

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
11 January 2001 (11.01.2001)

PCT

(10) International Publication Number  
**WO 01/02031 A3**

- (51) International Patent Classification<sup>7</sup>: **A61L 27/50** Dunwoody, GA 30338 (US). **GIRARDOT, Marie-Nadia**; 6328 North Peachtree Road, Dunwoody, GA 30338 (US).
- (21) International Application Number: PCT/US00/17606
- (22) International Filing Date: 27 June 2000 (27.06.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/142,171 1 July 1999 (01.07.1999) US
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- (81) Designated States (*national*): AU, CA, JP.
- (84) Designated States (*regional*): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
6 December 2001
- 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.



**WO 01/02031 A3**

(54) Title: TARGETED ANTICALCIFICATION TREATMENT

(57) Abstract: Methods for providing biomaterials with increased resistance to calcification by treating with cell-targeted agents and/or with matrix-targeted agents. Cell-targeted agents are used which block calcium channels or which prevent oxidative damage to cells and/or inhibit enzymes. Other treatments of biomaterials may remove cell-derived calcium-binding components or target extracellular matrices, as by cleaving proteins with cyanogen bromide or reducing disulfide bonds to produce sulfhydryl groups which are thereafter alkylated. Combinations of the foregoing different treatments are also effective in increasing the calcification resistance of cardiovascular tissues that were previously subjected to chemical fixing and/or other anticalcification treatments.

# INTERNATIONAL SEARCH REPORT

International Application No

PC1/US 00/17606

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61L27/50

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 A61L

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, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 753 652 A (LANGER ROBERT ET AL) 28 June 1988 (1988-06-28) claims 1,7-10,26-28 ---	1,4,5, 13,14,20
X	EP 0 564 786 A (LIFECCELL CORP) 13 October 1993 (1993-10-13) page 6, line 20 - line 37 claims 1,8,9 ---	1-3,13, 15,16
X	US 5 558 875 A (WANG SU) 24 September 1996 (1996-09-24) abstract ---	1,13,20
X	US 5 843 182 A (GOLDSTEIN STEVEN) 1 December 1998 (1998-12-01) column 2, line 54 - line 62 claims 1-3,11-14,22,23 ---	1,13,20
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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

1 March 2001

Date of mailing of the international search report

16.03.01

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# INTERNATIONAL SEARCH REPORT

International Application No

PC1/US 00/17606

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 13227 A (LERNER EYAL; LEVY ROBERT J (US); UNIV MICHIGAN (US)) 9 May 1996 (1996-05-09) claims 1,4,5 ---	1,13,20
A	HENRY P D: "ANTI-ATHEROSCLEROTIC EFFECTS OF CALCIUM ANTAGONISTS: A BRIEF REVIEW" CLINICAL AND INVESTIGATIVE MEDICINE, vol. 10, no. 6, 1 November 1987 (1987-11-01), pages 601-605, XP000604021 page 602, left-hand column, paragraph 3 -page 602, right-hand column, paragraph 3 -----	1,4,5, 13,14,20

## INTERNATIONAL SEARCH REPORT

national application No.  
PCT/US 00/17606

### 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. ☐ 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 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:

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 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.

**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 (partially), 4, 5 (all completely),  
13 (partially), 14 (completely), 20 (partially)

Treatment of biomaterials with a cell-targeted agent which is a calcium channel blocking agent.

2. Claims: 1 (partially), 2, 3 (all completely),  
13 (partially), 15, 16 (all completely),  
20 (partially)

Treatment of biomaterials with a cell-targeted agent which prevents oxidative or selective enzymatic damage.

3. Claims: 1 (partially), 10 (completely), 13 (partially),  
20 (partially)

Treatment of biomaterials with a cell-targeted agent which removes cell-derived calcium-binding components.

4. Claims: 1 (partially), 6-9, 11, 12 (all completely),  
13 (partially), 17-19 (all completely)

Treatment of biomaterials with a matrix-targeted agent.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCI/US 00/17606

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4753652	A	28-06-1988	NONE
EP 0564786	A	13-10-1993	US 5336616 A 09-08-1994 AU 668703 B 16-05-1996 AU 3293493 A 19-08-1993 CA 2089336 A 13-08-1993 JP 6261933 A 20-09-1994
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