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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-034188-00001-0000

Fecha 2007-07-03 16 00 28 Dep 2020 NUECREACIONES
Tra 11 PATENTEIYII Ene 378 FASENACIONALI
Act 329 CTOINFORMACION Folios 28

AS: 103.309

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

E S D

REF: Expediente No 07 034188 - Solicitud de Patente FASE NACIONAL Corresp
a la Solicitud Internacional PCT/US2005/036300
a favor de **GENENTECH, INC.**

Titulada. MODULADORES DE ACTIVADOR DE FACTOR DE CRECIMIENTO
HEPATOCÍTICO

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, me
permito anexar al presente escrito los siguientes documentos

- 1 Documento donde consta la cesión del derecho a la Patente otorgado por los
inventores al solicitante, debidamente apostillado, junto con su correspondiente
traducción al castellano
- 2 Reporte Preliminar Internacional sobre la 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, 29 de junio de 2007
CHP/MEVaac

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 P2179R1	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2005/038900	International filing date (day/month/year) 03 October 2005 (03.10.2005)	Priority date (day/month/year) 04 October 2004 (04.10.2004)	
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 RUPORT consists of a total of 12 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: <table> <tr> <td>☒ Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td>☒ Box No. II</td> <td>Priority</td> </tr> <tr> <td>☒ Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td>☐ Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td>☒ Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td>☐ Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td>☒ Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td>☒ Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> 4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(e) 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).	☒ 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
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☐ 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															

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 11 April 2007 (11.04.2007)
	Authorized officer Beate Giffo-Schmitt e-mail: p03.pct@wipo.int

PATENT COOPERATION TREATY

REC'D 13 JUN 2006

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From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)Applicant's or agent's file reference
see form PCT/ISA/220FOR FURTHER ACTION
See paragraph 2 belowInternational application No.
PCT/US2005/036300International filing date (day/month/year)
03.10.2005Priority date (day/month/year)
04.10.2004International Patent Classification (IPC) or both national classification and IPC
INV. C07K1840 A61P3500 A61K38095
ADD. C12N984Applicant
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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Date of completion of
this opinionsee form
PCT/ISA/210

Authorized Officer

Bumb, P

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/036300

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:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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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. 12-15 (with respect to industrial applicability), 1-15 (in part)

because:

- ☒ the said international application, or the said claims Nos. 12-15 (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. 1-15 (in part) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

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

International application No.
PCT/US2005/036300

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

1. Statement

Novelty (N)	Yes: Claims	2-3,7-17
	No: Claims	1,4-8
Inventive step (IS)	Yes: Claims	
	No: Claims	1-17
Industrial applicability (IA)	Yes: Claims	1-11,16,17
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

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

see separate sheet

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

International application No.

PCT/US2005/036300

Re Item III.

- 1.1 Claims 12-15 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).
- 1.2 Claims 1-15 relate to an extremely large number of possible antibodies, as any antibody may be expected to aspecifically bind HGFA, at least to some degree. Support and disclosure in the sense of Articles 5 and 6 PCT, however, are only to be found for a very limited number of the products claimed. The non-compliance with the substantive provisions is to such an extent that the search was performed taking into consideration this non-compliance in determining the extent of the search of said claims 1-15.

The search of claims 1-15 was restricted to those antibodies which specifically bind HGFA, as exemplified by present example 1 (see page 81, line 32 to page 82, line 3).

- 1.3 Claims 12, 14 and 15 relate to an extremely large number of possible methods of treatment. These methods relate to a vast number of possible diseases due to the fundamental unclarity of expressions such as "disease associated with" and "immune related". No support and disclosure in the sense of Articles 5 and 6 PCT is to be found for any of the *in vivo* treatment methods claimed. The non-compliance with the substantive provisions is to such an extent that the search was performed taking into consideration the non-compliance in determining the extent of the search of said claims 1-15.

The search of claims 12, 14 and 15 was restricted to the disease of cancer (see claim 13), diseases related to angiogenesis and autoimmune diseases as defined in the description (see pages 48 & 49).

Re Item V.

1. State of the Art

1.1 Reference is made to the following documents:

- D1: KATAOKA H ET AL: "Activation of Hepatocyte Growth Factor/Scatter Factor in Colorectal Carcinoma", CANCER RESEARCH, vol. 60, 1 November 2000 (2000-11-01), pages 6148-6159, XP002380896
- D2: MIYAZAWA K ET AL: "Activation of Hepatocyte Growth Factor in the Injured Tissues Is Mediated by Hepatocyte Growth Factor Activator", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 7, 16 February 1996 (1996-02-16), pages 3615-3618, XP002039579
- D3: EP 1213302 A1 (MITSUBISHI CHEMICAL CORPORATION) (12 June 2002) (2002-06-12)
- D4: CAO B ET AL: "Neutralizing monoclonal antibodies to hepatocyte growth factor/scatter factor (HGF/SF) display antitumor activity in animal models", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA, vol. 98, no. 13, 19 June 2001 (2001-06-19), pages 7443-7448, XP002982804

2. Novelty

- 2.1 D1-D3 disclose monoclonal antibodies which specifically bind human HGFA (see D1, pages 6149-6151) (see D1, Fig. 2C) (see D2, pages 3616-3617) (see D2, Fig. 2) (see D3, examples 3-7). The antibody P1-4 of D1 & D2 is shown to inhibit the proteolytic processing of single chain HGF by HGFA *in vitro* (see D1, Fig. 2C) (see D2, Fig. 2). The subject-matter of claims 1 & 4-6 is thus not new (Article 33(2) PCT).
- 2.2 Neither the binding site of anti-HGFA antibodies, nor their mode of inhibiting HGF-conversion has been previously reported. The subject-matter of claims 2-3 and 10-11 is thus novel (Article 33(2) PCT).
- 2.3 The direct inhibition of (a) cell proliferation, (b) angiogenesis or (c) HGF/c-met signalling by means of anti-HGFA antibodies has not been previously reported. The subject-matter of claims 7-9 is thus new (Article 33(2) PCT).
- 2.4 The *in vivo* application of anti-HGFA antibodies has not been previously reported. The subject-matter of claims 12-15 is thus new (Article 33(2) PCT).

- 2.5 Anti-HGFA antibodies which comprise two or more of the CDRs as put forth by Figure 1A or SEQ ID Nos: 71-112 have not been previously disclosed. The subject-matter of claims 16-17 is thus new (Article 33(2) PCT).

3. Inventive Step

- 3.1 D1 is considered to represent the closest prior art with respect to the subject-matter of claim 2 and discloses the neutralizing anti-HGFA mAb P1-4 (see D1, page 6149).

The subject-matter of (a) claim 2 differs from that of (b) mAb P1-4 in that the former recognizes an epitope within the active site of HGFA. The technical effect achieved by said difference may be expected to lie in a complete inhibition of the targeted HGFA-molecule's biological activity. The technical problem to be solved with respect to the state of the art may therefore be regarded as the provision of an antibody which blocks HGFA's active site.

Claim 2 is attempting to define the product for which protection is sought in terms of the result to be achieved ("antibody ... [which] binds to an active site") without providing a solution to the technical problem of attaining said desired properties. It does therefore not constitute an inventive technical solution in the sense of Article 33(3) PCT.

Furthermore, the aforementioned technical problem has not been solved by the present application. The present application does not provide conclusive technical support (Article 5 PCT) for an antibody which binds the active site of HGFA (see application, page 83, line 4). The subject-matter of claim 2 therefore does not solve the aforementioned technical problem and does not comply to Article 33(3) PCT.

- 3.2 D1 is considered to represent the closest prior art with respect to the subject-matter of claim 3 and discloses the neutralizing anti-HGFA mAb P1-4 (see D1, page 6149).

The subject-matter of (a) claim 3 differs from that of (b) mAb P1-4 in that the former recognizes an epitope outside the active site of HGFA. The technical effect achieved by said difference is not apparent, as not every such binding is expected to result in

an appreciable inhibitory effect. The technical problem to be solved with respect to the state of the art may therefore be regarded as the provision of an alternative antibody which specifically binds HGFA.

Claim 3 is attempting to define the product for which protection is sought in terms of the result to be achieved ("antibody ... [which] binds to [...] HGFA") without providing a solution to the technical problem of attaining said desired properties. It does therefore not constitute an inventive technical solution in the sense of Article 33(3) PCT.

Furthermore, the aforementioned technical problem has not been solved by the present application. The present application does not provide conclusive technical support (Article 6 PCT) for an antibody which binds HGFA outside of the active site of HGFA (see application, page 83, line 4). The subject-matter of claim 2 therefore does not solve the aforementioned technical problem and does not comply to Article 33(3) PCT.

3.3 Claims 7-11 are formulated in terms of the result to be achieved ("antibody which inhibits"/"antibody [which] is an [...] inhibitor") without providing a technical solution to the technical problem of achieving said desired properties. The subject-matter of said claims in itself therefore does not provide an inventive technical solution in the sense of Article 33(3) PCT).

3.4 D1 is considered to represent the closest prior art with respect to the subject-matter of claim 12 and discloses the neutralizing anti-HGFA mAb P1-4 (see D1, page 6149) which is used *in vitro* to downregulate the proteolytic processing of single chain HGF.

The subject-matter of (a) claim 12 differs from that of (b) D1 in that the former uses said known anti-HGFA antibody in an *in vivo* treatment of a disease. The technical effect achieved by said difference may be expected to lie in an *in vivo* therapeutic effect. The technical problem to be solved may therefore be regarded as the provision of an effective medicament.

The person skilled in the art is aware of the fact that interfering with HGF's biological

activity results in an antitumour activity *in vivo* (see D4, pages 7445-7446). He would therefore contemplate using the HGFA-neutralizing antibody P1-4 of D1 in a method of treatment, especially since D1 already suggests that the proteolytic activation step of HGF may serve as a target of therapeutic intervention in the treatment of tumours, i.e. colon cancer (see D1, page 8158).

The subject-matter of claims 12-13 therefore does not involve an inventive step (Article 33(3) PCT).

- 3.5 In the state of the art angiogenesis is generally implicated in the formation of tumours and the HGF/c-Met signalling pathway is well known to be implicated in angiogenesis (see i.e. D4, page 7445). The unclarity of the expression "Immune related" notwithstanding, tumorigenesis may be regarded as influencing and thus relating to an immune response.

The subject-matter of claims 14-15 therefore does not introduce any inventive subject-matter over claim 12 and thus does not involve an inventive step (Article 33(3) PCT).

- 3.6 D1 is considered to represent the closest prior art with respect to the subject-matter of claim 16 and discloses the neutralizing anti-HGFA mAb P1-4 (see D1, page 6149).

The subject-matter of (a) claim 16 differs from that of (b) D1 in that the former comprises one specific CDR, wherein said CDR comprises one of the amino acid sequences depicted in Fig. 1A.

As the antigen-specificity and affinity of an antibody is only sufficiently well defined when the complete antigen-binding region is defined, in other words, when the complete variable heavy and variable light chain regions are provided, the technical effect achieved by the partial definition of a single CDR is not apparent. The technical problem to be solved is therefore regarded to lie in the provision of an alternative antibody which specifically binds HGFA.

As mentioned above, the provision of a partial CDR is not sufficient to guarantee the

antigen-specificity of a given antibody. The subject-matter of claim 16 is therefore not considered to have solved the aforementioned technical problem (lack of technical support, Article 6 PCT) and a lack of inventive step arises over said claim (Article 33(3) PCT).

- 3.7 Similarly, the subject-matter of claim 17 does not solve the aforementioned technical problem of providing an antibody which specifically binds HGFA (lack of technical support, Article 6 PCT), resulting in lack of inventive step for claim 17 (Article 33(3) PCT).

4. Industrial Applicability

- 4.1 For the assessment of the present claims 12-15 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.

- 5.1 The present method claims 13-15 are formulated as direct dependent claims of product claim 10, thereby rendering the subject-matter of said claims unclear (Article 6 PCT).

Re Item VIII.

- 6.1 Claims 1-11, and consequently claims 12-15 which refer thereto, attempt to define the subject-matter for which protection is sought in terms of the desired properties ("antibody which binds") of the claimed products without providing the technical features or indeed any technical solution to the technical problem of achieving said desiderata. The reader is left in doubt as to the technical features referred to, thereby rendering the subject-matter of said claims unclear (Article 6 PCT).

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

International application No.

PCT/US2005/036300

- 6.2 Claims 1, 2, 3, 7, 8, 9, 11, 12, 14 and 15 do not meet the requirements of Article 6 PCT in that they fail to clearly define the subject-matter for which protection is sought. Said claims make use of certain unclear, vague or relative terminology which leaves the reader in doubt as to the features referred to. Said unclear terminology comprises: "antibody that binds" (claims 1-3, 12), "a position other than" (claim 3), "inhibits" (claims 7-9), "partial competitive inhibitor" (claim 11), "disease associated with", "dysregulation" (claims 12 & 14), "effective amount" (claim 12), "immune related" (claim 15).
- 6.3 Claims 16 & 17 do not meet the requirements of Article 6 PCT in that they do not clearly define the subject-matter for which protection is sought. Said claims refer to a CDR, wherein said one CDR may comprise multiple sequences of Fig. 1A-1D, i.e. H1, H2 and H3, thereby introducing ambiguity about the meaning of said claims.
- 6.4 Claims 16 & 17 contain references to the drawings. According to Rule 6.2(a) PCT, claims should not contain such references except where absolutely necessary, which is not the case here.

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APOSTILLE
(Convention de La Haye du 5 octobre 1961)

1. Country: United States of America

This public document

2. has been signed by M Tarver

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.

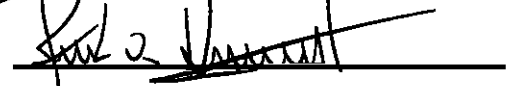
6. the fourteenth of March, 2007

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

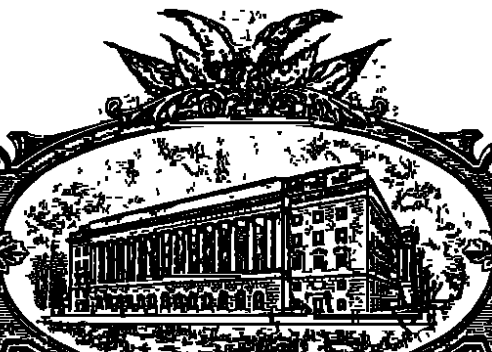
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February 21, 2007

THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE
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and Director of the United States Patent and Trademark Office



M. TARVER
Certifying Officer

RECORDATION FORM COVER SHEET
PATENTS ONLY

Commissioner for Patents: Please record the attached original documents or copy thereof.

1. Name of conveying party(ies):

Daniel K. Kirchhofer
Yan WuAdditional name(s) of conveying party(ies) attached? _ Yes ☒ No

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

Name: GENENTECH, INC.

Internal Address:

Street Address: 1 DNA WayCity: South San Francisco State: CaliforniaZIP: 94080-4990Additional name(s) & address(es) attached? _ Yes ☒ No

3. Nature of conveyance:

☒ Assignment

Merger

Security Agreement

Change of Name

Other:

Execution Date: May 16, 2005, July 27, 2005

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)

B. Patent No.(s)

60/615,657

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 940806. Total number of applications and patents involved: 17. Total fee (37 CFR 3.41): \$ 40.00

_ Enclosed

☒ Authorized to be charged to deposit account

8. Deposit account number:

07-0630

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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

August 17, 2005

Date

Total number of pages comprising cover sheet, attachments and document: 5

700203905

PATENT
REEL: 016645 FRAME: 0392

19
Docket No. PR2179

ASSIGNMENT

WHEREAS, Daniel K. Kirchhofer, a citizen of U.S.A., residing at 326 S. Springer Road, Los Altos, California 94024, and Yan Wu, a citizen of U.S.A., residing at 101 Challenge Court, Foster City, California 94404 (hereinafter "ASSIGNORS"), have invented a new and useful invention in

MODULATORS OF HEPATOCYTE GROWTH FACTOR ACTIVATOR

for which a provisional application Serial No. 60/615,657 (Docket No. PR2179) has been filed by them on 4 October 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 94080-4490, 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 ASSIGNORS 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 ASSIGNORS covenant and agree 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 ASSIGNORS 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 ASSIGNORS 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 ASSIGNORS, their respective heirs, legal representatives and assigns.

Said ASSIGNORS hereby warrant and represent that they have not entered and will not enter into any assignment, contract, or understanding in conflict herewith.

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WD

IN WITNESS WHEREOF we undersign as follows;

South San Francisco

Dated: 5/16/05

Daniel K. Kirchhofer

Daniel K. Kirchhofer

South San Francisco

Dated: _____

Yan Wu

IN WITNESS WHEREOF we undersign as follows:

South San Francisco

Daniel K. Kirchhofer

Dated: _____

South San Francisco

Yan Wu

Dated: 12/2/23

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TRADUCCION AL ESPAÑOL del Documento de Cesión a **GENENTECH, INC.** firmado por los cedentes 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 M. Tarver
- 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 catorce de Marzo de 2007
- 7 por el Funcionario de autenticación asistente, Departamento de Estado de Estados Unidos
- 8 No. 07016182-8
- 9 Sello/timbre
- 10. Firma

(Firma)

Patrick O. Hatchett

[sello]

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 21 de 2007

ESTE ES PARA CERTIFICAR QUE EL ANEXO ES UNA COPIA
VERDADERA DE LOS ARCHIVOS DE ESTA OFICINA DE UN
DOCUMENTO ARCHIVADO EL 17 DE AGOSTO DE 2005.

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

M. TARVER
Funcionario que Certifica

SPS

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HOJA DE PORTADA DEL FORMULARIO DE REGISTRO SOLAMENTE PATENTES		Departamento de Comercio Oficina de Marcas y Patentes Expediente de abogado No PR2179
Comisionado Asistente para patentes Por favor archive los documentos originales anexos o copias de los mismos		
1. Nombre de la(s) parte(s) cedente(s) Daniel K Kirchhofer Yan Wu ¿Se anexa(n) nombre(s) adicional(es) de parte(s) cedente(s)? _ Si ☒ No	2. Nombre y dirección de la(s) parte(s) receptora(s) Nombre <u>GENENTECH, INC.</u> Dirección interna Dirección <u>1 DNA Way</u> Ciudad <u>South San Francisco</u> Estado <u>California</u> ZIP <u>94080-4990</u> ¿Se anexan Nombre(s) y dirección(es) adicional(es)? _ Si ☒ No	
3. Naturaleza del traspaso ☒ Cesión Fusión Acuerdo de Seguridad Cambio de Nombre Otro Fecha de Ejecución. Mayo 16, 2005, Julio 27, 2005		
4. Numero(s) de solicitud o número(s) de patente: Si este documento se presenta junto con una nueva solicitud, la fecha de ejecución de la solicitud es A Solicitud de patente No(s) B Patente No(s) 60/615,657 ¿Se anexa numeros adicionales? _ Si ☒ No		
5. Nombre y dirección de la parte a quien se le debe enviar la correspondencia Paul Naik, Ph D GENENTECH, INC 1DNA Way South San Francisco, CA 94080	6. Numero total de solicitudes y patentes involucradas. <u>1</u>	
	7. Tarifa total (37 C F R 3.41) <u>\$40.00</u> _ Adjunta ☒ Autorizado para cargarla a cuenta de depósito	
	8. Número de cuenta de Depósito <u>07-0630</u>	
NO USE ESTE ESPACIO		
9. Declaración y firma hasta donde se y creo, la información anterior es verdadera y correcta y cualquier copia anexa es una copia verdadera del documento original Paul Naik, Ph D (Firma) Agosto 17, 2005 Nombre de la persona que firma Firma Fecha Registro No 49,075 Número total de páginas que comprenden portada, anexos y documento <u>5</u>		

PATENTE

700203905

ROLLO: 016645 CUADRO 0392

604
501

CESIÓN

CONSIDERANDO QUE, Daniel K. Kirchhofer, un ciudadano de E U A , residente en 326 S Springer Road, los Altos, California 94024, y Yan Wu, un ciudadano de E.U.A., residente en 101 Challenge Court, Foster City, California 94404 (en adelante refendos como "CEDENTE"), han inventado una invención nueva y útil

MODULADORES DE ACTIVADORES DEL FACTOR DE CRECIMIENTO DE HEPATOCITOS

para la cual se presentaron la solicitud provisional No. 60/615.657 (Expediente No PR2179) el 4 de octubre 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.

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EN TESTIMONIO DE LO CUAL suscribimos como sigue

South San Francisco	<u>(Firma)</u> Daniel K. Kirchhofer
Fechado: <u>5/16/05</u>	
South San Francisco	<u>Yan Wu</u>
Fechado: _____	

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503

EN TESTIMONIO DE LO CUAL suscribimos como sigue:

South San Francisco

Daniel K Kirchhofer

Fechado _____

South San Francisco

(firma)
Yan Wu

Fechado. 7-27-05

REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

509

Folio 508

2020
Bogotá D.C.,

Doctor(a)
CADENA SARMIENTO JUAN PABLO
Apoderado(a) y/o Representante de
GENENTECH, INC.

REFERENCIA	Radicación No	7 34188
	Solicitud internacional	PCT/US2005/036300
	Fecha inicio fase nacional	04/05/07
	Trámite	11
	Evento	378
	Actuación	416
	Oficio No.	3858
	Folios	1

Teniendo en cuenta que la solicitud de privilegio de patente que se tramita bajo el expediente indicado en la referencia, reúne los requisitos de forma establecidos en la Decisión 486 de la Comisión de la Comunidad Andina, el Tratado de Cooperación en Materia de Patentes (PCT), el Reglamento y la Circular Única de la Superintendencia de Industria y Comercio, se envía el extracto de la solicitud a la Oficina de Comunicaciones para efecto de su publicación en la Gaceta de Propiedad Industrial.

Cúmplase
Dado en Bogotá DC,

13 SET. 2007

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la división de Nuevas Creaciones

jfernand