



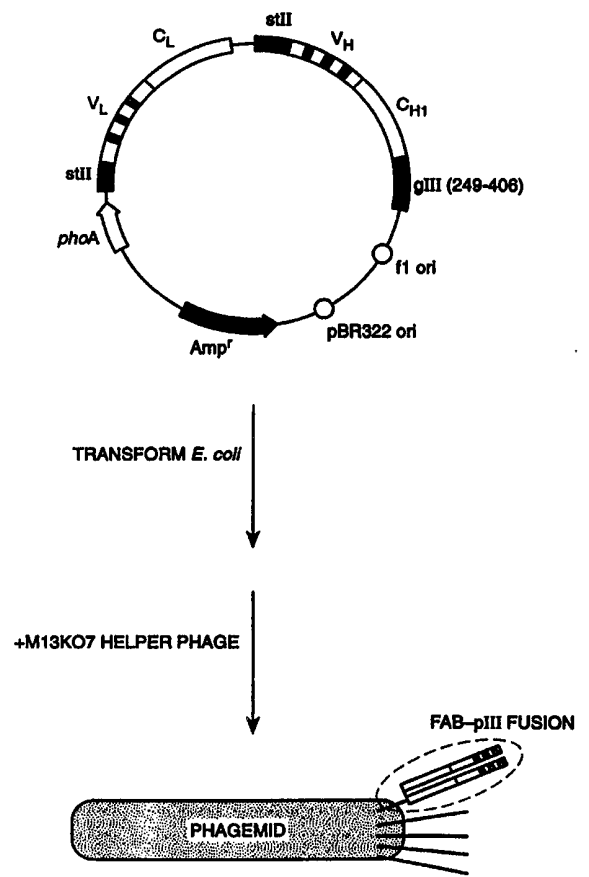
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>6</sup> : <b>C07K 16/22, C12N 15/13, 15/63, 15/70, A61K 39/395</b></p>	<p>A3</p>	<p>(11) International Publication Number: <b>WO 98/45331</b></p> <p>(43) International Publication Date: 15 October 1998 (15.10.98)</p>
<p>(21) International Application Number: PCT/US98/06604</p> <p>(22) International Filing Date: 3 April 1998 (03.04.98)</p> <p>(30) Priority Data: 08/833,504 7 April 1997 (07.04.97) US 08/908,469 6 August 1997 (06.08.97) US</p> <p>(71) Applicant (for all designated States except US): GENENTECH, INC. [US/US]; One DNA Way, South San Francisco, CA 94080 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): BACA, Manuel [AU/US]; Apartment #H3, 888 Foster City Boulevard, Foster City, CA 94404 (US). WELLS, James, A. [US/US]; 1341 Columbus Avenue, Burlingame, CA 94010 (US). PRESTA, Leonard, G. [US/US]; Apartment 206, 1900 Gough Street, San Francisco, CA 94109 (US). LOWMAN, Henry, B. [US/US]; 400 San Juan Avenue, El Granada, CA 94018 (US). CHEN, Yvonne, Man-Yee [CA/US]; 1951 O'Farrell Street #321, San Mateo, CA 94403 (US).</p> <p>(74) Agents: DREGER, Walter, H. et al.; Flehr, Hohbach, Test, Albritton &amp; Herbert LLP, Suite 400, 4 Embarcadero Center, San Francisco, CA 94111-4187 (US).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p> <p>(88) Date of publication of the international search report: 3 December 1998 (03.12.98)</p>	

(54) Title: ANTI-VEGF ANTIBODIES

(57) Abstract

Humanized and variant anti-VEGF antibodies and various uses therefor are disclosed. The anti-VEGF antibodies have strong binding affinities for VEGF; inhibit VEGF-induced proliferation of endothelial cells *in vitro*, and inhibit tumor growth *in vivo*.



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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 98/06604

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 6 C07K16/22 C12N15/13 C12N15/63 C12N15/70 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 6 C07K C12N A61K

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)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92 22653 A (GENENTECH INC) 23 December 1992	7, 10-13, 25-27
Y	the whole document and specially: see SEQ.ID.N. 17, 18 and 25 see page 5, line 24 - page 7, line 35  see page 9, line 22 - page 10, line 4; figure 5	1, 4, 14, 15, 22, 28-31, 34-38
Y	KIM ET AL.,: "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumor growth in vivo" NATURE, vol. 362, 1993, page 841 XP002013864 London, GB cited in the application see abstract	1, 4, 14, 15, 22, 28-31, 34-38

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
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- "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.
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Date of the actual completion of the international search

Date of mailing of the international search report

18 September 1998

02/10/1998

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 98/06604

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 2 268 744 A (CELLTECH LTD) 19 January 1994 see abstract see page 4, paragraph 3 - page 6, paragraph 1 ---	1,32-41
A	M.M. BENDIG: "Humanization of rodent monoclonal antibodies" METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, vol. 8, 1995, pages 83-93, XP000647344 New York, NY, US see the whole document ---	1,34-38
P,X	M. BACA ET AL., : "Antibody humanization using monovalent phage display" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 16, 18 April 1997, pages 10678-10684, XP002077471 see the whole document -----	1-42

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/06604

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 5 AND 39-42  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 5 and 39-42 are directed to a method of treatment of 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 II Observations where unity of invention is lacking (Continuation of item 2 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/US 98/06604

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Information on patent family members

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PCT/US 98/06604

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