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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, LA, 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, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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9 August 2007

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: IMPROVED METHOD OF TREATING DEGENERATIVE SPINAL DISORDERS

(57) Abstract: The present invention describes methods for treating a degenerative intervertebral disc disorder comprising implanting a disc stabilization device into a subject and administering at least one therapeutic agent which promotes healing of the disc to the subject. The invention also includes methods of promoting healing of damaged or degenerated intervertebral discs comprising decreasing the load of the disc through a disc stabilization device and inhibiting the inflammatory process. Also described are hydrogels for use in combination with extradiscal stabilization devices, as intradiscal stabilization devices, as drug carriers, and as combinations thereof.



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# INTERNATIONAL SEARCH REPORT

International application No  
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**A. CLASSIFICATION OF SUBJECT MATTER**  
 INV. A61F2/44 A61K39/395 C07K16/24 A61P19/00 A61P29/00

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)  
**A61F**

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, Sequence Search, BIOSIS, EMBASE**

**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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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  
**2 April 2007**

Date of mailing of the international search report  
**19/06/2007**

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/023704

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/026244 A1 (TRIEU HAI H [US]) 28 February 2002 (2002-02-28)	1, 3, 4, 13-19, 28, 29, 33, 34, 37-41, 48-51, 58-63, 65, 74-78, 88, 89, 93-95
Y	paragraphs [0009], [0101] - [0109]	21-27, 30-32, 35, 36, 53-57, 64, 82-85, 90-92
X	WO 2004/100841 A (INTRINSIC THERAPEUTICS INC [US]; LAMBRECHT GREGORY H [US]; KAVANAUGH S) 25 November 2004 (2004-11-25)	1-4, 13-20, 34, 37-41, 48-52, 58-63, 65, 74-78, 93-95
Y	pages 1, 2, 18 - page 19	21-27, 30-32, 35, 36, 53-57, 64, 82-85, 90-92
Y	US 6 258 562 B1 (SALFELD JOCHEN G [US] ET AL) 10 July 2001 (2001-07-10)	21-27, 53-57, 82-85
Y	sequences 1, 2	
Y	ROBERTS S ET AL: "Matrix metalloproteinases and aggrecanase : their role in disorders of the human intervertebral disc" SPINE, PHILADELPHIA, PA, US, vol. 25, no. 23, 2000, pages 3005-3013, XP002979618 ISSN: 0362-2436 abstract page 3012, left-hand column	31, 32, 91, 92
	-/--	

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/023704

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>MIYAMOTO K ET AL: "129. Tumor necrosis factor alpha inhibits proteoglycan metabolism and stimulates matrix metalloproteinase and aggrecanase production by human intervertebral disc cells"            THE SPINE JOURNAL, ELSEVIER,            vol. 4, no. 5,            10 September 2004 (2004-09-10), page S66,            XP004563948            ISSN: 1529-9430            abstract</p>	31,32, 91,92
Y	<p>BONNET C S ET AL: "Osteoarthritis, angiogenesis and inflammation"            RHEUMATOLOGY, OXFORD UNIVERSITY PRESS,            LONDON, GB,            vol. 44, no. 1, January 2005 (2005-01),            pages 7-16, XP002413664            ISSN: 1462-0324            pages 11-12; figure 1</p>	30,90
Y	<p>SAKAI D ET AL: "Transplantation of mesenchymal stem cells embedded in Atelocollagen&lt;(&gt;R) gel to the intervertebral disc: a potential therapeutic model for disc degeneration"            BIOMATERIALS, ELSEVIER SCIENCE PUBLISHERS            BV., BARKING, GB,            vol. 24, no. 20, September 2003 (2003-09),            pages 3531-3541, XP004429647            ISSN: 0142-9612            abstract; figures 1,3-6</p>	35,36
Y	<p>GRUBER H E ET AL: "BIOLOGIC STRATEGIES FOR THE THERAPY OF INTERVERTEBRAL DISC DEGENERATION"            EXPERT OPINION ON BIOLOGICAL THERAPY,            ASHLEY, LONDON, GB,            vol. 3, no. 8, December 2003 (2003-12),            pages 1209-1214, XP009051664            ISSN: 1471-2598            page 1211 - page 1212</p>	35,36
Y	<p>WO 2004/073532 A (SPINE NEXT [FR]; MEUNIER ALAIN [FR]; SENEGAS JACQUES [FR]; LE COUEDIC) 2 September 2004 (2004-09-02)            figures 1-3</p>	64
	-/--	

## 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>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  abstract</p> <p style="text-align: center;">-----</p>	23,55,83
A	<p>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  abstract</p> <p style="text-align: center;">-----</p>	23,55,83
A	<p>GENEVAY S ET AL: "Efficacy of etanercept in the treatment of acute, severe sciatica: a pilot study."  ANNALS OF THE RHEUMATIC DISEASES SEP 2004, vol. 63, no. 9, September 2004 (2004-09), pages 1120-1123, XP009081423  ISSN: 0003-4967  the whole document</p> <p style="text-align: center;">-----</p>	1,2,20, 21,26
A	<p>KARPPINEN JARO ET AL: "Tumor necrosis factor-alpha monoclonal antibody, infliximab, used to manage severe sciatica."  SPINE 15 APR 2003,  vol. 28, no. 8,  15 April 2003 (2003-04-15), pages 750-753 ; dis, XP009081417  ISSN: 1528-1159  the whole document</p> <p style="text-align: center;">-----</p>	1,2,20, 21,25
A	<p>MASUDA K ET AL: "Growth factors and the intervertebral disc"  THE SPINE JOURNAL, ELSEVIER,  vol. 4, no. 6, November 2004 (2004-11), pages S330-S340, XP004639287  ISSN: 1529-9430  the whole document</p> <p style="text-align: center;">-----</p>	1,2,28, 29,34, 88,89
A	<p>NAGASE HIDEAKI ET AL: "Aggrecanases and cartilage matrix degradation."  ARTHRITIS RESEARCH &amp; THERAPY 2003,  vol. 5, no. 2, 2003, pages 94-103,  XP009081422  ISSN: 1478-6362  the whole document</p> <p style="text-align: center;">-----</p>	1,2,31, 32,38, 39,76, 91,92
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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>GUIOT B H ET AL: "Molecular biology of degenerative disc disease." NEUROSURGERY NOV 2000, vol. 47, no. 5, November 2000 (2000-11), pages 1034-1040, XP009081419 ISSN: 0148-396X the whole document</p> <p style="text-align: center;">-----</p>	<p>1-4, 13-41, 48-65, 74-78, 82-85, 88-95</p>

# INTERNATIONAL SEARCH REPORT

International application No.  
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## 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.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 1-76 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

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.:  
  
1-4 (all partially), 13-19, 20-41 (all partially), 48-51, 52-57  
(all partially), 58-65, 74-76 (all partially), 77, 78  
82-85 (all partially), 88-95

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: 1-4 (all partially), 13-19, 20-41 (all partially), 48-51, 52-57 (all partially), 58-65, 74-76 (all partially), 77, 78, 82-85 (all partially), 88-95

Method of treating a degenerated intervertebral disc disorder comprising an intradiscal stabilization device and a therapeutic agent

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2. claims: 1-4 (all partially), 5-12, 20-41 (all partially), 42-47, 52-57 (all partially), 66-73, 74-76 (all partially), 79-81, 82-85 (all partially), 86, 87

Method of treating a degenerated intervertebral disc disorder comprising an extradiscal stabilization device and a therapeutic agent

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/023704

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2002026244	A1	28-02-2002	
		AT 310475 T	15-12-2005
		AU 8535101 A	13-03-2002
		CA 2419978 A1	07-03-2002
		DE 60115254 D1	29-12-2005
		DE 60115254 T2	10-08-2006
		EP 1313412 A2	28-05-2003
		EP 1563808 A1	17-08-2005
		ES 2252281 T3	16-05-2006
		JP 2004507318 T	11-03-2004
		WO 0217824 A2	07-03-2002
		US 2005154463 A1	14-07-2005
		US 2005131540 A1	16-06-2005
		US 2005131541 A1	16-06-2005
		US 2005278029 A1	15-12-2005
		US 2003023311 A1	30-01-2003
		US 2003199984 A1	23-10-2003
		US 6620196 B1	16-09-2003
		US 2004117019 A1	17-06-2004
		US 2006064171 A1	23-03-2006
		US 2006064172 A1	23-03-2006
WO 2004100841	A	25-11-2004	
		EP 1624832 A1	15-02-2006
		US 2006200246 A1	07-09-2006
US 6258562	B1	10-07-2001	
		AT 239041 T	15-05-2003
		AU 722077 B2	20-07-2000
		AU 2122997 A	28-08-1997
		BG 64564 B1	29-07-2005
		BG 102755 A	31-05-1999
		BG 107537 A	30-09-2003
		BG 64776 B1	31-03-2006
		BR 9707379 A	13-04-1999
		CA 2243459 A1	14-08-1997
		CN 1504752 A	16-06-2004
		CN 1215407 A	28-04-1999
		CY 2463 A	03-06-2005
		CZ 9802476 A3	11-11-1998
		DE 69721548 T2	01-04-2004
		DE 122004000003 I1	23-09-2004
		DE 122004000004 I1	12-08-2004
		DK 929578 T3	25-08-2003
		EP 0929578 A1	21-07-1999
		ES 2198552 T3	01-02-2004
		HU 9901874 A2	28-09-1999
		IL 125697 A	20-03-2005
		JP 3861118 B2	20-12-2006
		JP 2000507810 T	27-06-2000
		JP 2003177130 A	27-06-2003
		JP 2007045828 A	22-02-2007
		LU 91062 A9	26-04-2004
		NL 300143 I1	03-05-2004
		NO 983627 A	07-10-1998
		NO 20026202 A	07-10-1998
		NO 322755 B1	04-12-2006
		NO 320657 B1	09-01-2006
		NZ 331579 A	29-06-2001
		NZ 512006 A	27-05-2005
		NZ 536216 A	31-08-2006

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No <b>PCT/US2006/023704</b>
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6258562	B1	PL 328411 A1	18-01-1999
		PL 193499 B1	28-02-2007
		PT 929578 T	30-09-2003
		RO 119831 B1	29-04-2005
		RU 2003120859 A	10-01-2005
		SI 9720020 A	31-10-1999
		SK 106298 A3	10-03-1999
		TR 9801532 T2	23-11-1998
		WO 9729131 A1	14-08-1997
WO 2004073532	A	02-09-2004	AU 2003303927 A1
			EP 1585448 A1
			FR 2850009 A1
			JP 2006513007 T
			KR 20050092768 A
			US 2006235532 A1