



No. 07-033379- -00003-0000

Fecha: 2007-09-04 16:46:35 Dep. 2020 NUECREACIONE
Tra 11 PATENTEIYI Eve: 378 FASENACIONALI
Act 444 RESPUESTAREQUE Folios: 81

AS: 103.343

Señores

**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES**

E. S. D.

RESPUESTA A OFICIO 5783 DE 11 MAYO 2007

REF: Expediente No. 07 033379 - Solicitud de Patente FASE NACIONAL

Corresp. a la Solicitud Internacional PCT/US2005/031798

a favor de **GENENTECH, INC.**

Titulada: **COMPOSICIONES Y MÉTODOS PARA EL DIAGNÓSTICO Y
TRATAMIENTO DE TUMORES**

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 11 de mayo de 2007, cuyo término fue prorrogado mediante escrito radicado el 09 de julio de 2007, 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 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. Nuevos dibujos formales nítidos de las Figuras 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166 y 167.
4. 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, 3 de septiembre de 2007

CHP/MEV/aac

1662

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

TARJETA ARCHIVO TEMÁTICO

PATENTE DE INVENCION X PCT X MODELO DE UTILIDAD DISEÑO INDUSTRIAL

(21) N° de solicitud: 07 033379

(22) Fecha de solicitud: 02-04-2007

(51) Clasificación Internacional :

(71) Solicitante(s) **GENENTECH, INC.**

(72) Inventor(es) Belinda CAIRNS, Ruihuan, CHEN, Anan CHUNTHARAPAI, Gretchen FRANTZ, Kenneth HILLAN, Hartmut KOEPPEN, Heidi PHILLIPS, Paul POLAKIS, Chae Janeka REED, Chie SAKANAKA, Victoria SMITH, Susan SPENCER, P. Mickey WILLIAMS, Thomas WU, Zemin ZHANG

(74) Agente: JUAN PABLO CADENA SARMIENTO

(30) Prioridad

(31)

No. Prioridad

(32)

Fecha

(33)

País

10/936,626

08-09-2004

US

(85) Fecha inicio fase nacional: 08-04-2007

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

Fecha de presentación de la solicitud: 07-09-2005

No. de solicitud: PCT/US2005/031798

(87) Publicación internacional:

Fecha: 16-03-2006

No. Publicación: WO 2006/029183 A3

FIGURA CARACTERISTICA
6 x 6 cm

(54) Título: **COMPOSICIONES Y MÉTODOS PARA EL DIAGNÓSTICO Y TRATAMIENTO DE TUMORES**

(57) Resumen: 1. Un anticuerpo aislado que se fija a un polipéptido teniendo una identidad de secuencia de amino ácidos por lo menos de 80% con:

- a) el polipéptido que aparece en la Figura 115 (SEQ ID No.115);
- b) el polipéptido que aparece en la Figura 115 (SEQ ID No. 115), que carece de su péptido de señal asociado;
- c) un dominio extracelular del polipéptido que aparece en la Figura 115 (SEQ ID No. 115), con su péptido de señal asociado;
- d) un dominio extracelular del polipéptido que aparece en la 115 (SEQ ID No. 115), que carece de su péptido de señal asociado;
- e) un polipéptido codificado por una secuencia nucleótida que aparece en la Figura 37 (SEQ ID No. 37); o
- f) un polipéptido codificado por la región de codificación de longitud total de una secuencia nucleótida que aparece en la Figura 37 (SEQ ID No. 37).

CONTINUA AL RESPALDO ...

47. Un ARN de interferencia de unión TAT (ARNsi) que se fija a un ácido nucleico teniendo una identidad de secuencia por lo menos de 80% con:

- a) una secuencia nucleótida que se muestra en la Figura 37 (SEQ ID No:37; y
- b) el complemento de (a), donde el ARNsi reduce la expresión del TAT188.

51. Una composición de sustancias que comprende:

- a) el anticuerpo de la Reivindicación 1 en combinación con un excipiente

3

 Industria y Comercio SUPERINTENDENCIA		SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO DIVISION DE NUEVAS CREACIONES EXTRACTO PARA PUBLICACIÓN SOLICITUD DE PATENTE DE INVENCION PCT	
(21) N° de solicitud: 07 033379		(51) Int Cl:	
22) Fecha de solicitud: 02-04-2007		(71) Solicitante(s) GENENTECH, INC.	
(30) Prioridad	(31) No. Prioridad 10/936,626	(32) Fecha 08-09-2004	(33) País US
		(72) Inventor(es): Belinda CAIRNS, Ruihuan, CHEN, Anan CHUNTHARAPAI, Gretchen FRANTZ, Kenneth HILLAN, Hartmut KOEPPEN, Heidi PHILLIPS, Paul POLAKIS, Chae Janeke REED, Chie SAKANAKA, Victoria SMITH, Susan SPENCER, P. Mickey WILLIAMS, Thomas WU, Zemin ZHANG	
		(74) Agente: JUAN PABLO CADENA SARMIENTO	
(85) Fecha inicio fase nacional: 08-04-2007		(87) Publicación internacional	
(86) Datos relativos a la presentación de la solicitud PCT		Fecha: 16-03-2006	
Fecha de presentación de la solicitud: 07-09-2005		N° publicación: WO 2006/029183 A3	
No. de solicitud: PCT/US2005/031798			
(54) Título: COMPOSICIONES Y MÉTODOS PARA EL DIAGNÓSTICO Y TRATAMIENTO DE TUMORES			

1. Un anticuerpo aislado que se fija a un polipéptido teniendo una identidad de secuencia de amino ácidos por lo menos de 80% con:

- a) el polipéptido que aparece en la Figura 115 (SEQ ID No.115);
- b) el polipéptido que aparece en la Figura 115 (SEQ ID No. 115), que carece de su péptido de señal asociado;
- c) un dominio extracelular del polipéptido que aparece en la Figura 115 (SEQ ID No. 115), con su péptido de señal asociado;
- d) un dominio extracelular del polipéptido que aparece en la 115 (SEQ ID No. 115), que carece de su péptido de señal asociado;
- e) un polipéptido codificado por una secuencia nucleótida que aparece en la Figura 37 (SEQ ID No. 37); o
- f) un polipéptido codificado por la región de codificación de longitud total de una secuencia nucleótida que aparece en la Figura 37 (SEQ ID No. 37).

47. Un ARN de interferencia de unión TAT (ARNsi) que se fija a un ácido nucleico teniendo una identidad de secuencia por lo menos de 80% con:

- a) una secuencia nucleótida que se muestra en la Figura 37 (SEQ ID No:37; y
- b) el complemento de (a), donde el ARNsi reduce la expresión del TAT188.

51. Una composición de sustancias que comprende:

- a) el anticuerpo de la Reivindicación 1 en combinación con un excipiente

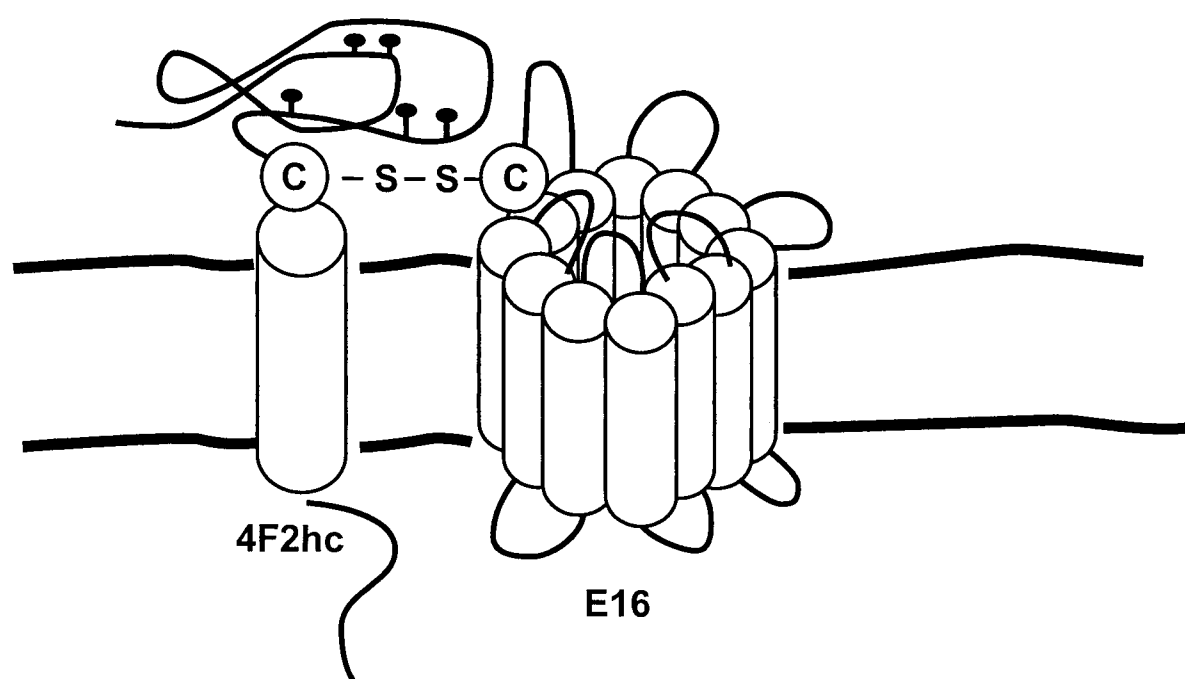


FIG. 155

S

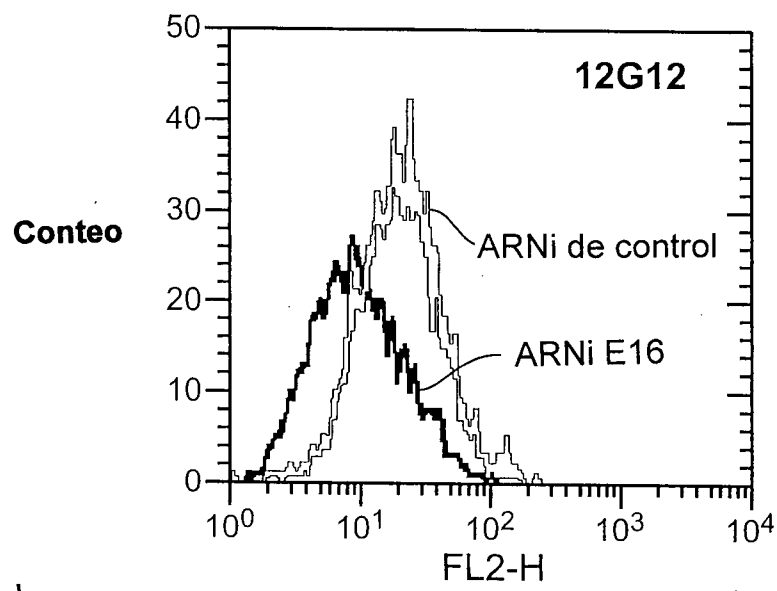
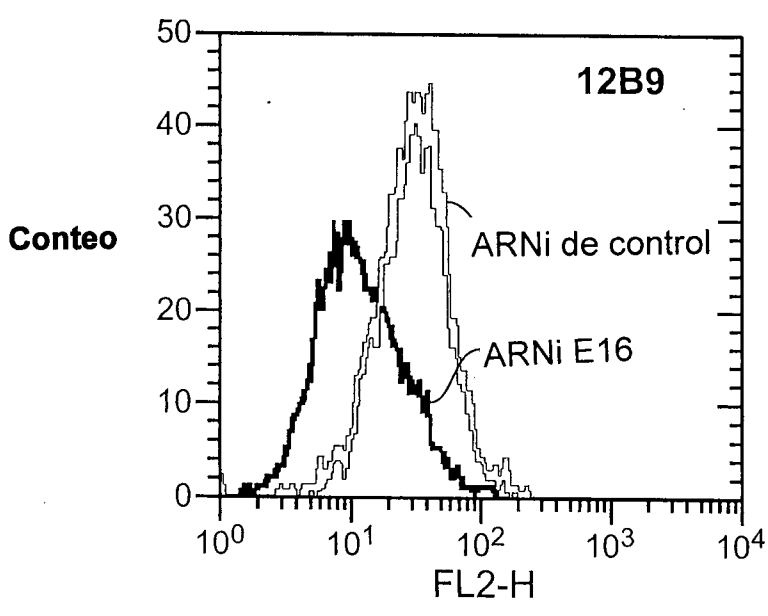
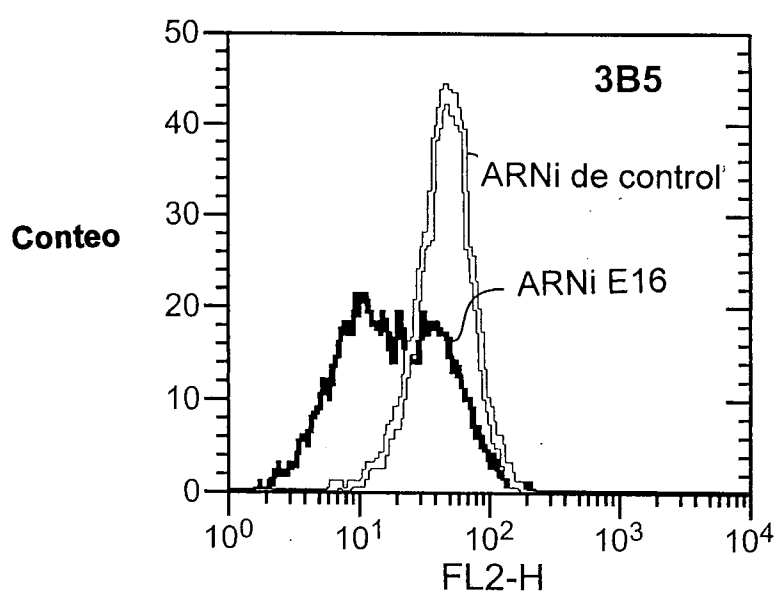


FIG. 156



Células PC3 tratadas con E16 mAb (3B5) durante la noche

FIG. 157

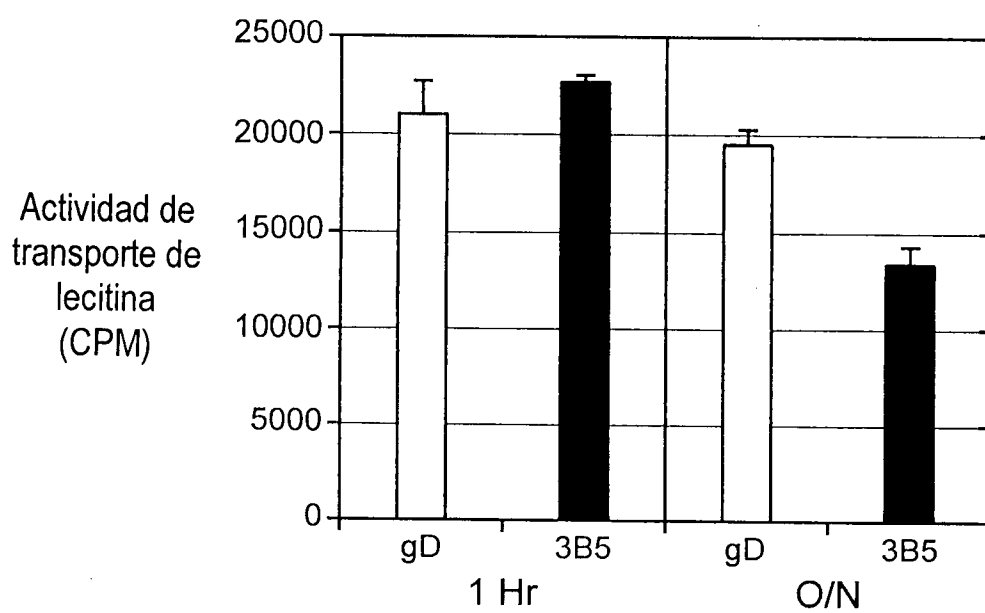
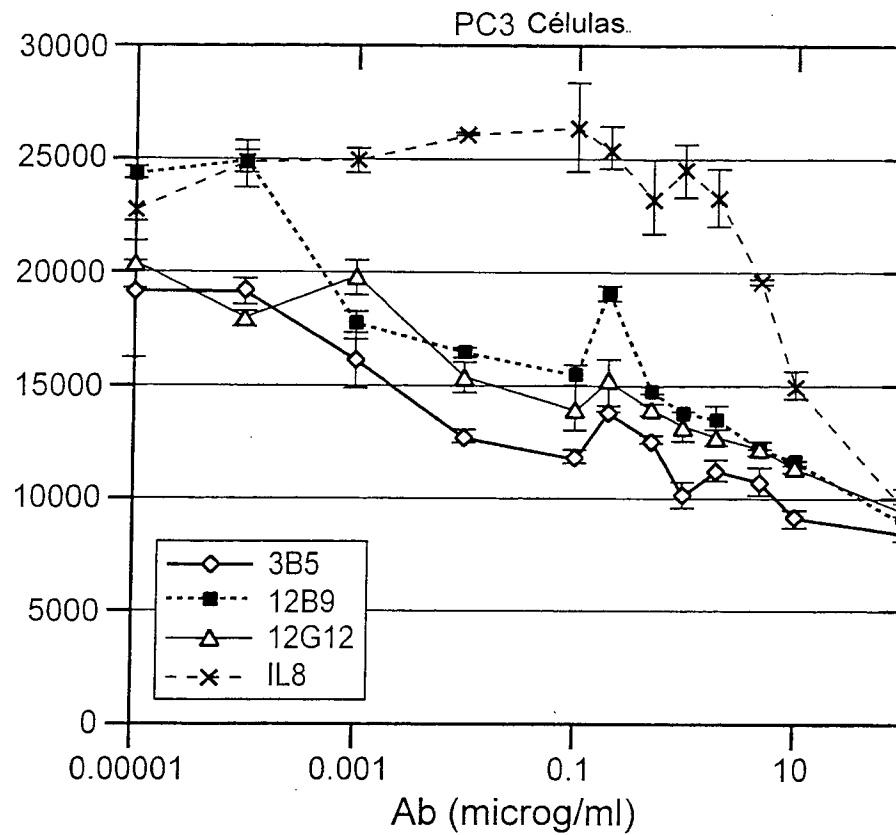


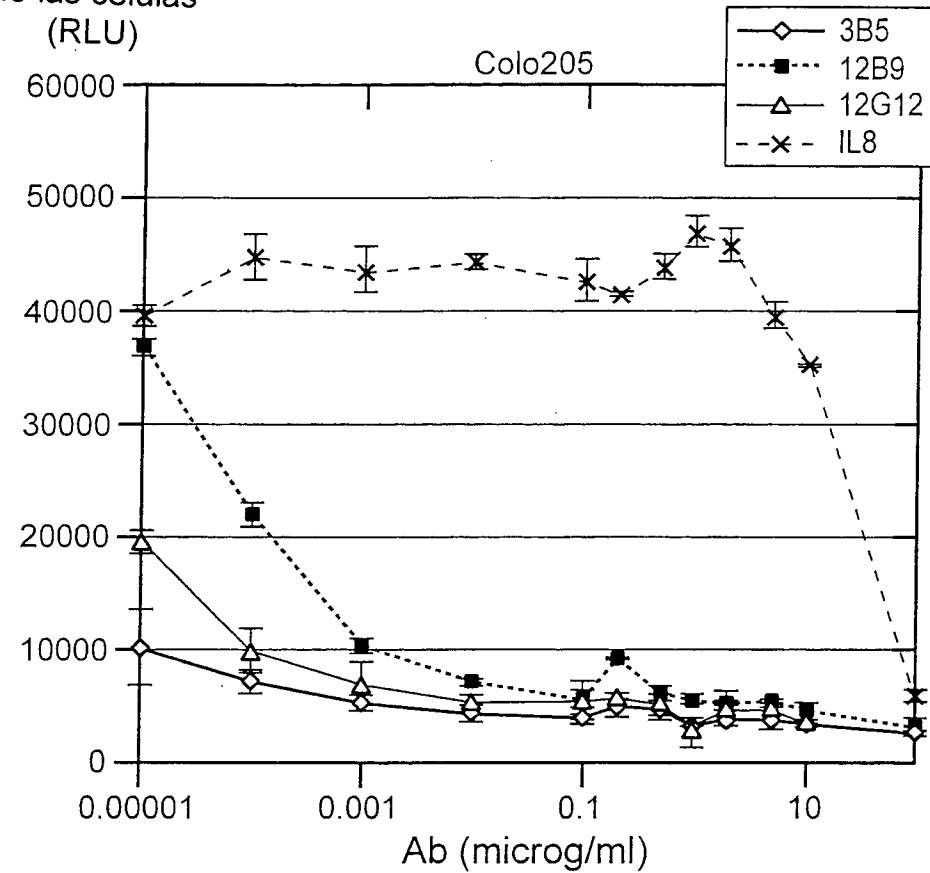
FIG. 158

Efecto de anti-E-16-vc-MMAE sobre el crecimiento de células cancerígenas in vitro

Viabilidad de las células (RLU)



Viabilidad de las células (RLU)



Tratamiento durante 72 h

FIG. 159

Anticuerpos conjugados anti-E16, células tumorales Colo205

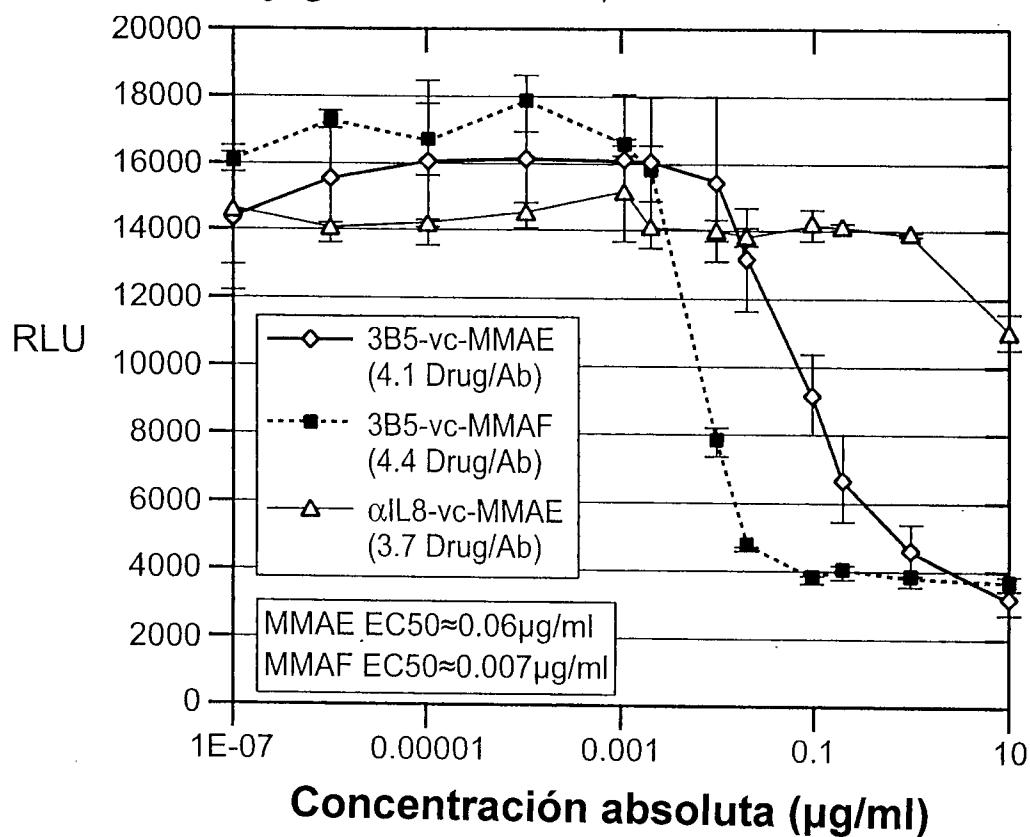
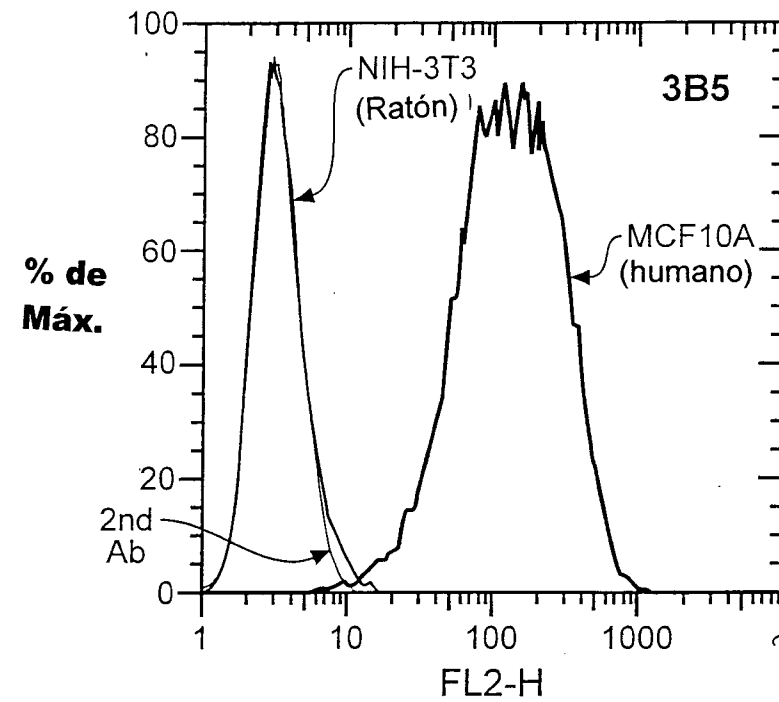
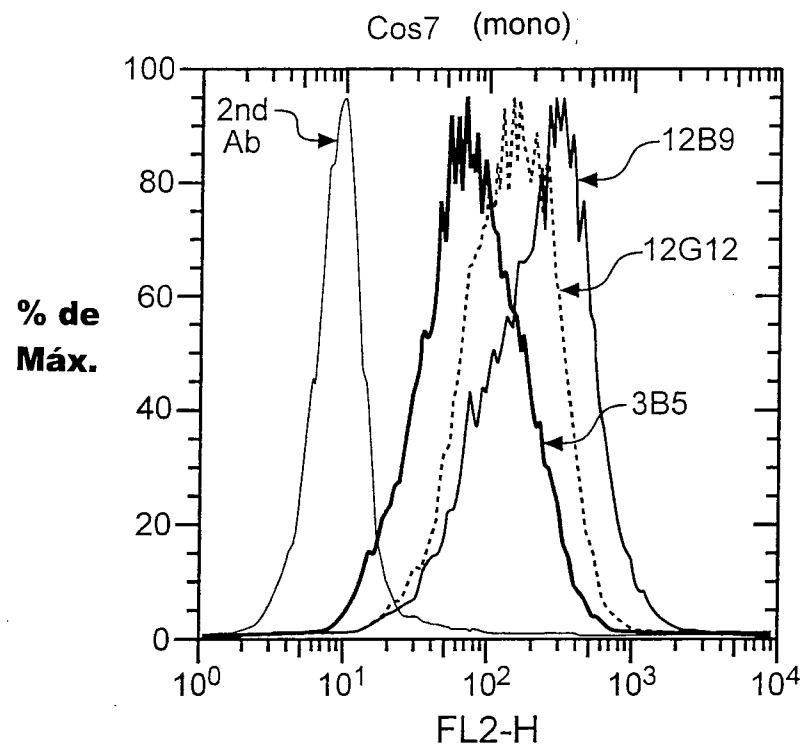
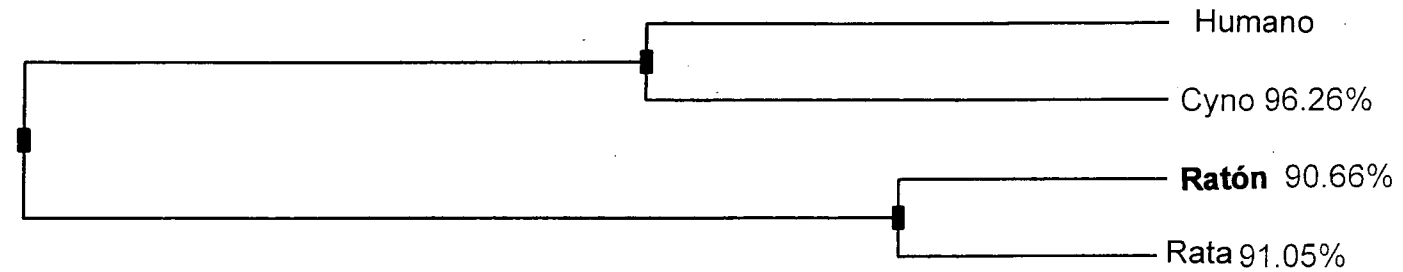


FIG. 160

Mono E16



El anticuerpo anti-E16 no reacciona con ratón E16, pero si tiene una reacción cruzada con mono E16.

FIG. 161

W

Anticuerpos anti-E16 sin conjugar, Xenoinjerto PC3

Protocolo # 03-0481

Eficacia anti-tumor de anticuerpos anti-E16
Vs. Tumores xenoinjerto PC3 en ratones atímicos

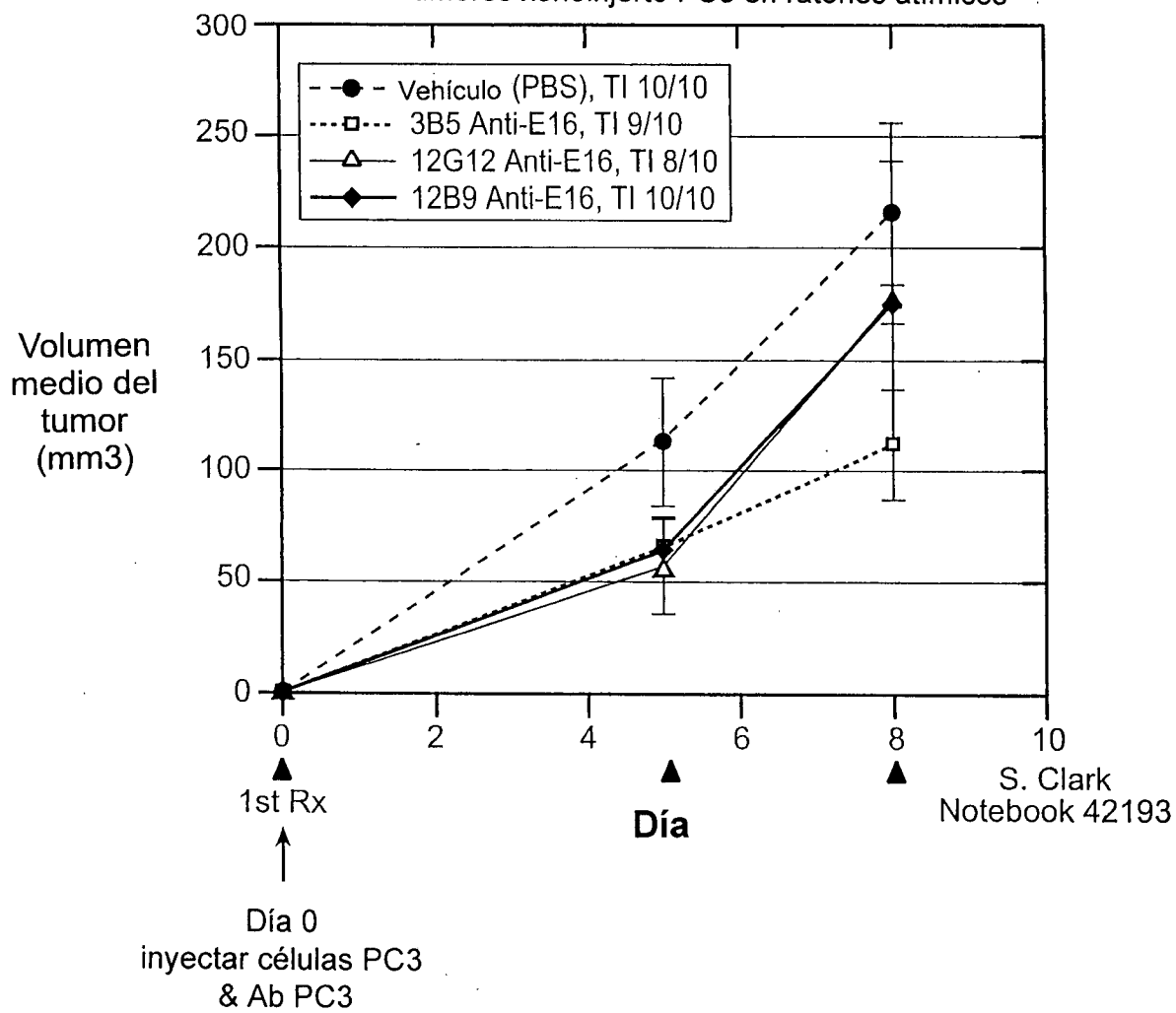


FIG. 162



Anticuerpos anti-E16 conjugados, Xenoinjerto Colo205

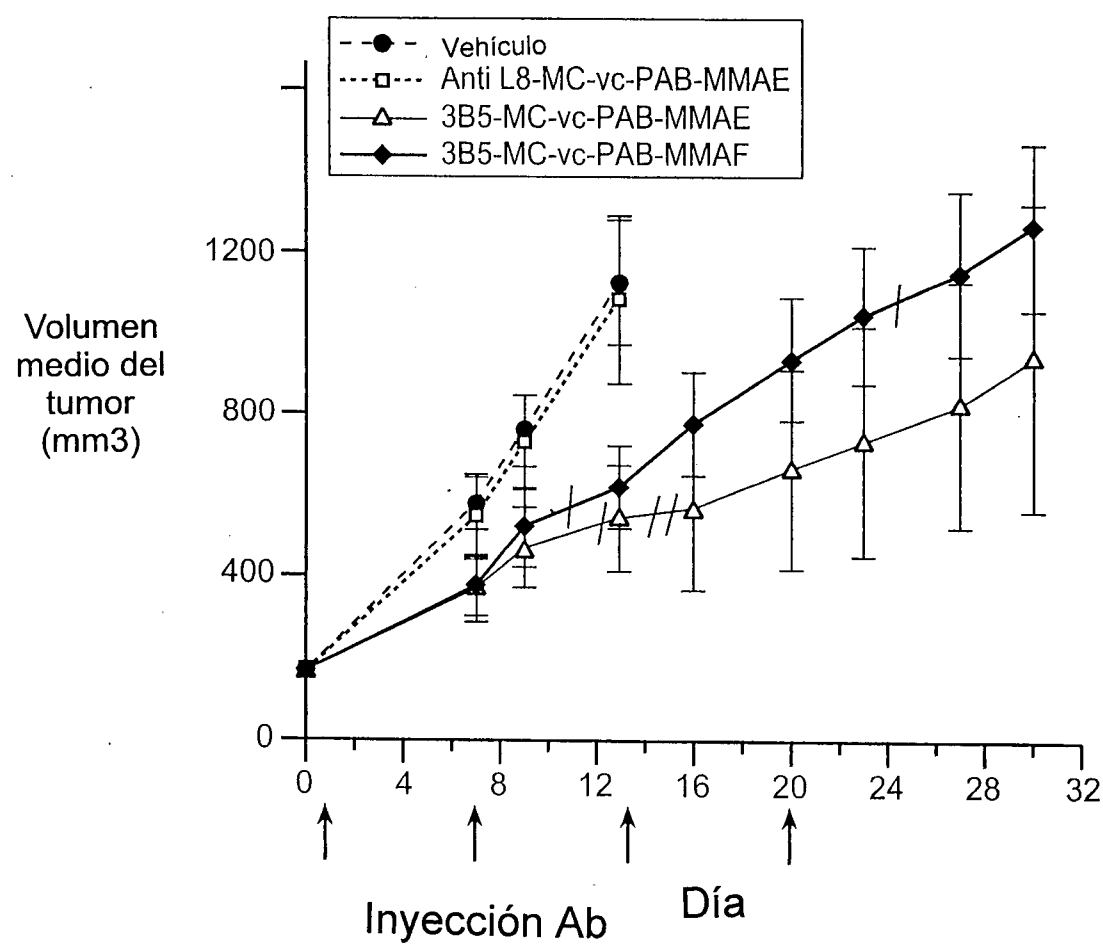


FIG. 163

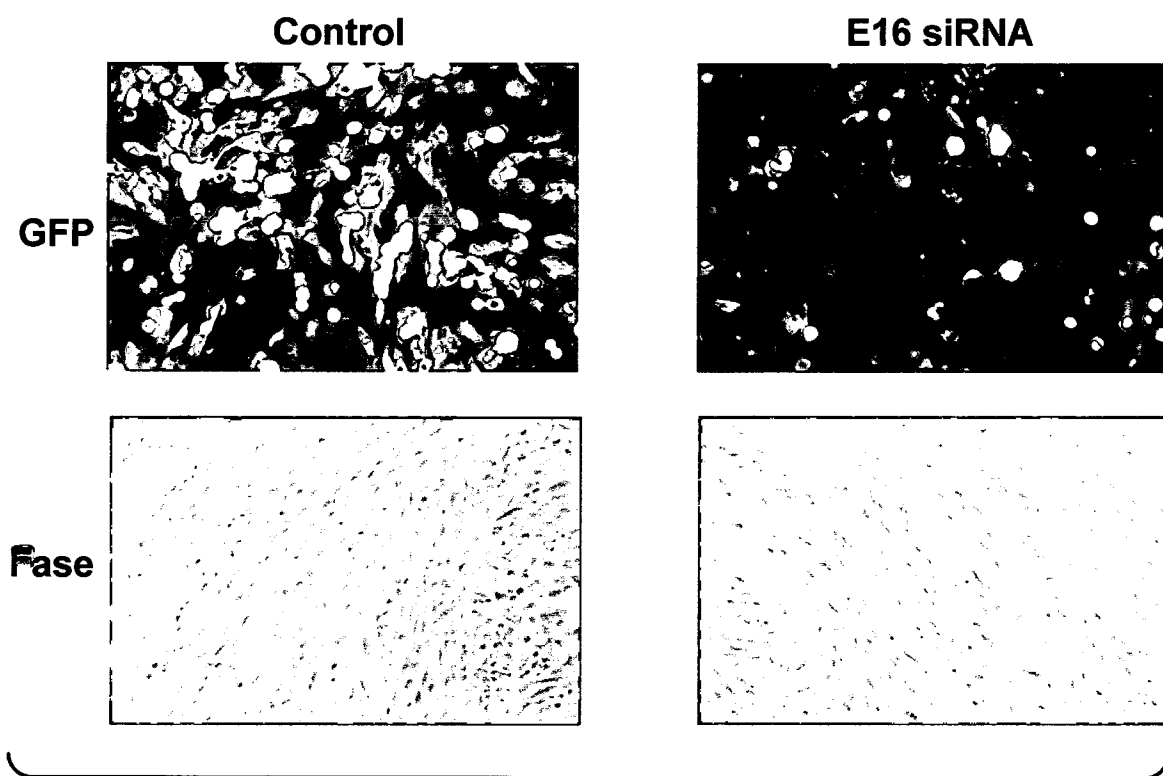


FIG. 164

E16-GFP →

β-tubulina →

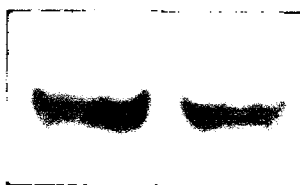
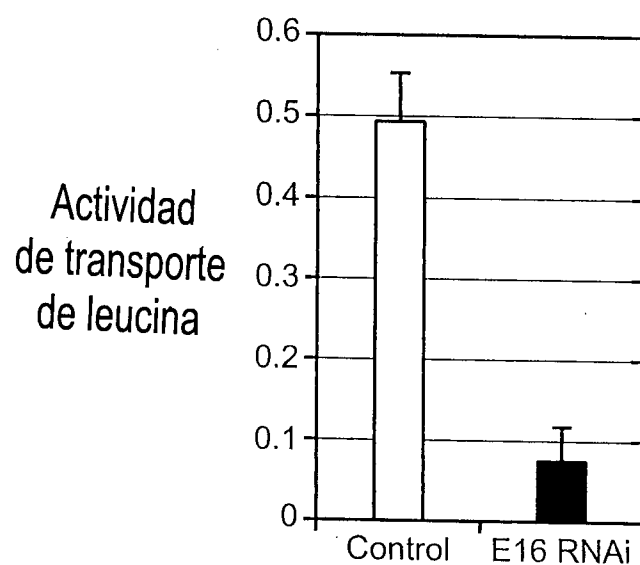
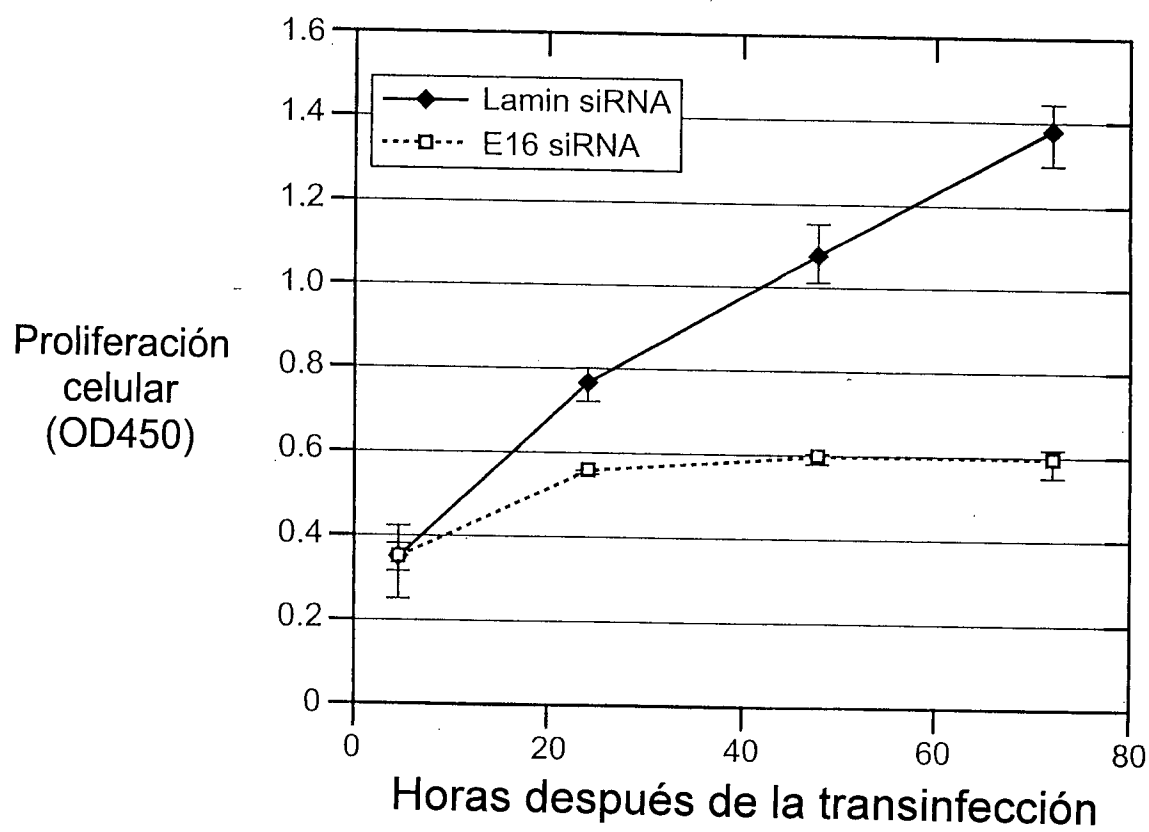


FIG. 165

**FIG. 166****FIG. 167**

PATENT COOPERATION TREATY

PCT

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

(PCT Rule 44bis)

1P-103543

1674

Applicant's or agent's file reference P5001R1P1	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2005/031798	International filing date (day/month/year) 07 September 2005 (07.09.2005)	Priority date (day/month/year) 08 September 2004 (08.09.2004)	
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 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:

- | | |
|---|---|
| ☒ 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		Date of issuance of this report 13 March 2007 (13.03.2007)
Facsimile No. +41 22 338 82 70		Authorized officer Philippe Becamel
Form PCT/IB/373 (January 2004)		e-mail: pt12.pct@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 11 AUG 2006

PCT

PCT

To:

see form PCT/ISA/220

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

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

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

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2005/031798

International filing date (day/month/year)
07.09.2005

Priority date (day/month/year)
08.09.2004

International Patent Classification (IPC) or both national classification and IPC
INV. C07K16/30 A61K47/48 A61K39/395 A61P35/00

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:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Bayer, A

Telephone No. +49 89 2399-7103



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

1676
International application No.
PCT/US2005/031798

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:

see separate sheet

1677

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/031798

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. 1-21, 51-54, 58 (all partially); 28, 29, 38, 47-50, 55, 56 (all complete); 33-37, 58-61 (regarding IA)

because:

☒ the said international application, or the said claims Nos. 33-37, 58-61 (regarding IA) 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. 58 (partially) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☒ the claims, or said claims Nos. 58 (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. 1-21, 51-54 (all partially); 28, 29, 38, 47-50, 55, 56 (all complete)

☐ 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

1678

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/031798

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☒ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-21, 51-54 (all partially), 22-46, 57-61 (all complete)

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	16-21
	No: Claims	1-15, 22-27, 30-37, 39-46, 51-54, 58-61
Inventive step (IS)	Yes: Claims	
	No: Claims	1-27, 30-37, 39-46, 51-54, 58-61
Industrial applicability (IA)	Yes: Claims	1-27, 30-32, 39-46, 51-54, 57
	No: Claims	

2. Citations and explanations

see separate sheet

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

1679
International application No.

PCT/US2005/031798

Re Item I

1. Sequence listings (pages 1-303) corresponding to figures 1-154 as filed are considered to be part of the application and will be considered for the examination.

Re Item III

1. The international search report has been drawn up in respect to only part of the claims of the international application as filed. Since only claims searched will be the subject of the international preliminary examination (Rule 66.1(e) PCT), this written opinion is based on claims 1-21, 51-54, 58 (all partially) and claims 22-27, 30-37, 39-46, 57, 59-61 (all complete) (see also item IV below).
2. Claims 58-61 and claims 33-37 as far as in vivo is concerned 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).
3. Present claim 58 (partially) encompass compounds defined only by their desired function, contrary to the requirements of clarity of Article 6 PCT, because the result-to-be-achieved type of definition does not allow the scope of the claim to be ascertained. Arguing that any compound could be screened does not overcome this objection, as the skilled person would not have knowledge beforehand as to whether it would fall within the scope claimed, except for the antibodies against TAT188 disclosed in the description. It is therefore considered that an equally unquantifiable and thus unreasonable amount of experimentation would be required to screen peptides randomly, imposing a severe and undue burden on all those wishing to ascertain the scope of the claims, which is not in compliance with the clarity requirements of Article 6 PCT. Furthermore, the description does not provide support and disclosure in the sense of Articles 5 and 6 PCT for all imaginable compounds having the desired function. This noncompliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the noncompliance in determining the extent of the search for said claim (PCT Guidelines, 9.19 and 9.24).

1680

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



International application No.

PCT/US2005/031798

The search of said claim was consequently restricted to antibodies as defined in present claim 59.

Accordingly, this written opinion is based on the subject-matter of claim 58 only with regard to antibodies.

4. Present claims 22, 23, 26, 27, 30, 33, 39, 44, 45, 58 and 59 in which the polypeptide is designated by its internal denomination, i.e. TAT188, are not clear (Article 6 PCT). The polypeptide should be defined by its sequence.

Re Item IV

The separate inventions are:

Inventions 1-74: Claims 1-21, 51-54 (all partially)

Each of the antibodies binding to the polypeptides defined by SEQ-ID NOs: 79-114 and 116-154 and the related subject-matter define one independent invention.

Invention 75: Claims 1-21, 51-54 (all partially); claims 22-46, 57-61 (all complete)

An isolated antibody binding to the polypeptide defined by SEQ-ID NO: 115, i.e. TAT188 and the related subject-matter.

Invention 76: Claims 47-50, 55, 56 (all complete); claims 51-54 (all partially)

TAT188 siRNA and the related subject-matter.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The present application relates to the identification of various TAT (Tumour-associated Antigenic Target) polypeptides defined by SEQ-ID NOs: 79-154, wherein SEQ-ID NO: 115 corresponds to TAT188, and discloses isolated antibodies against such polypeptides as well as uses thereof. Thus, the problem underlying the present application can be seen as the provision of antibodies against TAT polypeptides.

Additionally, the present application discloses TAT188 binding interfering RNA (siRNA)

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

 International application No.
PCT/US2005/031798

and uses thereof. Thus, another problem underlying the present application can be seen as the provision of TAT siRNA.

The technical relationship and thus common concept within the meaning of Rule 13.2 PCT a priori linking the antibodies is considered as all relating to TAT polypeptides. The technical relationship and thus common concept within the meaning of Rule 13.2 PCT a priori linking the anti-TAT188 antibody and the TAT188 siRNA is considered as both relating to TAT188.

The prior art, however, already discloses said common concepts. WO03000113 (D1) discloses the identical TAT polypeptides of the present application, i.e. SEQ-ID NOs: 79-154 including TAT188 as well as antibodies against such polypeptides.

Thus, in view of the prior art, the problem underlying the present application can be formulated as the provision of alternative TAT modulators. All inventions listed above, represent an independent solution concerning the foregoing problem of the underlying application.

Since no other technical feature can be distinguished which, in the light of the prior art could be regarded as special common technical feature, the ISA is of the opinion that there is no single inventive concept (Rule 13.1 PCT) underlying the plurality of different inventions in the sense of Rule 13.2 PCT.

Consequently there is lack of unity and the different inventions not belonging to a common inventive concept are formulated as different inventions pursuant to Article 17(3)(a) PCT.

Since the applicant did not pay search fees for all of the inventions, an opinion will only be formulated for the subject-matter of the searched inventions, i.e. invention 1 (an isolated antibody binding to a polypeptide defined by SEQ-ID NO: 79 and the related subject-matter) and 75 (an isolated antibody binding to the polypeptide defined by SEQ-ID NO:115, i.e. TAT188 and the related subject-matter).

Re Item V

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

International application No.

PCT/US2005/031798

1882

1. Reference is made to the following documents:

- D1: WO 03/000113 A (GENENTECH, INC) 3 January 2003 (2003-01-03)
D2: HENDERSON MARILYN ET AL: "Microfibril-associated glycoprotein-1 (MAGP-1) is specifically located on the beads of the beaded-filament structure for fibrillin-containing microfibrils as visualized by the rotary shadowing technique" JOURNAL OF HISTOCHEMISTRY AND CYTOCHEMISTRY, vol. 44, no. 12, 1996, pages 1389-1397, XP002379484 ISSN: 0022-1554
D3: MANNION BRIAN A ET AL: "The light chain of CD98 is identified at E16/TA1 protein" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 50, 11 December 1998 (1998-12-11), pages 33127-33129, XP002392000 ISSN: 0021-9258
D4: EP-A-1 111 048 (JAPAN SCIENCE AND TECHNOLOGY CORPORATION; JAPAN SCIENCE AND TECHNOLOGY) 27 June 2001 (2001-06-27)
D5: DORONINA S O ET AL: "Development of potent monoclonal antibody auristatin conjugates for cancer therapy" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 21, no. 7, July 2003 (2003-07), pages 778-784, XP002280966 ISSN: 1087-0156 cited in the application
D6: DORONINA SVETLANA ET AL: "Immunoconjugates comprised of drugs with impaired cellular permeability: A new approach to targeted therapy." ABSTRACTS OF PAPERS AMERICAN CHEMICAL SOCIETY, vol. 228, no. Part 1, August 2004 (2004-08), page U908, XP009066098 & MEETING OF THE DIVISION OF CHEMICAL TOXICOLOGY OF THE AMERICAN-CHEMICAL-SOCIETY HELD AT THE 228TH N; PHILADELPHIA, PA, USA; AUGUST 22 -26, 2004 ISSN: 0065-7727

As not otherwise indicated, reference is made to the passages cited in the International Search Report.

2. Novelty

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-15, 22-27, 30-37, 39-46, 51-54 and 58-61 is not new in the sense of Article 33(2) PCT.

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

International application No.

PCT/US2005/031798

Document D1 discloses the identical subject-matter as the present application, including SEQ-ID NOs: 1, 79, 37 and 115 and antibodies against in general as well as uses thereof. Only missing from D1 are the toxins and linkers specified in dependent claims 16-21 and the specific antibodies 3B5.1, 12B9.1 and 12G12.1. Accordingly, in view of D1, the subject-matter of present claims 1-15, 22-27, 30-37, 39-46, 51-54 and 58-61 is not novel.

Document D2 discloses the preparation and use of MAGP-1 monoclonal antibody (mAb 11B). Since MAGP-1 is synonymous to MFAP2 (microfibrillar-associated protein 2) which is identical to TAT161 presented by SEQ-ID 79 of the present application, D2 anticipates the novelty of present claims 1-3.

Document D3 discloses monoclonal antibodies against E16 which is identical to TAT188 and their use in immunoblots of colon carcinomas compared to normal colon cells. Since any antibody against E16 inherently has the functional features of present claims 23, 26, 27 and 30, claims 1-3, 22-27, 30-32 and 39-46 are not novel in view of D3.

Document D4 discloses human LAT1 (L-amino acid transporter 1 which is identical to TAT188) and antibodies against as well as their use in therapy, diagnosis and quantification of LAT1. Accordingly, in view of D4, the subject-matter of present claims 1-5, 12-15, 22-27, 30-37, 39-46, 51-54 and 58-61 is not novel.

For the specific anti-TAT188 antibodies 3B5.1, 12B9.1 and 12G12.1 presented by their ATCC Accession Numbers novelty can be acknowledged since none of the prior art available discloses such antibodies (Article 33(2) PCT).

3. Inventive step

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-27, 30-37, 39-46, 51-54, 57-61 does not involve an inventive step in the sense of Article 33(3) PCT.

3.1 Taking D1 as the closest prior art, the problem underlying the present claims 16-21

may be considered as the provision of alternative Immunoconjugates, the solution being the use of the toxins and carriers recited in claims 16-21.

However such toxins and carriers have already been employed for the same purpose, i.e. for the preparation of mAb Immunoconjugates, see, e.g. D5 and D6. It would therefore be obvious to the person skilled in the art, to apply these compounds with corresponding effect to the antibody of D1, thereby arriving at the subject-matter of present claims 16-21.

3.2 The antibody of present claims 1-27, 30-32 is only defined by its binding to TAT188 without giving any technical feature of the antibody. Since an antibody against a known protein represents the outcome of routine experimentation that does not involve inventive skill, said claims are not considered as inventive.

3.3 The specific antibodies produced by hybridomas 3B5.1, 12B9.1 and 12G12.1 as well as their uses are not considered as inventive either.

Taking D1 as the closest prior art the problem to be solved by the present application was to provide monoclonal antibodies against T188. D1, however very detailed teaches how to obtain such antibodies using methods well-known to the skilled person as well as uses thereof and thus the generation and uses of said antibodies do not involve inventive skill.

Taking D3 as the closest prior art the problem to be solved by the present application was to provide alternative monoclonal antibodies against T188. However, the generation of monoclonal antibodies against a known protein represents the outcome of routine experimentation not involving inventive skill. Additionally, there seems to be no surprising effect/feature of the specific antibodies of the present application in comparison to the antibodies disclosed in D3.

Thus, no inventive step for claims 1-27, 30-37, 39-46, 51-54 and 57-61 can be acknowledged.

4. For the assessment of the present claims 33-37 and 58-61 on the question whether

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

1685
International application No.

PCT/US2005/031798

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.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 11 AUG 2006

PCT

PCT

To:

see form PCT/ISA/220

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

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

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

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2005/031798

International filing date (day/month/year)
07.09.2005

Priority date (day/month/year)
08.09.2004

International Patent Classification (IPC) or both national classification and IPC
INV. C07K16/30 A61K47/48 A61K39/395 A61P35/00

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:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

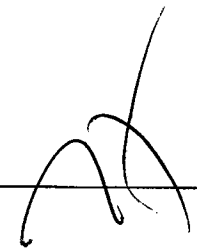
Bayer, A

Telephone No. +49 89 2399-7103



WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/031798



Box No. 1 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:

see separate sheet

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/031798

1688

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. 1-21, 51-54, 58 (all partially); 28, 29, 38, 47-50, 55, 56 (all complete); 33-37, 58-61 (regarding IA)

because:

☒ the said international application, or the said claims Nos. 33-37, 58-61 (regarding IA) 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. 58 (partially) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☒ the claims, or said claims Nos. 58 (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. 1-21, 51-54 (all partially); 28, 29, 38, 47-50, 55, 56 (all complete)

☐ 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).

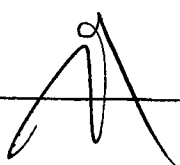
☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and 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/US2005/031798



Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
 - ☒ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
 - ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
 - ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-21, 51-54 (all partially), 22-46, 57-61 (all complete)

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	16-21
	No: Claims	1-15, 22-27, 30-37, 39-46, 51-54, 58-61
Inventive step (IS)	Yes: Claims	
	No: Claims	1-27, 30-37, 39-46, 51-54, 58-61
Industrial applicability (IA)	Yes: Claims	1-27, 30-32, 39-46, 51-54, 57
	No: Claims	

2. Citations and explanations

see separate sheet

169

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



International application No.

PCT/US2005/031798

Re Item I

1. Sequence listings (pages 1-303) corresponding to figures 1-154 as filed are considered to be part of the application and will be considered for the examination.

Re Item III

1. The international search report has been drawn up in respect to only part of the claims of the international application as filed. Since only claims searched will be the subject of the international preliminary examination (Rule 66.1(e) PCT), this written opinion is based on claims 1-21, 51-54, 58 (all partially) and claims 22-27, 30-37, 39-46, 57, 59-61 (all complete) (see also item IV below).
2. Claims 58-61 and claims 33-37 as far as in vivo is concerned 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).
3. Present claim 58 (partially) encompass compounds defined only by their desired function, contrary to the requirements of clarity of Article 6 PCT, because the result-to-be-achieved type of definition does not allow the scope of the claim to be ascertained. Arguing that any compound could be screened does not overcome this objection, as the skilled person would not have knowledge beforehand as to whether it would fall within the scope claimed, except for the antibodies against TAT188 disclosed in the description. It is therefore considered that an equally unquantifiable and thus unreasonable amount of experimentation would be required to screen peptides randomly, imposing a severe and undue burden on all those wishing to ascertain the scope of the claims, which is not in compliance with the clarity requirements of Article 6 PCT. Furthermore, the description does not provide support and disclosure in the sense of Articles 5 and 6 PCT for all imaginable compounds having the desired function. This noncompliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the noncompliance in determining the extent of the search for said claim (PCT Guidelines, 9.19 and 9.24).

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

International application No.

PCT/US2005/031798

The search of said claim was consequently restricted to antibodies as defined in present claim 59.

Accordingly, this written opinion is based on the subject-matter of claim 58 only with regard to antibodies.

4. Present claims 22, 23, 26, 27, 30, 33, 39, 44, 45, 58 and 59 in which the polypeptide is designated by its internal denomination, i.e. TAT188, are not clear (Article 6 PCT). The polypeptide should be defined by its sequence.

Re Item IV

The separate inventions are:

Inventions 1-74: Claims 1-21, 51-54 (all partially)

Each of the antibodies binding to the polypeptides defined by SEQ-ID NOs: 79-114 and 116-154 and the related subject-matter define one independent invention.

Invention 75: Claims 1-21, 51-54 (all partially); claims 22-46, 57-61 (all complete)

An isolated antibody binding to the polypeptide defined by SEQ-ID NO: 115, i.e. TAT188 and the related subject-matter.

Invention 76: Claims 47-50, 55, 56 (all complete); claims 51-54 (all partially)

TAT188 siRNA and the related subject-matter.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The present application relates to the identification of various TAT (Tumour-associated Antigenic Target) polypeptides defined by SEQ-ID NOs: 79-154, wherein SEQ-ID NO: 115 corresponds to TAT188, and discloses isolated antibodies against such polypeptides as well as uses thereof. Thus, the problem underlying the present application can be seen as the provision of antibodies against TAT polypeptides.

Additionally, the present application discloses TAT188 binding interfering RNA (siRNA)

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

International application No.

PCT/US2005/031798

and uses thereof. Thus, another problem underlying the present application can be seen as the provision of TAT siRNA.

The technical relationship and thus common concept within the meaning of Rule 13.2 PCT a priori linking the antibodies is considered as all relating to TAT polypeptides. The technical relationship and thus common concept within the meaning of Rule 13.2 PCT a priori linking the anti-TAT188 antibody and the TAT188 siRNA is considered as both relating to TAT188.

The prior art, however, already discloses said common concepts. WO03000113 (D1) discloses the identical TAT polypeptides of the present application, i.e. SEQ-ID NOs: 79-154 including TAT188 as well as antibodies against such polypeptides.

Thus, in view of the prior art, the problem underlying the present application can be formulated as the provision of alternative TAT modulators. All inventions listed above, represent an independent solution concerning the foregoing problem of the underlying application.

Since no other technical feature can be distinguished which, in the light of the prior art could be regarded as special common technical feature, the ISA is of the opinion that there is no single inventive concept (Rule 13.1 PCT) underlying the plurality of different inventions in the sense of Rule 13.2 PCT.

Consequently there is lack of unity and the different inventions not belonging to a common inventive concept are formulated as different inventions pursuant to Article 17(3)(a) PCT.

Since the applicant did not pay search fees for all of the inventions, an opinion will only be formulated for the subject-matter of the searched inventions, i.e. invention 1 (an isolated antibody binding to a polypeptide defined by SEQ-ID NO: 79 and the related subject-matter) and 75 (an isolated antibody binding to the polypeptide defined by SEQ-ID NO:115, i.e. TAT188 and the related subject-matter).

Re Item V

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

International application No.

PCT/US2005/031798

1. Reference is made to the following documents:

- D1: WO 03/000113 A (GENENTECH, INC) 3 January 2003 (2003-01-03)
- D2: HENDERSON MARILYN ET AL: "Microfibril-associated glycoprotein-1 (MAGP-1) is specifically located on the beads of the beaded-filament structure for fibrillin-containing microfibrils as visualized by the rotary shadowing technique" JOURNAL OF HISTOCHEMISTRY AND CYTOCHEMISTRY, vol. 44, no. 12, 1996, pages 1389-1397, XP002379484 ISSN: 0022-1554
- D3: MANNION BRIAN A ET AL: "The light chain of CD98 is identified at E16/TA1 protein" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 50, 11 December 1998 (1998-12-11), pages 33127-33129, XP002392000 ISSN: 0021-9258
- D4: EP-A-1 111 048 (JAPAN SCIENCE AND TECHNOLOGY CORPORATION; JAPAN SCIENCE AND TECHNOLOGY) 27 June 2001 (2001-06-27)
- D5: DORONINA S O ET AL: "Development of potent monoclonal antibody auristatin conjugates for cancer therapy" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 21, no. 7, July 2003 (2003-07), pages 778-784, XP002280966 ISSN: 1087-0156 cited in the application
- D6: DORONINA SVETLANA ET AL: "Immunoconjugates comprised of drugs with impaired cellular permeability: A new approach to targeted therapy." ABSTRACTS OF PAPERS AMERICAN CHEMICAL SOCIETY, vol. 228, no. Part 1, August 2004 (2004-08), page U908, XP009066098 & MEETING OF THE DIVISION OF CHEMICAL TOXICOLOGY OF THE AMERICAN-CHEMICAL-SOCIETY HELD AT THE 228TH N; PHILADELPHIA, PA, USA; AUGUST 22 -26, 2004 ISSN: 0065-7727

As not otherwise indicated, reference is made to the passages cited in the International Search Report.

2. Novelty

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-15, 22-27, 30-37, 39-46, 51-54 and 58-61 is not new in the sense of Article 33(2) PCT.

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

International application No.

PCT/US2005/031798

Document D1 discloses the identical subject-matter as the present application, including SEQ-ID NOs: 1, 79, 37 and 115 and antibodies against in general as well as uses thereof. Only missing from D1 are the toxins and linkers specified in dependent claims 16-21 and the specific antibodies 3B5.1, 12B9.1 and 12G12.1. Accordingly, in view of D1, the subject-matter of present claims 1-15, 22-27, 30-37, 39-46, 51-54 and 58-61 is not novel.

Document D2 discloses the preparation and use of MAGP-1 monoclonal antibody (mAb 11B). Since MAGP-1 is synonymous to MFAP2 (microfibrillar-associated protein 2) which is identical to TAT161 presented by SEQ-ID 79 of the present application, D2 anticipates the novelty of present claims 1-3.

Document D3 discloses monoclonal antibodies against E16 which is identical to TAT188 and their use in immunoblots of colon carcinomas compared to normal colon cells. Since any antibody against E16 inherently has the functional features of present claims 23, 26, 27 and 30, claims 1-3, 22-27, 30-32 and 39-46 are not novel in view of D3.

Document D4 discloses human LAT1 (L-amino acid transporter 1 which is identical to TAT188) and antibodies against as well as their use in therapy, diagnosis and quantification of LAT1. Accordingly, in view of D4, the subject-matter of present claims 1-5, 12-15, 22-27, 30-37, 39-46, 51-54 and 58-61 is not novel.

For the specific anti-TAT188 antibodies 3B5.1, 12B9.1 and 12G12.1 presented by their ATCC Accession Numbers novelty can be acknowledged since none of the prior art available discloses such antibodies (Article 33(2) PCT).

3. Inventive step

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-27, 30-37, 39-46, 51-54, 57-61 does not involve an inventive step in the sense of Article 33(3) PCT.

3.1 Taking D1 as the closest prior art, the problem underlying the present claims 16-21

may be considered as the provision of alternative Immunoconjugates, the solution being the use of the toxins and carriers recited in claims 16-21.

However such toxins and carriers have already been employed for the same purpose, i.e. for the preparation of mAb Immunoconjugates, see, e.g. D5 and D6. It would therefore be obvious to the person skilled in the art, to apply these compounds with corresponding effect to the antibody of D1, thereby arriving at the subject-matter of present claims 16-21.

3.2 The antibody of present claims 1-27, 30-32 is only defined by its binding to TAT188 without giving any technical feature of the antibody. Since an antibody against a known protein represents the outcome of routine experimentation that does not involve inventive skill, said claims are not considered as inventive.

3.3 The specific antibodies produced by hybridomas 3B5.1, 12B9.1 and 12G12.1 as well as their uses are not considered as inventive either.

Taking D1 as the closest prior art the problem to be solved by the present application was to provide monoclonal antibodies against T188. D1, however very detailed teaches how to obtain such antibodies using methods well-known to the skilled person as well as uses thereof and thus the generation and uses of said antibodies do not involve inventive skill.

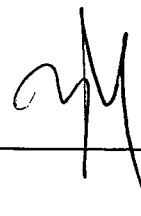
Taking D3 as the closest prior art the problem to be solved by the present application was to provide alternative monoclonal antibodies against T188. However, the generation of monoclonal antibodies against a known protein represents the outcome of routine experimentation not involving inventive skill. Additionally, there seems to be no surprising effect/feature of the specific antibodies of the present application in comparison to the antibodies disclosed in D3.

Thus, no inventive step for claims 1-27, 30-37, 39-46, 51-54 and 57-61 can be acknowledged.

4. For the assessment of the present claims 33-37 and 58-61 on the question whether

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

1696



International application No.

PCT/US2005/031798

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.

**BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE**

INTERNATIONAL FORM

**RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.**

To: (Name and Address of Depositor or Attorney)

Genentech, Inc.
Attn: Deidre L. Conley
1 DNA Way MS 49
South San Francisco, CA 94080

Deposited on Behalf of: Genentech, Inc.

Identification Reference by Depositor:

Hybridoma Cell Line from Mouse: 3B5.1
Hybridoma Cell Line from Mouse: 12B9.1
Hybridoma Cell Line from Mouse: 12G12.1
Docket or Case No.: P5001R1P1

Patent Deposit Designation

PTA-6193
PTA-6194
PTA-6195

The deposits were accompanied by: a scientific description, a proposed taxonomic description indicated above. The deposits were received September 8, 2004 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested September 21, 2004. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris
Marie Harris, Patent Specialist, ATCC Patent Depository

Date: October 6, 2004

1698

AMERICAN TYPE CULTURE COLLECTION

10801 University Blvd.
Manassas, VA 20110-2209
Telephone: 703-365-2700
Fax: 703-365-2745

FACSIMILE

Date: September 24, 2004

To: Deirdre L. Conley
Fax Number: 650-952-9881

From: ATCC Patent Depository **Number of pages:** 1 (Including this page)

REFERENCE: Patent Deposit (Ref: Docket or Case No.: P5001R1P1)

Description: Hybridoma Cell Line from Mouse: 3B5.1 assigned PTA-6193
Hybridoma Cell Line from Mouse: 12B9.1 assigned PTA-6194
Hybridoma Cell Line from Mouse: 12G12.1 assigned PTA-6195

Date of Deposit: September 8, 2004

The ATCC Certificate of Deposit will be forwarded to you within 30 days. An invoice will be sent under separate cover referencing PO# 515441 as follows:

Total Fees for PTA-6193 to PTA-6195 \$ 7,500.00
(Storage/informing/viability testing)


Marie Harris, Patent Specialist
ATCC Patent Depository

The information contained in this facsimile is intended only for the use of the individual or entity named above. If the reader of this message is not the intended recipient, you are notified that any dissemination or distribution, except to the intended recipient of this communication, is prohibited. If you have received this communication in error, please call us immediately at the telephone number listed above.

TOTAL P.01

ATCC

10801 University Blvd • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-365-2745

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.

To: (Name and Address of Depositor or Attorney)

Genentech, Inc.
Attn: Deidre L. Conley
1 DNA Way MS 49
South San Francisco, CA 94080

Deposited on Behalf of: Genentech, Inc.

Identification Reference by Depositor:

Hybridoma Cell Line from Mouse: 3B5.1
Hybridoma Cell Line from Mouse: 12B9.1
Hybridoma Cell Line from Mouse: 12G12.1
Docket or Case No.: P5001R1P1

Patent Deposit Designation

PTA-6193
PTA-6194
PTA-6195

The deposits were accompanied by: a scientific description, a proposed taxonomic description indicated above. The deposits were received September 8, 2004 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested September 21, 2004. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris
Marie Harris, Patent Specialist, ATCC Patent Depository

Date: October 6, 2004

1700

AMERICAN TYPE CULTURE COLLECTION

10801 University Blvd.
Manassas, VA 20110-2209
Telephone: 703-365-2700
Fax: 703-365-2745

FACSIMILE**Date:** September 24, 2004**To:** Deirdre L. Conley
Fax Number: 650-952-9881**From:** ATCC Patent Depository **Number of pages:** 1 (Including this page)**REFERENCE:** Patent Deposit (Ref: Docket or Case No.: P5001R1P1)

Description: Hybridoma Cell Line from Mouse: 3B5.1 assigned PTA-6193
Hybridoma Cell Line from Mouse: 12B9.1 assigned PTA-6194
Hybridoma Cell Line from Mouse: 12G12.1 assigned PTA-6195

Date of Deposit: September 8, 2004

The ATCC Certificate of Deposit will be forwarded to you within 30 days. An invoice will be sent under separate cover referencing PO# 515441 as follows:

Total Fees for PTA-6193 to PTA-6195 \$ 7,500.00
(Storage/informing/viability testing)

Marie Harris, Patent Specialist
ATCC Patent Depository

The information contained in this facsimile is intended only for the use of the individual or entity named above. If the reader of this message is not the intended recipient, you are notified that any dissemination or distribution, except to the intended recipient of this communication, is prohibited. If you have received this communication in error, please call us immediately at the telephone number listed above.

TOTAL P.01

APOSTILLE*(Convention de La Haye du 5 octobre 1961)*

1. Country: United States of America

This public document

2. has been signed by M.K. Carter

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 twenty-second of August, 2007

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

8. No. 07034157-2

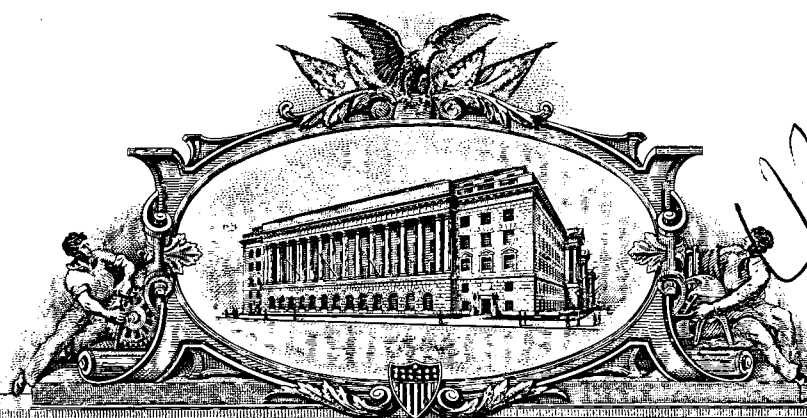
9. Seal/Stamp:

10. Signature:

Patrick O. Hatchett

Colombia 1702

A 1645155



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

August 14, 2007

**THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE
RECORDS OF THIS OFFICE OF A DOCUMENT RECORDED ON
JULY 20, 2007.**

By Authority of the

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

M. K. CARTER

Certifying Officer



PATENT ASSIGNMENT

Electronic Version v1.1

• Stylesheet Version v1.1

SUBMISSION TYPE:	NEW ASSIGNMENT																																
NATURE OF CONVEYANCE:	ASSIGNMENT																																
CONVEYING PARTY DATA																																	
<table border="1"><thead><tr><th>Name</th><th>Execution Date</th></tr></thead><tbody><tr><td>Belinda Cairns</td><td>06/06/2006</td></tr><tr><td>Ruihuan Chen</td><td>05/22/2006</td></tr><tr><td>Gretchen Frantz</td><td>05/22/2006</td></tr><tr><td>Kenneth J. Hillan</td><td>05/24/2006</td></tr><tr><td>Hartmut Koeppen</td><td>05/23/2006</td></tr><tr><td>Heidi S. Phillips</td><td>06/21/2006</td></tr><tr><td>Paul Polakis</td><td>05/21/2006</td></tr><tr><td>Susan D. Spencer</td><td>05/22/2006</td></tr><tr><td>Victoria Smith</td><td>05/23/2006</td></tr><tr><td>P. Mickey Williams</td><td>05/31/2006</td></tr><tr><td>Thomas D. Wu</td><td>05/22/2006</td></tr><tr><td>Zemin Zhang</td><td>05/22/2006</td></tr><tr><td>Chie Sakanaka</td><td>05/22/2006</td></tr><tr><td>Anan Chuntharapai</td><td>05/22/2006</td></tr><tr><td>Chai Janeka Reed</td><td>05/22/2006</td></tr></tbody></table>		Name	Execution Date	Belinda Cairns	06/06/2006	Ruihuan Chen	05/22/2006	Gretchen Frantz	05/22/2006	Kenneth J. Hillan	05/24/2006	Hartmut Koeppen	05/23/2006	Heidi S. Phillips	06/21/2006	Paul Polakis	05/21/2006	Susan D. Spencer	05/22/2006	Victoria Smith	05/23/2006	P. Mickey Williams	05/31/2006	Thomas D. Wu	05/22/2006	Zemin Zhang	05/22/2006	Chie Sakanaka	05/22/2006	Anan Chuntharapai	05/22/2006	Chai Janeka Reed	05/22/2006
Name	Execution Date																																
Belinda Cairns	06/06/2006																																
Ruihuan Chen	05/22/2006																																
Gretchen Frantz	05/22/2006																																
Kenneth J. Hillan	05/24/2006																																
Hartmut Koeppen	05/23/2006																																
Heidi S. Phillips	06/21/2006																																
Paul Polakis	05/21/2006																																
Susan D. Spencer	05/22/2006																																
Victoria Smith	05/23/2006																																
P. Mickey Williams	05/31/2006																																
Thomas D. Wu	05/22/2006																																
Zemin Zhang	05/22/2006																																
Chie Sakanaka	05/22/2006																																
Anan Chuntharapai	05/22/2006																																
Chai Janeka Reed	05/22/2006																																
RECEIVING PARTY DATA																																	
<table border="1"><tr><td>Name:</td><td>Genentech, Inc.</td></tr><tr><td>Street Address:</td><td>1 DNA Way</td></tr><tr><td>City:</td><td>South San Francisco</td></tr><tr><td>State/Country:</td><td>CALIFORNIA</td></tr><tr><td>Postal Code:</td><td>94080-4990</td></tr></table>		Name:	Genentech, Inc.	Street Address:	1 DNA Way	City:	South San Francisco	State/Country:	CALIFORNIA	Postal Code:	94080-4990																						
Name:	Genentech, Inc.																																
Street Address:	1 DNA Way																																
City:	South San Francisco																																
State/Country:	CALIFORNIA																																
Postal Code:	94080-4990																																
PROPERTY NUMBERS Total: 1																																	
<table border="1"><thead><tr><th>Property Type</th><th>Number</th></tr></thead><tbody><tr><td>Application Number:</td><td>10936626</td></tr></tbody></table>		Property Type	Number	Application Number:	10936626																												
Property Type	Number																																
Application Number:	10936626																																
CORRESPONDENCE DATA																																	

540.00 10936626 CH

1704

SD

Fax Number: (650)324-0638

Correspondence will be sent via US Mail when the fax attempt is unsuccessful.

Phone: 650 324-7000

Email: smanibusan@hewm.com

Correspondent Name: Ginger Dreger

Address Line 1: 275 Middlefield Road

Address Line 4: Menlo Park, CALIFORNIA 94025

ATTORNEY DOCKET NUMBER:

39766-0214R1P1

NAME OF SUBMITTER:

Ginger Dreger

Total Attachments: 16

source=assignment#page1.tif

source=assignment#page2.tif

source=assignment#page3.tif

source=assignment#page4.tif

source=assignment#page5.tif

source=assignment#page6.tif

source=assignment#page7.tif

source=assignment#page8.tif

source=assignment#page9.tif

source=assignment#page10.tif

source=assignment#page11.tif

source=assignment#page12.tif

source=assignment#page13.tif

source=assignment#page14.tif

source=assignment#page15.tif

source=assignment#page16.tif

ASSIGNMENT

WHEREAS, Belinda Cairns, a citizen of GB, residing at 17 Chester Circle, Los Altos, CA 94022, and Ruihuan Chen, a citizen of CN, residing at 1072 Tanland Drive, #114, Palo Alto, CA 94303, and Gretchen Frantz, a citizen of US, residing at 2819 Buchanan Street, San Francisco, CA 94123, and Kenneth J. Hillan, a citizen of GB, residing at 64 Seward Street, San Francisco, CA 94114, Hartmut Koeppen, a citizen of DE, residing at 1746 Milvia Street, Berkeley, CA 94709, Heidi S. Phillips, a citizen of US, residing at 1511 Walnut Drive, Palo Alto, CA 94303, Paul Polakis, a citizen of US, residing at 1449 Cortez Avenue, Burlingame, CA 94010, Susan D. Spencer, a citizen of US, residing at 2395 Paradise Drive, Tiburon, CA 94920-1201, Victoria Smith, a citizen of AU, residing at 19 Dwight Road, Burlingame, CA 94010, P. Mickey Williams, a citizen of US, residing at 509 Alto Avenue, Half Moon Bay, CA 94019, Thomas D. Wu, a citizen of US, residing at 41 Nevada Street, San Francisco, CA 94110, Zemin Zhang, a citizen of US, residing at 876 Taurus Drive, Foster City, CA 94404, Mark Sliwowski, a citizen of US, residing at 42 Oak Creek Lane, San Carlos, CA 94070, Chie Sakanaka, a citizen of JP, residing at 1481 8th Ave, San Francisco, CA 94122, Anan Chuntharapai, a citizen of US, residing at 826 Ellis Drive, Colma, CA 94015, and Chae Janeka Reed, a citizen of US, residing at 2396 Post Street, San Francisco, CA 94115, (hereinafter "ASSIGNORS"), have invented a new and useful invention in 619 MENNA STREET SAN FRANCISCO CA 94103

COMPOSITIONS AND METHODS FOR THE DIAGNOSIS AND TREATMENT OF TUMOR

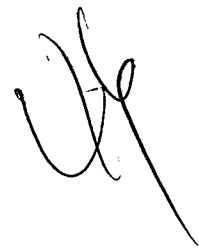
for which an application Serial No. 10/936,626 (Docket No. P5001R1P1) for Letters Patent has been filed by them on September 8, 2004; and

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 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



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.

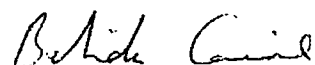
The terms and covenants of this assignment shall inure to the benefit of said GENENTECH, INC., its successors, assigns and other legal representatives, and shall be binding upon said ASSIGNORS, their respective heirs, legal representatives and assigns.

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

IN WITNESS WHEREOF we undersign as follows;

Los Altos

Dated: 06/06/06


Belinda Cairns

South San Francisco

Dated: _____

Ruihuan Chen

South San Francisco

Dated: _____

Gretchen Frantz

South San Francisco

Dated: _____

Kenneth J. Hillan

South San Francisco

Dated: _____

Hartmut Koeppen

South San Francisco

Dated: _____

Heidi S. Phillips

South San Francisco

Dated: _____

Paul Polakis

South San Francisco

Dated: _____

Susan D. Spencer

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.

IN WITNESS WHEREOF we undersign as follows;

Los Altos

Belinda Cairns

Dated: _____

South San Francisco



Ruihuan Chen

Dated: 05/22/2006

South San Francisco

Gretchen Frantz

Dated: _____

South San Francisco

Kenneth J. Hillan

Dated: _____

South San Francisco

Hartmut Koeppen

Dated: _____

South San Francisco

Heidi S. Phillips

Dated: _____

South San Francisco

Paul Polakis

Dated: _____

1708

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.

IN WITNESS WHEREOF we undersign as follows;

Los Altos

Belinda Cairns

Dated: _____

South San Francisco

Ruihuan Chen

Dated: _____

South San Francisco

Gretchen Frantz

Dated: 5/22/06

South San Francisco

Kenneth J. Hillan

Dated: _____

South San Francisco

Hartmut Koeppen

Dated: _____

South San Francisco

Heidi S. Phillips

Dated: _____

South San Francisco

Paul Polakis

Dated: _____

CSH

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.

IN WITNESS WHEREOF we undersign as follows;

Los Altos

Belinda Cairns

Dated: _____

South San Francisco

Ruihuan Chen

Dated: _____

South San Francisco

Gretchen Frantz

Dated: _____

South San Francisco

Kenneth J. Hillan

Kenneth J. Hillan

Dated: 5/24/06

South San Francisco

Hartmut Koeppen

Dated: _____

South San Francisco

Heidi S. Phillips

Dated: _____

South San Francisco

Paul Polakis

Dated: _____

1710

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.

IN WITNESS WHEREOF we undersign as follows;

Los Altos	_____
Dated: _____	Belinda Cairns
South San Francisco	_____
Dated: _____	Ruihuan Chen
South San Francisco	_____
Dated: _____	Gretchen Frantz
South San Francisco	_____
Dated: _____	Kenneth J. Hillan
South San Francisco	_____
Dated: <u>05.23.2000</u>	 Hartmut Koeppen
South San Francisco	_____
Dated: _____	Heidi S. Phillips
South San Francisco	_____
Dated: _____	Paul Polakis

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.

IN WITNESS WHEREOF we undersign as follows;

Los Altos

Belinda Cairns

Dated: _____

South San Francisco

Ruihuan Chen

Dated: _____

South San Francisco

Gretchen Frantz

Dated: _____

South San Francisco

Kenneth J. Hillan

Dated: _____

South San Francisco

Hartmut Koeppen

Dated: _____

South San Francisco

Heidi S. Phillips
Heidi S. Phillips

Dated: 6/21/00

South San Francisco

Paul Polakis

Dated: _____

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.

IN WITNESS WHEREOF we undersign as follows;

Los Altos

Belinda Cairns

Dated: _____

South San Francisco

Ruihuan Chen

Dated: _____

South San Francisco

Gretchen Frantz

Dated: _____

South San Francisco

Kenneth J. Hillan

Dated: _____

South San Francisco

Hartmut Koeppen

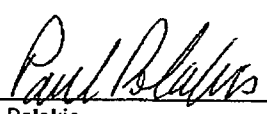
Dated: _____

South San Francisco

Heidi S. Phillips

Dated: _____

South San Francisco



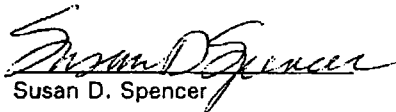
Paul Polakis

Dated: 5-21-04



South San Francisco

Dated: 5/22/06


Susan D. Spencer

South San Francisco

Dated: _____

Victoria Smith

Half Moon Bay

Dated: _____

P. Mickey Williams

South San Francisco

Dated: _____

Thomas D. Wu

South San Francisco

Dated: _____

Zemin Zhang

South San Francisco

Dated: _____

Mark Sliwkowski

South San Francisco

Dated: _____

Chie Sakanaka

South San Francisco

Dated: _____

Anan Chuntharapai

South San Francisco

Dated: _____

Chae Janeka Reed



South San Francisco

Dated: _____

Susan D. Spencer

South San Francisco

Dated: MAY 23.06

Victoria Smith

Half Moon Bay

Dated: _____

P. Mickey Williams

South San Francisco

Dated: _____

Thomas D. Wu

South San Francisco

Dated: _____

Zemin Zhang

South San Francisco

Dated: _____

Mark Sliwkowski

South San Francisco

Dated: _____

Chie Sakanaka

South San Francisco

Dated: _____

Anan Chuntharapai

South San Francisco

Dated: _____

Chae Janeka Reed

715

South San Francisco

Dated: _____

Susan D. Spencer

South San Francisco

Dated: _____

Victoria Smith

Half Moon Bay

Dated: 2/27/06

P. Mickey Williams

South San Francisco

Dated: _____

Thomas D. Wu

South San Francisco

Dated: _____

Zemin Zhang

South San Francisco

Dated: _____

Mark Sliwkowski

South San Francisco

Dated: _____

Chie Sakanaka

South San Francisco

Dated: _____

Anan Chuntharapai

South San Francisco

Dated: _____

Chae Janeka Reed



South San Francisco

Dated: _____

Susan D. Spencer

South San Francisco

Dated: _____

Victoria Smith

Half Moon Bay

Dated: _____

P. Mickey Williams

South San Francisco

Dated: 5/22/06

Thomas D. Wu

South San Francisco

Dated: _____

Zemin Zhang

South San Francisco

Dated: _____

Mark Sliwkowski

South San Francisco

Dated: _____

Chie Sakanaka

South San Francisco

Dated: _____

Anan Chuntharapai

South San Francisco

Dated: _____

Chae Janeka Reed

1717



South San Francisco

Dated: _____

Susan D. Spencer

South San Francisco

Dated: _____

Victoria Smith

Half Moon Bay

Dated: _____

P. Mickey Williams

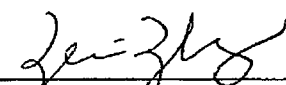
South San Francisco

Dated: _____

Thomas D. Wu

South San Francisco

Dated: 5/22/06



Zemin Zhang

South San Francisco

Dated: _____

Mark Sliwkowski

South San Francisco

Dated: _____

Chie Sakanaka

South San Francisco

Dated: _____

Anan Chuntharapai

South San Francisco

Dated: _____

Chae Janeka Reed

South San Francisco

Dated: _____

Susan D. Spencer

South San Francisco

Dated: _____

Victoria Smith

Half Moon Bay

Dated: _____

P. Mickey Williams

South San Francisco

Dated: _____

Thomas D. Wu

South San Francisco

Dated: _____

Zemin Zhang

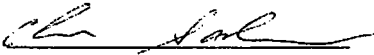
South San Francisco

Dated: _____

Mark Sliwkowski

South San Francisco

Dated: 5/22/06


Chie Sakanaka

South San Francisco

Dated: _____

Anan Chuntharapai

South San Francisco

Dated: _____

Chae Janeka Reed



South San Francisco

Dated: _____

Susan D. Spencer

South San Francisco

Dated: _____

Victoria Smith

Half Moon Bay

Dated: _____

P. Mickey Williams

South San Francisco

Dated: _____

Thomas D. Wu

South San Francisco

Dated: _____

Zemin Zhang

South San Francisco

Dated: _____

Mark Sliwkowski

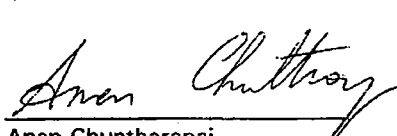
South San Francisco

Dated: _____

Chie Sakanaka

South San Francisco

Dated: 5/22/2006



Anan Chuntharapai

South San Francisco

Dated: _____

Chae Janeka Reed

30

South San Francisco

Dated: _____

Susan D. Spencer

South San Francisco

Dated: _____

Victoria Smith

Half Moon Bay

Dated: _____

P. Mickey Williams

South San Francisco

Dated: _____

Thomas D. Wu

South San Francisco

Dated: _____

Zemin Zhang

South San Francisco

Dated: _____

Mark Sliwkowski

South San Francisco

Dated: _____

Chie Sakanaka

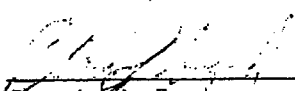
South San Francisco

Dated: _____

Anan Chuntharapai

South San Francisco

Dated: May 22, 2006



Chae Jareka Reed

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. K. Carter
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 veintidós de Agosto de 2007
7. por el Funcionario de Autenticación Asistente, Departamento de Estado
de Estados Unidos
8. No. 0703157-2
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

Agosto 14 de 2007

ESTE ES PARA CERTIFICAR QUE EL ANEXO ES UNA COPIA VERDADERA
DE LOS ARCHIVOS DE ESTA OFICINA DE UN DOCUMENTO ARCHIVADO
EL 20 DE JULIO DE 2007.

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

M. K. Carter
Funcionario que Certifica

Hay un sello que dice:

Oficina de Marcas y Patentes de Estados Unidos
Departamento de Comercio

CESIÓN DE PATENTE

Versión electrónica v1.1

Versión de la hoja v1.1

TIPO DE PRESENTACIÓN:	CESIÓN NUEVA																																
NATURALEZA DEL ACUERDO:	CESIÓN																																
DATOS DE LA PARTE CEDENTE:																																	
<table border="1"> <thead> <tr> <th>Nombre</th> <th>Fecha de ejecución</th> </tr> </thead> <tbody> <tr><td>Melinda Cairns</td><td>06/06/2006</td></tr> <tr><td>Ruihuan Chen</td><td>05/22/2006</td></tr> <tr><td>Gretchen Frantz</td><td>05/22/2006</td></tr> <tr><td>Kenneth J. Hillan</td><td>05/24/2006</td></tr> <tr><td>Hartmut Koeppen</td><td>05/23/2006</td></tr> <tr><td>Heidi S. Phillips</td><td>06/21/2006</td></tr> <tr><td>Paul Polakis</td><td>05/21/2006</td></tr> <tr><td>Susan D. Spencer</td><td>05/22/2006</td></tr> <tr><td>Victoria Smith</td><td>05/23/2006</td></tr> <tr><td>P. Mickey Williams</td><td>05/31/2006</td></tr> <tr><td>Thomas D. Wu</td><td>05/22/2006</td></tr> <tr><td>Zemin Zhang</td><td>05/22/2006</td></tr> <tr><td>Chie Sakanaka</td><td>05/22/2006</td></tr> <tr><td>Anan Chuntharapai</td><td>05/22/2006</td></tr> <tr><td>Chai Janeka Reed</td><td>05/22/2006</td></tr> </tbody> </table>		Nombre	Fecha de ejecución	Melinda Cairns	06/06/2006	Ruihuan Chen	05/22/2006	Gretchen Frantz	05/22/2006	Kenneth J. Hillan	05/24/2006	Hartmut Koeppen	05/23/2006	Heidi S. Phillips	06/21/2006	Paul Polakis	05/21/2006	Susan D. Spencer	05/22/2006	Victoria Smith	05/23/2006	P. Mickey Williams	05/31/2006	Thomas D. Wu	05/22/2006	Zemin Zhang	05/22/2006	Chie Sakanaka	05/22/2006	Anan Chuntharapai	05/22/2006	Chai Janeka Reed	05/22/2006
Nombre	Fecha de ejecución																																
Melinda Cairns	06/06/2006																																
Ruihuan Chen	05/22/2006																																
Gretchen Frantz	05/22/2006																																
Kenneth J. Hillan	05/24/2006																																
Hartmut Koeppen	05/23/2006																																
Heidi S. Phillips	06/21/2006																																
Paul Polakis	05/21/2006																																
Susan D. Spencer	05/22/2006																																
Victoria Smith	05/23/2006																																
P. Mickey Williams	05/31/2006																																
Thomas D. Wu	05/22/2006																																
Zemin Zhang	05/22/2006																																
Chie Sakanaka	05/22/2006																																
Anan Chuntharapai	05/22/2006																																
Chai Janeka Reed	05/22/2006																																
DATOS DE LA PARTE QUE RECIBE																																	
<table border="1"> <tr><td>Nombre:</td><td>Genentech, Inc.</td></tr> <tr><td>Dirección:</td><td>1 DNA Way</td></tr> <tr><td>Ciudad:</td><td>South San Francisco</td></tr> <tr><td>Estado/País:</td><td>CALIFORNIA</td></tr> <tr><td>Código Postal:</td><td>94080-4990</td></tr> </table>		Nombre:	Genentech, Inc.	Dirección:	1 DNA Way	Ciudad:	South San Francisco	Estado/País:	CALIFORNIA	Código Postal:	94080-4990																						
Nombre:	Genentech, Inc.																																
Dirección:	1 DNA Way																																
Ciudad:	South San Francisco																																
Estado/País:	CALIFORNIA																																
Código Postal:	94080-4990																																
NUMEROS DEL PROPIETARIO Total: 1																																	
<table border="1"> <thead> <tr> <th>Tipo de Propiedad</th> <th>Número</th> </tr> </thead> <tbody> <tr> <td>Número de solicitud</td> <td>10936626</td> </tr> </tbody> </table>		Tipo de Propiedad	Número	Número de solicitud	10936626																												
Tipo de Propiedad	Número																																
Número de solicitud	10936626																																
DATOS DE CORRESPONDENCIA																																	
NUMERO DE FAX: (650) 324-0638																																	
La correspondencia se enviará por Correo de Estados Unidos cuando los intentos de hacerlo por fax no sean exitosos.																																	
Teléfono: 650 324-7000																																	
Email: smanibusan@hewm																																	
Nombre de destinatario: Ginger Dreger																																	
Dirección línea 1: 275 Middlefield Road																																	
500318544	PATENTE ROLLO: 019583 CUADRO: 0937																																

NUMERO DE EXPEDIENTE DEL ABOGADO:	39766-0214R1P1
NOMBRE DEL REMITENTE:	Ginger Dreger
Anexos totales: 3	
Fuente=Cesión#pagina1.tif	
Fuente=Cesión#pagina2.tif	
Fuente=Cesión#pagina3.tif	
Fuente=Cesión#pagina4.tif	
Fuente=Cesión#pagina5.tif	
Fuente=Cesión#pagina6.tif	
Fuente=Cesión#pagina7.tif	
Fuente=Cesión#pagina8.tif	
Fuente=Cesión#pagina9.tif	
Fuente=Cesión#pagina10.tif	
Fuente=Cesión#pagina11.tif	
Fuente=Cesión#pagina12.tif	
Fuente=Cesión#pagina13.tif	
Fuente=Cesión#pagina14.tif	
Fuente=Cesión#pagina15.tif	
Fuente=Cesión#pagina16.tif	

CESIÓN

CONSIDERANDO QUE, Melinda Cairns, un ciudadano de Gran Bretaña., residente en 17 Chester Circle, Los Altos, CA 94022, y Ruihuan Chen, un ciudadano de Canadá, residente en 1072 Tanland Drive, #114, Palo Alto, CA 94303, y Kenneth J. Hillan, un ciudadano de Gran Bretaña, residente en 64 Seward Street, San Francisco, CA 94114, Hartmut Koeppen, un ciudadano de Alemania, residente en 1746 Milvia Street, Berkley, CA 94709, Heidi S. Phillips, un ciudadano de los E.U.A., residente en 1449 Cortez Avenue, Burlingame, CA 94010, Susan D. Spencer, un ciudadano de los E.U.A., residente en 2935 Paradise Drive, Tiburón, CA 94920-1201, Victoria Smith, un ciudadano de los E.U.A., residente en 19 Dwight Road, Burlingame, CA 94010, P. Mickey Williams, un ciudadano de los E.U.A., residente en 509 Alto Avenue, Half Moon Bay, CA 94110, Thomas D. Wu, un ciudadano de los E.U.A., residente en 41 Nevada Street, San Francisco, CA 94110, Zemin Zhang, un ciudadano de los E.U.A., residente en 876 Taurus Drive, Foster City, CA 94404, Mark Slowkowski, un ciudadano de los E.U.A., residente en 42 Oak Creek Lane, San Carlos, CA 94070, Chie Sakanaka, un ciudadano del Japón, residente en 1481 8th Ave, San Francisco, CA 94122, Anan Chuntharapai, un ciudadano de los E.U.A., residente en 826 Ellis Drive, Colma, CA 94015 y Chae Janeka Reed, un ciudadano de los E.U.A., residente en 619 Minna Street, San Francisco, CA 94103 (en adelante referidos como "CEDENTE"), han inventado una invención nueva y útil

COMPOSICIONES Y MÉTODOS PARA EL DIAGNÓSTICO Y EL TRATAMIENTO DE TUMORES

para la cual se presentó la solicitud con Serie No. 10/936,626 (Expediente No. P5001R1P1) por ellos el 8 de Septiembre, 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:

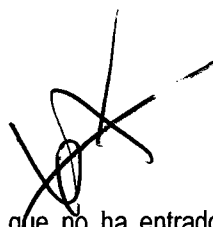
Que por una consideración buena y valiosa el recibo de la cual se reconoce por la presente, dicho CEDENTE ha y por la presente vende, cede, transfiere y traspasa a dicha GENENTECH, INC. sus sucesores y cesionarios, el derecho, título e interés completo y exclusivo incluyendo todos los derechos bajo la 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 involucren dicha invención; y (e) para procedimientos legales que involucren 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 actuar en 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.

PATENTE

ROLLO: 019583 CUADRO: 0939



Dicho CEDENTE por la presente garantiza y manifiesta 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:

Los Altos	(firma)
<u>06/06/06</u>	<u>Belinda Cairns</u>
Fecha	
South San Francisco	
<u></u>	<u>Ruihuan Chen</u>
Fecha	
South San Francisco	
<u></u>	<u>Gretchen Frantz</u>
Fecha	
South San Francisco	
<u></u>	<u>Kenneth J. Hillan</u>
Fecha	
South San Francisco	
<u></u>	<u>Hartmut Koeppen</u>
Fecha	
South San Francisco	
<u></u>	<u>Heidi S. Phillips</u>
Fecha	
South San Francisco	
<u></u>	<u>Paul Polakis</u>
Fecha	
South San Francisco	
<u></u>	<u>Susan D. Spencer</u>
Fecha	

Dicho CEDENTE por la presente garantiza y manifiesta 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:

Los Altos

Fecha

Belinda Cairns

South San Francisco
05/22/2006

Fecha

(firma)
Ruihuan Chen

South San Francisco

Fecha

Gretchen Frantz

South San Francisco

Fecha

Kenneth J. Hillan

South San Francisco

Fecha

Hartmut Koeppen

South San Francisco

Fecha

Heidi S. Phillips

South San Francisco

Fecha

Paul Polakis

[Handwritten mark]

Dicho CEDENTE por la presente garantiza y manifiesta 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:

Los Altos

Fecha

Belinda Cairns

South San Francisco

Fecha

Ruihuan Chen

South San Francisco

5/22/06

Fecha

(firma)
Gretchen Frantz

South San Francisco

Fecha

Kenneth J. Hillan

South San Francisco

Fecha

Hartmut Koeppen

South San Francisco

Fecha

Heidi S. Phillips

South San Francisco

Fecha

Paul Polakis

Dicho CEDENTE por la presente garantiza y manifiesta 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:

Los Altos

Fecha

Belinda Cairns

South San Francisco

Fecha

Ruihuan Chen

South San Francisco

Fecha

Gretchen Frantz

South San Francisco
5/24/06

Fecha

(firma)
Kenneth J. Hillan

South San Francisco

Fecha

Hartmut Koeppen

South San Francisco

Fecha

Heidi S. Phillips

South San Francisco

Fecha

Paul Polakis



Dicho CEDENTE por la presente garantiza y manifiesta 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:

Los Altos

Fecha

Belinda Cairns

South San Francisco

Fecha

Ruihuan Chen

South San Francisco

Fecha

Gretchen Frantz

South San Francisco

Fecha

Kenneth J. Hillan

South San Francisco

5/24/06
Fecha

(firma)
Hartmut Koeppen

South San Francisco

Fecha

Heidi S. Phillips

South San Francisco

Fecha

Paul Polakis



1832

Dicho CEDENTE por la presente garantiza y manifiesta 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:

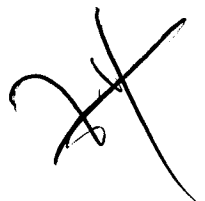
Los Altos	
Fecha	Belinda Cairns
South San Francisco	
Fecha	Ruihuan Chen
South San Francisco	
Fecha	Gretchen Frantz
South San Francisco	
Fecha	Kenneth J. Hillan
South San Francisco	
Fecha	Hartmut Koeppen
South San Francisco	
06/21/06	(firma)
Fecha	Heidi S. Phillips
South San Francisco	
Fecha	Paul Polakis



Dicho CEDENTE por la presente garantiza y manifiesta 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:

Los Altos	_____
_____	Belinda Cairns
Fecha	
South San Francisco	_____
_____	Ruihuan Chen
Fecha	
South San Francisco	_____
_____	Gretchen Frantz
Fecha	
South San Francisco	_____
_____	Kenneth J. Hillan
Fecha	
South San Francisco	_____
_____	Hartmut Koeppen
Fecha	
South San Francisco	_____
_____	Heidi S. Phillips
Fecha	
South San Francisco	_____
_____	(firma)
5/21/06	Paul Polakis
Fecha	



South San Francisco
5/22/06
Fecha

(firma)
Susan D. Spencer

South San Francisco
Fecha

Victoria Smith

South San Francisco
Fecha

P. Mickey Williams

South San Francisco
Fecha

Thomas D. Wu

South San Francisco
Fecha

Zemin Zhang

South San Francisco
Fecha

Mark Sliwkowski

South San Francisco
Fecha

Chie Sakanaka

South San Francisco
Fecha

Anan Chuntharapai

South San Francisco
Fecha

Chae Janeka Reed



South San Francisco

Fecha

Susan D. Spencer

South San Francisco

May. 23, 2006
Fecha

(firma)
Victoria Smith

South San Francisco

Fecha

P. Mickey Williams

South San Francisco

Fecha

Thomas D. Wu

South San Francisco

Fecha

Zemin Zhang

South San Francisco

Fecha

Mark Sliwkowski

South San Francisco

Fecha

Chie Sakanaka

South San Francisco

Fecha

Anan Chuntharapai

South San Francisco

Fecha

Chae Janeka Reed



South San Francisco

Fecha

Susan D. Spencer

South San Francisco

Fecha

Victoria Smith

South San Francisco
5/31/06

Fecha

(firma)
P. Mickey Williams

South San Francisco

Fecha

Thomas D. Wu

South San Francisco

Fecha

Zemin Zhang

South San Francisco

Fecha

Mark Sliwkowski

South San Francisco

Fecha

Chie Sakanaka

South San Francisco

Fecha

Anan Chuntharapai

South San Francisco

Fecha

Chae Janeka Reed



South San Francisco

Fecha

Susan D. Spencer

South San Francisco

Fecha

Victoria Smith

South San Francisco

Fecha

P. Mickey Williams

South San Francisco

5/22/06
Fecha

(firma)
Thomas D. Wu

South San Francisco

Fecha

Zemin Zhang

South San Francisco

Fecha

Mark Sliwkowski

South San Francisco

Fecha

Chie Sakanaka

South San Francisco

Fecha

Anan Chuntharapai

South San Francisco

Fecha

Chae Janeka Reed

South San Francisco

Fecha

Susan D. Spencer

South San Francisco

Fecha

Victoria Smith

South San Francisco

Fecha

P. Mickey Williams

South San Francisco

Fecha

Thomas D. Wu

South San Francisco
5/22/06

Fecha

(firma)
Zemin Zhang

South San Francisco

Fecha

Mark Sliwkowski

South San Francisco

Fecha

Chie Sakanaka

South San Francisco

Fecha

Anan Chuntharapai

South San Francisco

Fecha

Chae Janeka Reed



South San Francisco

Susan D. Spencer

Fecha

South San Francisco

Victoria Smith

Fecha

South San Francisco

P. Mickey Williams

Fecha

South San Francisco

Thomas D. Wu

Fecha

South San Francisco

Zemin Zhang

Fecha

South San Francisco

Mark Sliwkowski

Fecha

South San Francisco

(firma)
Chie Sakanaka

5/22/06

Fecha

South San Francisco

Anan Chuntharapai

Fecha

South San Francisco

Chae Janeka Reed

Fecha

22

South San Francisco

Fecha

Susan D. Spencer

South San Francisco

Fecha

Victoria Smith

South San Francisco

Fecha

P. Mickey Williams

South San Francisco

Fecha

Thomas D. Wu

South San Francisco

Fecha

Zemin Zhang

South San Francisco

Fecha

Mark Sliwowski

South San Francisco

Fecha

Chie Sakanaka

South San Francisco
5/22/06

Fecha

(firma)
Anan Chuntharapai

South San Francisco

Fecha

Chae Janeka Reed

81

South San Francisco

Fecha

Susan D. Spencer

South San Francisco

Fecha

Victoria Smith

South San Francisco

Fecha

P. Mickey Williams

South San Francisco

Fecha

Thomas D. Wu

South San Francisco

Fecha

Zemin Zhang

South San Francisco

Fecha

Mark Sliwkowski

South San Francisco

Fecha

Chie Sakanaka

South San Francisco

Fecha

Anan Chuntharapai

South San Francisco

5/22/06
Fecha

(firma)
Chae Janeka Reed