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(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, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, 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.

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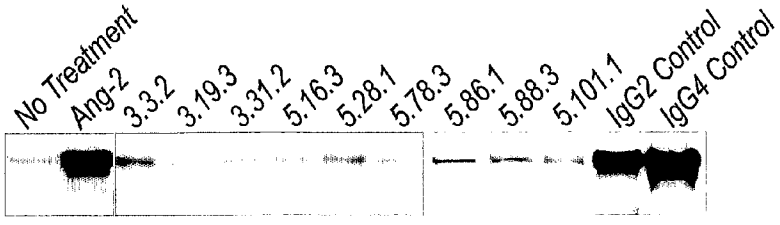
*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: ANTIBODIES DIRECTED TO ANGIOPOIETIN-2 AND USES THEREOF




(57) Abstract: Antibodies directed to the antigen Ang-2 and uses of such antibodies are described. In particular, fully human monoclonal antibodies directed to the antigen Ang-2. Nucleotide sequences encoding, and amino acid sequences comprising, heavy and light chain immunoglobin molecules, particularly sequences corresponding to contiguous heavy and light chain sequences spanning the framework regions and/or complementary determining regions (CDR's), specifically from FR1 through FR4 or CDR1 through CDR3. Hybridomas or other cell lines expressing such immunoglobin molecules and monoclonal antibodies.

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# INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/22 C07K16/28 C12N15/13 C12N15/85 C12N5/10
A61K39/395 A61P35/00

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)
C07K A61P 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)
EPO-Internal, WPI Data, PAJ, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | WO 03/030833 A (AMGEN INC; OLINER, JOHNATHAN, DANIEL)<br>17 April 2003 (2003-04-17)<br>page 88, lines 2-9; tables 8,9<br>page 84, paragraph B<br>figure 2c; example 5<br>page 64, lines 3-5<br>---<br>-/-- | 1-40 |

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

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 1 June 2006 | 22/06/2006 |

| Name and mailing address of the ISA/ | Authorized officer |
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| European Patent Office, P.B. 5818 Patentlaan 2<br>NL – 2280 HV Rijswijk<br>Tel. (+31–70) 340–2040, Tx. 31 651 epo nl,<br>Fax: (+31–70) 340–3016 | Siaterli, M-Z |

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International application No
PCT/US2005/045657

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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|---|---|---|
| X | LIN PENGNIAN ET AL: "Inhibition of tumor angiogenesis using a soluble receptor establishes a role for Tie2 in pathologic vascular growth" JOURNAL OF CLINICAL INVESTIGATION, NEW YORK, NY, US, vol. 100, no. 8, 1997, pages 2072-2078, XP002294946 ISSN: 0021-9738 cited in the application | 26-28,30 |
| Y | page 2073, left-hand column, paragraph 1 - right-hand column, paragraph 2 page 2076, left-hand column, paragraph 2 page 2077, right-hand column, last paragraph | 1-25,29, 31-40 |
| X | OLINER J ET AL: "Suppression of angiogenesis and tumor growth by selective inhibition of angiopoietin-2" CANCER CELL, XX, US, vol. 6, no. 5, November 2004 (2004-11), pages 507-516, XP002348738 ISSN: 1535-6108 page 508, right-hand column, paragraph 2; figures 1,2; table 1 | 1-40 |
| X | WO 00/75323 A (IMMUNEX CORPORATION; CERRETTI, DOUGLAS, P; BORGES, LUIS, G; FANSLOW, W) 14 December 2000 (2000-12-14) | 26-32 |
| Y | examples 1,7 | 1-25, 33-40 |
| A | MAISONPIERRE P C ET AL: "ANGIOPOIETIN-2, A NATURAL ANTAGONIST FOR TIE2 THAT DISRUPTS IN VIVO ANGIOGENESIS" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 277, 4 July 1997 (1997-07-04), pages 55-60, XP002046280 ISSN: 0036-8075 cited in the application page 56, middle column, lines 2-4 | |

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International application No
PCT/US2005/045657

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| A | FIEDLER ULRIKE ET AL: "Angiopoietin-1 and angiopoietin-2 share the same binding domains in the Tie-2 receptor involving the first Ig-like loop and the epidermal growth factor-like repeats." THE JOURNAL OF BIOLOGICAL CHEMISTRY. 17 JAN 2003, vol. 278, no. 3, 17 January 2003 (2003-01-17), pages 1721-1727, XP002383517 ISSN: 0021-9258 page 1726, right-hand column, paragraph 2 | |
| Y | CAI M ET AL: "Single chain Fv antibody against angiopoietin-2 inhibits VEGF-induced endothelial cell proliferation and migration in vitro" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 309, no. 4, 3 October 2003 (2003-10-03), pages 946-951, XP004455833 ISSN: 0006-291X page 948, left-hand column, paragraph 3; table 1 | 1-25,29, 31-40 |
| A | ROBINSON CANDY S ET AL: "The effects of Angiopoietin-2 and neutralizing anti-TIE-2 antibody on microvessel growth, branching, and regression in the ex vivo rat aortic ring explant model of angiogenesis" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 42, March 2001 (2001-03), page 2, XP001208033 & 92ND ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; NEW ORLEANS, LA, USA; MARCH 24-28, 2001 ISSN: 0197-016X abstract | |

# INTERNATIONAL SEARCH REPORT

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PCT/US2005/045657

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

Although claims 18-25 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 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/US2005/045657

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