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Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:
29 April 2010

(54) Title: METHODS OF ALTERING BONE GROWTH BY ADMINISTRATION OF SOST OR WISE ANTAGONIST OR AGONIST

(57) Abstract: The present invention provides a method of promoting local bone growth by administering a therapeutic amount of a Sost antagonist to a mammalian patient in need thereof. Preferably, the Sost antagonist is an antibody or FAB fragment selectively recognizing any one of SEQ ID NOS: 1-23. The Sost antagonist may be coadministered together or sequentially with a matrix conducive to anchoring new bone growth. Orthopedic and Periodontal devices comprising an implantable portion adapted to be permanently implanted within a mammalian body and bearing an external coating of a Sost antagonist are also disclosed, as is a method of increasing bone density by administering to a mammalian patient a therapeutic amount of a Sost antagonist together with an antiresorptive drug.



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A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/59 A61K38/18 A61K39/395 A61K45/06 A61L27/12
 A61L27/54 A61P19/08

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 A61L A61P

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, BIOSIS, Sequence Search, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/003158 A (CELLTECH R & D INC [US]; BRUNKOW MARY E [US]; GALAS DAVID J [US]; KOVA) 13 January 2005 (2005-01-13) abstract page 2, lines 21-33 page 3, lines 7-11 page 9, line 13 - page 12, line 8 page 38, line 27 - page 42, line 15 page 43, line 30 - page 47, line 14 page 74, line 30 - page 75, line 9 claims 1-20 figures 1-12 examples 11-16 ----- -/--	1-3, 7-12, 23-34

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
- "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

26 February 2010

Date of mailing of the international search report

16/03/2010

Name and mailing address of the ISA/

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Authorized officer

Ferreira, Roger

INTERNATIONAL SEARCH REPORT

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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
 - on paper
 - in electronic form
 - c. time of filing/furnishing
 - contained in the international application as filed
 - filed together with the international application in electronic 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

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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 Y	WO 03/106657 A (STOWERS INST FOR MEDICAL RES [US]) 24 December 2003 (2003-12-24) abstract page 15, line 18 - page 23, line 7 page 37, line 3 - page 38, line 3 page 46, lines 6-21 claims 1-235 figures 1-14 examples 1-44	1,7-12, 25,27-34 23-24,26
X	----- ELLIES DEBRA L ET AL: "Bone density ligand, Sclerostin, directly interacts with LRP5 but not LRP5G171V to modulate Wnt activity." JOURNAL OF BONE AND MINERAL RESEARCH : THE OFFICIAL JOURNAL OF THE AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH NOV 2006, vol. 21, no. 11, November 2006 (2006-11), pages 1738-1749, XP002554008 ISSN: 0884-0431 cited in the application the whole document	1,7-8, 10-11, 25, 27-28, 31-32
X	----- POOLE KENNETH E S ET AL: "Sclerostin is a delayed secreted product of osteocytes that inhibits bone formation" FASEB JOURNAL, FED. OF AMERICAN SOC. FOR EXPERIMENTAL BIOLOGY, BETHESDA, MD, US, vol. 19, no. 13, 1 November 2005 (2005-11-01), pages 1(1842-1844), XP002501738 ISSN: 0892-6638 [retrieved on 2008-08-25] the whole document	1,7-8, 10-11, 25, 27-28, 31-32
X Y	----- WO 2006/119107 A (UCB SA [GB]; AMGEN INC [US]; PASZTY CHRISTOPHER [US]; ROBINSON MARTYN) 9 November 2006 (2006-11-09) abstract page 2, lines 3-24 claims 1-72	1,7-12, 25, 27-29, 31-33 23-24,26
X	----- WO 2006/102070 A (ENZO BIOCHEM INC [US]; WU DIANQING DAN [US]; LI XIAOFENG [US]) 28 September 2006 (2006-09-28) abstract claims 1-113	1,7-12, 25, 27-29, 31-33
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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	WO 03/039534 A (MERCK & CO INC [US]; STOCH SELWYN AUBREY [US]; ORLOFF JOHN [US]) 15 May 2003 (2003-05-15) abstract claims 1-19	1,7-12, 25, 27-29, 31-33
A	BEZOOIJEN R L V ET AL: "SOST/sclerostin, an osteocyte-derived negative regulator of bone formation" CYTOKINE AND GROWTH FACTOR REVIEWS, OXFORD, GB, vol. 16, no. 3, 1 June 2005 (2005-06-01), pages 319-327, XP004964512 ISSN: 1359-6101 the whole document	1-3, 7-12,25, 27-34
A	BALEMANS W ET AL: "INCREASED BONE DENSITY IN SCLEROSTEOSIS IS DUE TO THE DEFICIENCY OF A NOVEL SECRETED PROTEIN (SOST)" HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, vol. 10, no. 5, 1 January 2001 (2001-01-01), pages 537-543, XP001058218 ISSN: 0964-6906 the whole document	1-3, 7-12,25, 27-34
A	VAN BEZOOIJEN RUTGER L ET AL: "WNT BUT NOT BMP SIGNALING IS INVOLVED IN THE INHIBITORY ACTION OF SCLEROSTIN ON BMP-STIMULATED BONE FORMATION" JOURNAL OF BONE AND MINERAL RESEARCH, AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH, NEW YORK, NY, US, vol. 22, no. 1, January 2007 (2007-01), pages 19-28, XP008078168 ISSN: 0884-0431 Published online 09.10.2006 the whole document	1-3, 7-12,25, 27-34
X,P	US 2007/292444 A1 (KRUMLAUF ROBB [US] ET AL) 20 December 2007 (2007-12-20) the whole document	1-3, 7-12,25, 27-34
E	WO 2008/133722 A (UCB PHARMA SA [BE]; LATHAM JOHN [US]; WINKLER DAVID G [US]) 6 November 2008 (2008-11-06) the whole document	1-3, 7-12,25, 27-34
X	WO 03/073991 A2 (CELLTECH R & D INC [US]; KUNG SUTHERLAND MAY S [US]; GEOGHEGAN JAMES C) 12 September 2003 (2003-09-12) the whole document	23-24, 26-34
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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.
A	<p>HOSKING D J ET AL: "Osteoporosis therapy: an example of putting evidence-based medicine into clinical practice." QJM : MONTHLY JOURNAL OF THE ASSOCIATION OF PHYSICIANS JUN 2005, vol. 98, no. 6, June 2005 (2005-06), pages 403-413, XP002570651 ISSN: 1460-2725 the whole document</p>	<p>23-24, 26-34</p>
A	<p>HEANEY ROBERT P: "Advances in therapy for osteoporosis." CLINICAL MEDICINE & RESEARCH APR 2003, vol. 1, no. 2, April 2003 (2003-04), pages 93-99, XP002570652 ISSN: 1539-4182 the whole document</p>	<p>23-24, 26-34</p>
A	<p>MACDONALD B R ET AL: "Emerging therapies in osteoporosis." BEST PRACTICE & RESEARCH. CLINICAL RHEUMATOLOGY JUL 2001, vol. 15, no. 3, July 2001 (2001-07), pages 483-496, XP002570653 ISSN: 1521-6942 the whole document</p>	<p>23-24, 26-34</p>
A	<p>DÍEZ J L: "Skeletal effects of selective oestrogen receptor modulators (SERMs)." HUMAN REPRODUCTION UPDATE 2000 MAY-JUN, vol. 6, no. 3, May 2000 (2000-05), pages 255-258, XP002570654 ISSN: 1355-4786 the whole document</p>	<p>23-24, 26-34</p>
A	<p>KHOSLA S ET AL: "TREATMENT OPTIONS FOR OSTEOPOROSIS" MAYO CLINIC PROCEEDINGS, MAYO MEDICAL VENTURES, ROCHESTER, MN, vol. 70, no. 10, 1 January 1995 (1995-01-01), pages 978-982, XP009009909 ISSN: 0025-6196 the whole document</p>	<p>23-24, 26-34</p>

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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:

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:

see additional sheet

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 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 report covers only those claims for which fees were paid, specifically claims Nos.:

23-24, 26(completely); 1-3, 7-12, 25, 27-34(partially)
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-3, 7-12, 25, 27-34(all partially)

Subject-matter of claims 1-3, 7-12, 25 and 27-34 insofar as it relates to methods of promoting local bone growth by use of a SOST (also termed Sclerostin) antagonist.

2-3. claims: 1-3, 7-12, 25, 27-34(all partially)

Subject-matter of claims 1-3, 7-12, 25 and 27-34 insofar as it relates to methods of promoting local bone growth by use of, respectively, a Wise (also termed SOSTDC-1, Sclerostin Domain-Containing protein 1, USAG-1, Ectodin, Ectodermal BMP inhibitor, CDA019) antagonist (Invention 2) and a LRP (also termed LDL Receptor-related protein) antagonist (Invention 3).

4. claims: 4-6(completely); 7-12(partially)

Subject-matter of claims 4-12 insofar as it relates to methods of promoting local bone growth by use of a SOST, Wise or LRP antagonist together with a BMP recombinant protein.

5. claims: 13-22

Subject-matter of claims 13-22 insofar as it relates to an orthopedic or periodontal medical device comprising a SOST antagonist.

6. claims: 23-24, 26(completely); 27-34(partially)

Subject-matter of claims 23, 24 and 26-34 insofar as it relates to methods of increasing bone density by use of a SOST, Wise or LRP antagonist together with an antiresorptive drug.

7. claims: 35-39

Subject-matter of claims 35-39 insofar as it relates to methods of reducing bone by use of a SOST or Wise agonist.

8. claim: 40

Method of protecting a mammalian kidney from chemical injury resulting in renal damage (or glomerulonephritis) by use of a SOST or Wise antagonist.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/088542

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005003158 A	13-01-2005	AU 2004253870 A1	13-01-2005
		BR PI0411535 A	01-08-2006
		CA 2529578 A1	13-01-2005
		CN 1835968 A	20-09-2006
		EP 1638999 A2	29-03-2006
		JP 2008505843 T	28-02-2008
		KR 20060064568 A	13-06-2006
		NZ 544617 A	27-11-2009
		US 2006233801 A1	19-10-2006
		ZA 200600384 A	29-10-2008
WO 03106657 A	24-12-2003	AU 2003276430 A1	31-12-2003
WO 2006119107 A	09-11-2006	AR 053266 A1	25-04-2007
		AU 2006242431 A1	09-11-2006
		CA 2607197 A1	09-11-2006
		EA 200702402 A1	28-04-2008
		EP 1891101 A2	27-02-2008
		GT 200600186 A	09-02-2007
		JP 2008539726 T	20-11-2008
		KR 20080011420 A	04-02-2008
		US 2009304713 A1	10-12-2009
		US 2007110747 A1	17-05-2007
		UY 29514 A1	30-11-2006
WO 2006102070 A	28-09-2006	CA 2601360 A1	28-09-2006
		EP 1883418 A2	06-02-2008
		JP 2008536816 T	11-09-2008
WO 03039534 A	15-05-2003	CA 2465499 A1	15-05-2003
		EP 1446114 A1	18-08-2004
		JP 2005511593 T	28-04-2005
US 2007292444 A1	20-12-2007	NONE	
WO 2008133722 A	06-11-2008	EP 2094731 A2	02-09-2009
		US 2010015665 A1	21-01-2010
WO 03073991 A2	12-09-2003	AU 2003223214 A1	16-09-2003
		CA 2476410 A1	12-09-2003
		EP 1575481 A2	21-09-2005
		JP 2005532998 T	04-11-2005