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(54) Title: COMPOSITIONS AND METHODS OF USE FOR ANTIBODIES OF DICKKOPF-1 AND/OR -4

(57) Abstract: Antibodies and fragments that bind to the protein target Dickkopf (DKK1) are provided, as are methods of use and kits, for treating a target cell, in particular, a cell associated with an osteolytic condition.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61P19/08 A61P35/04 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)
A61K 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, Sequence Search, WPI Data, CHEM ABS Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 2005/084494 A1 (PROCKOP DARWIN [US] ET AL) 21 April 2005 (2005-04-21)</p> <p>0013-0015, 0017, 0076, 0077, 0099-0102, 0135-0150, 0157-0180, 0182-0194, 0247-0250, example 3, figure 15H, example 7</p> <p style="text-align: center;">----- -/--</p>	<p>1,2, 24-31, 33-37, 39-47, 49,50</p>

Further documents are listed in the continuation of Box C.

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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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

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& document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 6 951 921 B2 (FERRARA NAPOLEONE [US] ET AL) 4 October 2005 (2005-10-04)</p> <p>column 6, l. 53-column 7, l. 42; column 74, l. 55-column 76, l. 53; figure 41; c. 339, l. 48-57; columns 372-380; example 24; example 132</p>	<p>1, 2, 26, 27, 29-37, 39, 44, 45, 49, 50</p>
X	<p>WO 95/24481 A (SCHERING CORP [US]; DALIE BARBARA [US]; MILLER KENNETH [US]; MURGOLO N) 14 September 1995 (1995-09-14) p. 2-3; p. 5-6; figure 1, antibodies H-3 and H-4, CDR1</p>	<p>3, 4, 22-25, 29-31, 39</p>
X	<p>WO 03/070760 A (HOFFMANN LA ROCHE [CH]; MORPHOSYS AG [DE]; BARDROFF MICHAEL [DE]; BOHR) 28 August 2003 (2003-08-28)</p> <p>pages 2-4; p. 34; p. 67-68</p>	<p>3, 4, 22-25, 29-31, 39-43</p>
X	<p>WO 02/086085 A (BAYER AG [US]; MORPHOSYS AG [DE]; PAN CLARK [US]; KNORR ANDREAS M [DE]) 31 October 2002 (2002-10-31)</p> <p>paragraphs 07-38; page 57</p>	<p>3-5, 22-25, 29-31, 39-43</p>
X	<p>WO 02/066509 A (GENENTECH INC [US]) 29 August 2002 (2002-08-29)</p> <p>p. 1, l. 7-12; p. 5-7, l. 27; p. 17-p. 26, l. 22; examples 1 and 2</p>	<p>1, 2, 26, 27, 29-31, 33, 34, 40-44, 49</p>
X	<p>YI QING ET AL: "DKK-1 is a widely expressed, potent tumor-associated antigen in multiple myeloma recognized by cytotoxic T lymphocytes." BLOOD, vol. 106, no. 11, Part 1, November 2005 (2005-11), page 967A, XP002459930 & 47TH ANNUAL MEETING OF THE AMERICAN-SOCIETY-OF-HEMATOLOGY; ATLANTA, GA, USA; DECEMBER 10 -13, 2005 ISSN: 0006-4971 the whole document</p>	<p>49</p>
A	<p>US 2005/069915 A1 (MCCARTHY SEAN A [US]) 31 March 2005 (2005-03-31) 0007, 0020, 0022, 0025, 0035, 0040, 0043-45, 0127-0132, 0138-0146, 0170-0184, example 4, example 5, example 10</p>	<p>52</p>
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/000777

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BALINT R F ET AL: "ANTIBODY ENGINEERING BY PARSIMONIOUS MUTAGENESIS" GENE, ELSEVIER, AMSTERDAM, NL, vol. 137, no. 1, 27 December 1993 (1993-12-27), pages 109-118, XP002031537 ISSN: 0378-1119 the whole document	1-53
A	HOLT L J ET AL: "Domain antibodies: proteins for therapy" TRENDS IN BIOTECHNOLOGY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 21, no. 11, November 2003 (2003-11), pages 484-490, XP004467495 ISSN: 0167-7799 the whole document	1-53
A	DAVIES J ET AL: "Affinity improvement of single antibody VH domains: residues in all three hypervariable regions affect antigen binding" IMMUNOTECHNOLOGY, ELSEVIER SCIENCE PUBLISHERS BV, NL, vol. 2, no. 3, September 1996 (1996-09), pages 169-179, XP004070292 ISSN: 1380-2933 the whole document	1-53
A	LITTLE M ET AL: "Of mice and men: hybridoma and recombinant antibodies" IMMUNOLOGY TODAY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 21, no. 8, 1 August 2000 (2000-08-01), pages 364-370, XP004215163 ISSN: 0167-5699 the whole document	1-53
X	WO 2006/100582 A (GLYCART BIOTECHNOLOGY AG [CH]; UMANA PABLO [CH]; MOSSNER EKKEHARD [CH]) 28 September 2006 (2006-09-28) p. 41, seq ID:76	3,4
X	WO 2006/017538 A (DYAX CORP [US]; SEXTON DANIEL J [US]; NIXON ANDREW [US]; WILLIAMS ANTH) 16 February 2006 (2006-02-16) page 130, line 11, seq ID:475	3,4
E	WO 2007/054816 A (BIOREN INC [US]; CAPPUCILLI GUIDO [US]; CREA ROBERTO [US]; BAYEZ NURTE) 18 May 2007 (2007-05-18) 0043, figure 21B-2	4,5

INTERNATIONAL SEARCH REPORT

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Box No. 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 33-36 and 48-50 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 No. 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 allsearchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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 and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/000777

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2005084494	A1	21-04-2005	US 2004235166 A1 25-11-2004
US 6951921	B2	04-10-2005	NONE
WO 9524481	A	14-09-1995	AT 171473 T 15-10-1998 AU 1971295 A 25-09-1995 CA 2185112 A1 14-09-1995 DE 69504959 D1 29-10-1998 DE 69504959 T2 18-02-1999 DK 749481 T3 14-06-1999 EP 0749481 A1 27-12-1996 ES 2121358 T3 16-11-1998 JP 9510095 T 14-10-1997 US 5597710 A 28-01-1997
WO 03070760	A	28-08-2003	AU 2003218995 A1 09-09-2003 BR 0307837 A 07-12-2004 CA 2477012 A1 28-08-2003 CN 1630665 A 22-06-2005 HR 20040712 A2 30-06-2005 JP 2005527199 T 15-09-2005 MX PA04008077 A 14-12-2005 US 2005169925 A1 04-08-2005 ZA 200406604 A 14-06-2005
WO 02086085	A	31-10-2002	CA 2445168 A1 31-10-2002 EP 1381631 A2 21-01-2004 JP 2004529647 T 30-09-2004
WO 02066509	A	29-08-2002	CA 2438245 A1 29-08-2002 EP 1360199 A2 12-11-2003 HU 0303194 A2 29-12-2003 JP 2005509402 T 14-04-2005 MX PA03007327 A 14-02-2005 ZA 200306232 A 17-11-2004
US 2005069915	A1	31-03-2005	NONE
WO 2006100582	A	28-09-2006	AR 052714 A1 28-03-2007 AU 2006226060 A1 28-09-2006 US 2006223096 A1 05-10-2006
WO 2006017538	A	16-02-2006	AU 2005271523 A1 16-02-2006 CA 2575791 A1 16-02-2006 EP 1807451 A2 18-07-2007
WO 2007054816	A	18-05-2007	NONE