por la presente, dicho CEDENTE ha y por la presente vende, cede, transfiere y traspasa a dicha GENENTECH, INC. sus sucesores y cesionarios, el derecho, título e interés completo y exclusivo incluyendo todos los derechos bajo la Convención de Paris para la Protección de la Propiedad Industrial, en y para dicha invención, y en y para cualquiera y todas las patentes que se concedan y emitan para la misma o cualquier continuación, división, renovación, o sustitución de la misma, y en cuanto a patentes cualquier reemisión o reexaminación de las mismas, no solo para, por y en los Estados Unidos de América, sus territorios y posesiones, sin para, por y en todos los otros países; y se ha y por la presente se autoriza y solicita que las agencias gubernamentales respectivas emitan dichas patentes a GENENTECH, INC. de acuerdo con esta cesión.

Dicho CEDENTE garantiza y acuerda cooperar con GENENTECH, INC., para posibilitar a dicha GENENTECH, INC., a disfrutar hasta su máxima extensión el derecho, título e interés aquí cedido en Estados Unidos y los países extranjeros. Tal cooperación por dichos CEDENTE incluye la pronta producción de hechos y documentos pertinentes, dando testimonio, ejecutando peticiones, juramentos, especificaciones, declaraciones u otros documentos, y otra ayuda todas hasta el punto considerado necesario o deseable por dichas GENENTECH, INC. (a) para perfeccionar el derecho, título e interés aquí cedido; (b) para procesar cualquiera de dichas solicitudes; (c) para presentar y procesar solicitudes de reemisión de cualquiera de dichas patentes; (d) para procesos de interferencia u otros procesos de prioridad que involucran dicha invención; y (e) para procedimientos legales que involucran dicha invención y cualquier solicitud de la misma y cualquier patente concedida sobre la misma, incluyendo sin limitación procedimientos de oposición, procedimientos de cancelación, disputas de prioridad, procesos de uso público, acciones de violación y acciones de la corte; con la condición que los gastos incurridos por dicho CEDENTE al proporcionar dicha cooperación deban ser pagados por GENENTECH, INC.

Los términos y garantías de esta cesión deben lastimar a beneficio de dicha GENENTECH, INC. sus sucesores, cesionarios y otros representantes legales, y deberá ser obligante sobre dichos CEDENTE, sus respectivos herederos, representantes legales y cesionarios.

Dicho CEDENTE por la presente garantizan y manifiestan que no ha entrado y no entrará en ninguna cesión, contrato o entendimiento en conflicto con la presente.

EN TESTIMONIO DE LO CUAL suscribimos como sigue:

South San Francisco

(Firma)
Mark S. Dennis

Fechado: 11/09/ 04

CERTIFICADO: 11/19/2004

PATENTE
ROLLO: 015395 CUADRO 09289