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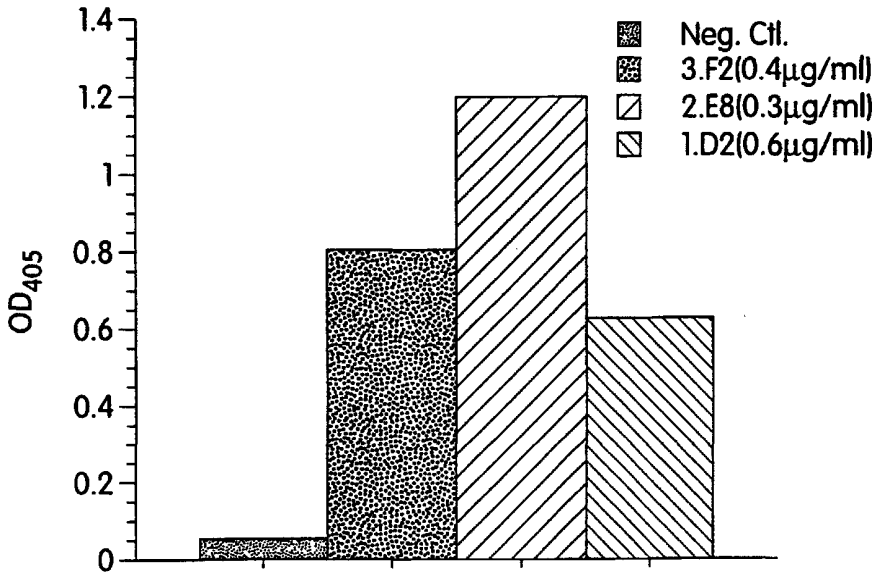
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[Continued on next page]

(54) Title: HUMAN MONOCLONAL ANTIBODIES TO HER2/NEU



(57) Abstract: Isolated human monoclonal antibodies and antigen-binding portions thereof which specifically bind to HER2/neu are disclosed. Also disclosed are bi- and multispecific molecules including human monoclonal antibodies and antigen-binding portions thereof which specifically bind to HER2/neu. The human antibodies can be produced in a non-human transgenic animal, e.g., a transgenic mouse, capable of producing multiple isotypes of human monoclonal antibodies by undergoing V-D-J recombination and isotype switching. Also disclosed are pharmaceutical compositions comprising the human antibodies, non-human transgenic animals and hybridomas which produce the human antibodies, and therapeutic and diagnostic methods for using the human antibodies.

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INTERNATIONAL SEARCH REPORT

Inte. onal Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K16/22 C07K16/28 A01K67/027 A61K39/395 C12N5/20
C12N15/13 G01N33/577 C07K16/46 A61P35/00 C12N15/85

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 A01K

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, PAJ, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 00271 A (UNIV CALIFORNIA) 3 January 1997 (1997-01-03)	1-5, 8-11,17, 18,21, 24,26-34
Y	page 1, line 16-30 page 2, line 17 -page 3, line 2 page 3, line 10 -page 4, line 2 page 4, line 19-25 page 5, line 8-14 page 49, line 1-26 page 50, line 19-31 --- -/--	6,7, 12-14, 25,35

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"E" earlier document but published on or after the international filing date

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 January 2001	24. 01. 01

Name and mailing address of the ISA	Authorized officer
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	Montrone, M

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INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/US 00/20272

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 04679 A (GENENTECH INC) 3 March 1994 (1994-03-03) abstract page 2, line 22 page 4, line 15-26 page 10, line 3-10 page 13, line 21-30 page 17, line 34-38 page 48, line 9-27 page 50, line 30 -page 51, line 26 page 52, line 9 -page 54, line 11 page 60, line 12-15 page 61, line 10-19 page 63; table 3 page 64; table 4 page 70, line 17 -page 73, line 3	1-5, 8-11,24, 26-28, 30-34
X Y	WO 98 02463 A (KELER TIBOR ;MEDAREX INC (US); DEO YASHWANT M (US); GRAZIANO ROBER) 22 January 1998 (1998-01-22) abstract page 1, line 5-16 page 2, line 29-36 page 3, line 1-10 page 5, line 10-14 page 18, line 20-30	15-23, 28-32 6,7, 12-14, 25,35
X	CURNOW R T: "CLINICAL EXPERIENCE WITH CD64-DIRECTED IMMUNOTHERAPY. AN OVERVIEW" CANCER IMMUNOLOGY AND IMMUNOTHERAPY,BERLIN,DE, vol. 45, no. 3/04, November 1997 (1997-11), pages 210-215, XP000918956 ISSN: 0340-7004 abstract	17,18, 20,21, 28,29, 31,32
X	BASELGA J ET AL: "PHASE II STUDY OF WEEKLY INTRAVENOUS RECOMBINANT HUMANIZED ANTI-P185HER2 MONOCLONAL ANTIBODY IN PATIENTS WITH HER2/NEU-OVEREXPRESSING METASTATIC BREAST CANCER" JOURNAL OF CLINICAL ONCOLOGY,PHILADELPHIA, PA,US, vol. 14, no. 3, March 1996 (1996-03), pages 737-744, XP000918166 abstract page 737, column 1, paragraph 1 -column 2, paragraph 1 page 738, column 1, paragraph 2 page 740, column 1, line 4-6	1-5, 8-11,24, 26-28, 31-34

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INTERNATIONAL SEARCH REPORT

Inte. onal Application No
PCT/US 00/20272

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	A JAKOBOVITS: "The long-awaited magic bullets: therapeutic human monoclonal antibodies from transgenic mice" EXPERT OPINION ON INVESTIGATIONAL DRUGS,GB,ASHLEY PUBLICATIONS LTD., LONDON, vol. 7, no. 4, 1 April 1998 (1998-04-01), pages 607-614, XP002084509 ISSN: 1354-3784 abstract page 607, paragraph 2 page 609, column 1, paragraphs 2-4 page 612, column 1, paragraph 2 -page 613, column 2, paragraph 1 ---	6,7, 12-14
P,X	WO 99 55367 A (MARKS JAMES D ;POUL MARIE ALIX (US); UNIV CALIFORNIA (US)) 4 November 1999 (1999-11-04) abstract page 1, line 15-18 page 2, line 16-22 page 5, line 5-11 page 5, line 31,32 page 7, line 5-7 page 17, line 11-18 page 18, line 3-30 page 19, line 18 -page 20, line 23 page 22, line 1 -page 23, line 13 page 66, line 11 -page 67, line 16 -----	1-5,10, 24,26, 28,30-34

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/20272

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 26 to 32 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

Inte. onal Application No
PCT/US 00/20272

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