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60/528,409 9 December 2003 (09.12.2003) US
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(54) Title: CONTROLLED RELEASE COMPOSITION CONTAINING A STRONTIUM SALT

(57) Abstract: A controlled release pharmaceutical composition comprising a strontium salt. The invention also relates to the use of a strontium salt for treating a male suffering from diseases and conditions affecting metabolism and/or structural integrity of cartilage and/or bone. The invention also relates to the use of a strontium-containing compound for preventing a cartilage and/or bone condition in a subject, and for the treatment and/or prophylaxis of secondary osteoporosis.

WO 2004/098617 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/DK2004/000326

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K33/24 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) IPC 7 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, PAJ, WPI Data, BIOSIS, EMBASE, CHEM ABS Data, SCISEARCH				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	EP 0 404 558 A (YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW UNIV. OF JERUSALEM) 27 December 1990 (1990-12-27) claims 1,5,14 -----	1-13,16, 18-37, 48,49		
X	EP 0 381 445 A (YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW UNIV. OF JERUSALEM) 8 August 1990 (1990-08-08) claims 1,3 page 4, lines 20-27 ----- -/--	1-13,16, 18		
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"> <input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. </td> <td style="width: 50%; border: none;"> <input checked="" type="checkbox"/> Patent family members are listed in annex. </td> </tr> </table>			<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.	<input checked="" type="checkbox"/> Patent family members are listed in annex.
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.	<input checked="" type="checkbox"/> Patent family members are listed in annex.			
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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 <p style="text-align: center; font-weight: bold;">4 February 2005</p>	Date of mailing of the international search report <p style="text-align: center; font-weight: bold;">23/02/2005</p>			
Name and mailing address of the ISA 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	Authorized officer <p style="text-align: center; font-weight: bold;">Strack, E</p>			

INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK2004/000326

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MOROHASHI T ET AL: "EFFECTS OF STRONTIUM ON CALCIUM METABOLISM IN RATS I. A DISTINCTION BETWEEN THE PHARMACOLOGICAL AND TOXIC DOSES" JAPANESE JOURNAL OF PHARMACOLOGY, THE JAPANESE PHARMACOLOGICAL SOCIETY, KYOTO, JP, vol. 64, no. 3, 1994, pages 155-162, XP008036785 ISSN: 0021-5198 abstract page 156, column 1, paragraph 2	1-12, 14-16, 18-37, 48, 49
X	WO 98/35657 A (COLLAGENEX PHARMACEUTICALS) 20 August 1998 (1998-08-20) claims 1,2,4,10	1-13,16, 18
X	US 5 856 356 A (TSOUDEROS ET AL) 5 January 1999 (1999-01-05) column 1, line 59 - column 2, line 18 claim 1 column 2, lines 50-55 example B	1-12, 14-37
X	WO 03/028742 A1 (SANTOSOLVE AS; JELLUM, EGIL; FAGERLUND, BJOERN, JARL; KJOELBERG, CLAS,) 10 April 2003 (2003-04-10) page 8, paragraph 2	1-12, 14-18
X	BRANDI M L: "New perspectives in the prevention and treatment of glucocorticoid-induced osteoporosis" CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2000 ITALY, vol. 18, no. 5 SUPPL. 21, 2000, pages S74-S78, XP002314920 ISSN: 0392-856X abstract page 77, column 1, paragraph 1	1-37, 48-53
X	WO 99/34772 A (ENAMELON, INC) 15 July 1999 (1999-07-15) page 26, paragraph 3 page 34, paragraph 1 page 38, line 2 - line 4	1-12, 14-18
A	SORBERA L A ET AL: "STRONTIUM RANELATE TREATMENT AND PREVENTION OF OSTEOPOROSIS BONE RESORPTION INHIBITOR BONE FORMATION STIMULANT" DRUGS OF THE FUTURE, BARCELONA, ES, vol. 28, no. 4, 1 April 2003 (2003-04-01), pages 328-335, XP008036784 ISSN: 0377-8282 table 1	1-37, 48-53

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2004/000326

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. Claims Nos.: **19-37 and 48-52 (all partially)**
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 19-37 and 48-52 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:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,
no additional fees are to be refunded.

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.:
1-37, 48-49 (partially); 50-53 (completely)
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-13, 16, 18-37, 48-49 (all partially)

The use of a controlled release composition for oral use of a strontium salt of an anorganic monoprotic acid alone for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of a cartilage and/or bone metabolism and the composition per se

2. claims: 1-13, 16, 18-37, 48-49 (all partially)

The use of a controlled release composition for oral use of a strontium salt of an anorganic diprotic acid alone for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of a cartilage and/or bone metabolism and the composition per se

3. claims: 1-13, 16, 18-37, 48-49 (all partially)

The use of a controlled release composition for oral use of a strontium salt of an anorganic triprotic acid alone for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of a cartilage and/or bone metabolism and the composition per se

4. claims: 1-12, 14-37, 48-49 (all partially)

The use of a controlled release composition for oral use of a strontium salt of an organic monoprotic acid alone for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of a cartilage and/or bone metabolism and the composition per se

5. claims: 1-12, 14-37, 48-49 (all partially)

The use of a controlled release composition for oral use of a strontium salt of an organic diprotic acid alone for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of a cartilage and/or bone metabolism and the composition per se

6. claims: 1-12, 14-37, 48-49 (all partially)

The use of a controlled release composition for oral use of a strontium salt of an organic triprotic acid alone for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of a cartilage and/or bone metabolism and the composition per se

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. claims: 19-37, 48-49 (partially), 42-47 (completely)

Use of a strontium salt for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of a cartilage and/or bone metabolism in combination with vitamin D

8. claims: 19-37, 48-49 (partially), 38-41 (completely)

Use of a strontium salt for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of a cartilage and/or bone metabolism in combination with calcium

9. claims: 1-37, 48-49 (partially), 50-53 (completely)

Use of a strontium salt for the treatment/prophylaxis of a cartilage/bone disease/condition resulting in a dysregulation of cartilage and/or bone metabolism in combination with a drug substance that induces osteoporosis and the combinations per se

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/DK2004/000326

Patent document cited in search report	Publication date	Publication date	Patent family member(s)	Publication date
EP 0404558	A	27-12-1990	US 5330746 A	19-07-1994
			US 5160737 A	03-11-1992
			AT 222505 T	15-09-2002
			AU 631655 B2	03-12-1992
			AU 5766790 A	17-01-1991
			CA 2019410 A1	21-12-1990
			DE 69033994 D1	26-09-2002
			DE 69033994 T2	06-11-2003
			EP 0404558 A1	27-12-1990
			IL 94749 A	24-01-1995
			JP 3128316 A	31-05-1991
			US 5438076 A	01-08-1995
			US 5648399 A	15-07-1997
			US 5639795 A	17-06-1997
EP 0381445	A	08-08-1990	AT 105170 T	15-05-1994
			DE 69008555 D1	09-06-1994
			DE 69008555 T2	18-08-1994
			EP 0381445 A2	08-08-1990
			US 5438076 A	01-08-1995
			US 5330746 A	19-07-1994
			US 5849266 A	15-12-1998
			US 5648399 A	15-07-1997
			US 5639795 A	17-06-1997
			US 5160737 A	03-11-1992
			US 5139768 A	18-08-1992
			US 5403577 A	04-04-1995
WO 9835657	A	20-08-1998	US 5792446 A	11-08-1998
			AU 6175398 A	08-09-1998
			WO 9835657 A1	20-08-1998
US 5856356	A	05-01-1999	FR 2749759 A1	19-12-1997
			AT 233558 T	15-03-2003
			AU 711950 B2	28-10-1999
			AU 2490297 A	08-01-1998
			BR 9703603 A	01-09-1998
			CA 2206837 A1	17-12-1997
			CN 1179944 A ,C	29-04-1998
			DE 69719408 D1	10-04-2003
			DE 69719408 T2	24-12-2003
			DK 813869 T3	02-06-2003
			EP 0813869 A1	29-12-1997
			ES 2193337 T3	01-11-2003
			HU 9701059 A2	02-03-1998
			JP 10059852 A	03-03-1998
			NO 972764 A	18-12-1997
			NZ 328106 A	27-04-2001
			ZA 9705323 A	14-01-1998
			WO 03028742	A1
US 2005013877 A1	20-01-2005			
WO 9934772	A	15-07-1999	AU 1527099 A	26-07-1999
			WO 9934772 A1	15-07-1999