

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
20 October 2005 (20.10.2005)

PCT

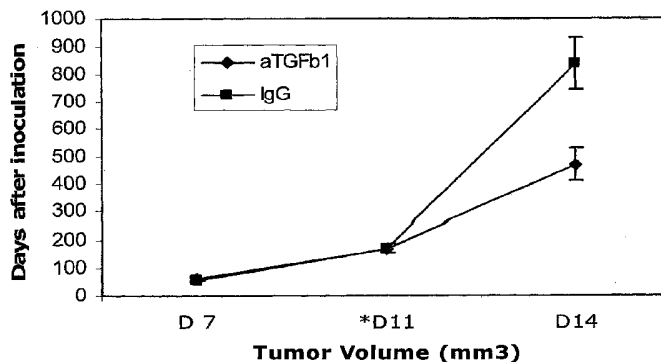
(10) International Publication Number  
**WO 2005/097832 A3**

- (51) International Patent Classification<sup>7</sup>: **C07K 16/22**, A61K 39/395
- (21) International Application Number: PCT/US2005/010994
- (22) International Filing Date: 31 March 2005 (31.03.2005)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/558,290 31 March 2004 (31.03.2004) US
- (71) Applicant (for all designated States except US): **GENENTECH, INC.** [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **ADAMS, Camellia, W.** [US/US]; 116C Flynn Avenue, Mountain View, CA 94043 (US). **FERRARA, Napoleone** [US/US]; #704, 2090 Pacific Avenue, San Francisco, CA 94109 (US). **FILVAROFF, Ellen** [US/US]; 538 18th Avenue, San Francisco, CA 94121 (US). **MAO, Weiguang** [CN/US]; 1613 De Anza Blvd., San Mateo, CA 94403 (US). **PRESTA, Leonard, G.** [US/US]; #206, 1900 Gough Street, San Francisco, CA 94109 (US). **TEJADA, Max, L.** [CA/US]; 121B Redding Road, Campbell, CA 95008 (US).
- (74) Agent: **HASAK, Janet, E.**; Genentech, Inc., MS 49, South San Francisco, CA 94080 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
- with international search report
  - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 1 December 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HUMANIZED ANTI-TGF-BETA ANTIBODIES

aTGFb1 treated B16 Tumor Growth



(57) Abstract: Humanized anti-TGF-beta antibodies are provided, as well as methods for their preparation and use, including methods for treating TGF-beta disorders, for example, cancer. Also provided are articles of manufacture designed for various uses that contain the humanized antibodies.

WO 2005/097832 A3

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/010994

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C07K16/22 A61K39/395

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

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, Sequence Search, BIOSIS, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/064069 A1 (THOMPSON JULIA ELIZABETH ET AL) 3 April 2003 (2003-04-03) abstract; claims 1-26 paragraph '0077! - paragraph '0078!	1-58
Y	US 5 821 337 A (CARTER ET AL) 13 October 1998 (1998-10-13) abstract; claim 13	1-58
	----- -/-	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

14 October 2005

Date of mailing of the international search report

21/10/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Favre, N

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/010994

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>HOEFER M ET AL: "ANTI-(TRANSFORMING GROWTH FACTOR BETA) ANTIBODIES WITH PREDEFINED SPECIFICITY INHIBIT METASTASIS OF HIGHLY TUMORIGENIC HUMAN XENOTRANSPLANTS IN NU/NU MICE" CANCER IMMUNOLOGY AND IMMUNOTHERAPY, BERLIN, DE, vol. 41, no. 5, 1995, pages 302-308, XP000644718 ISSN: 0340-7004 cited in the application the whole document</p>	1-58
Y	<p>US 5 772 998 A (DASCH ET AL) 30 June 1998 (1998-06-30) cited in the application the whole document</p>	1-58
Y	<p>US 2002/176858 A1 (DASCH JAMES R ET AL) 28 November 2002 (2002-11-28) the whole document</p>	1-58
Y	<p>US 2002/051785 A1 (SLAMON DENNIS J ET AL) 2 May 2002 (2002-05-02) the whole document</p>	1-58
A	<p>KLOS K S ET AL: "COMBINED TRASTUZUMAB AND PACLITAXEL TREATMENT BETTER INHIBITS ERBB-2-MEDIATED ANGIOGENESIS IN BREAST CARCINOMA THROUGH A MORE EFFECTIVE INHIBITION OF AKT THAN EITHER TREATMENT ALONE" CANCER, AMERICAN CANCER SOCIETY, PHILADELPHIA, PA, US, vol. 98, no. 7, 1 October 2003 (2003-10-01), pages 1377-1385, XP001206049 ISSN: 0008-543X the whole document</p>	1-58
A	<p>WO 00/34337 A (TSUKUBA RESEARCH LABORATORY, TOAGOSEI CO., LTD; PROTEIN DESIGN LABS, I) 15 June 2000 (2000-06-15) the whole document</p>	54-58
A	<p>GOLD L I: "THE ROLE FOR TRANSFORMING GROWTH FACTOR-BETA (TGF-BETA) IN HUMAN CANCER" CRITICAL REVIEWS IN ONCOGENESIS, BOCA RATON, FL, US, vol. 10, no. 4, 1999, pages 303-360, XP001038678 ISSN: 0893-9675 the whole document</p>	1-58

-/--

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/010994

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2003/125251 A1 (WAKEFIELD LALAGE M ET AL) 3 July 2003 (2003-07-03) the whole document	1-58
A	PRESTA L G ET AL: "Humanization of an anti-vascular endothelial growth factor monoclonal antibody for the therapy of solid tumors and other disorders" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 57, no. 20, 15 October 1997 (1997-10-15), pages 4593-4599, XP002111212 ISSN: 0008-5472 the whole document	1-58
E	WO 2005/050200 A (GENENTECH, INC; FILVAROFF, ELLEN, H) 2 June 2005 (2005-06-02) the whole document	1-58

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2005/010994

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material
    - in written format
    - in computer readable form
  - c. time of filing/furnishing
    - contained in the international application as filed
    - filed together with the international application in computer readable form
    - furnished subsequently to this Authority for the purpose of search
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2005/010994

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: —  
because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 34-49 and 54-58 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/US2005/010994

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003064069 A1	03-04-2003	US 2003091566 A1 US 6492497 B1	15-05-2003 10-12-2002
US 5821337 A	13-10-1998	AT 255131 T AU 675916 B2 AU 2250992 A CA 2103059 A1 DE 69233254 D1 DE 69233254 T2 DK 590058 T3 EP 0590058 A1 ES 2206447 T3 JP 6508267 T JP 2005000169 A LU 91067 A9 NL 300145 I1 WO 9222653 A1 US 6407213 B1 US 6719971 B1 US 6639055 B1	15-12-2003 27-02-1997 12-01-1993 15-12-1992 08-01-2004 16-09-2004 29-03-2004 06-04-1994 16-05-2004 22-09-1994 06-01-2005 02-04-2004 01-06-2004 23-12-1992 18-06-2002 13-04-2004 28-10-2003
US 5772998 A	30-06-1998	US 5783185 A	21-07-1998
US 2002176858 A1	28-11-2002	NONE	
US 2002051785 A1	02-05-2002	NONE	
WO 0034337 A	15-06-2000	NONE	
US 2003125251 A1	03-07-2003	NONE	
WO 2005050200 A	02-06-2005	NONE	