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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, 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, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
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(54) Title: METHODS AND COMPOSITIONS FOR TREATMENT OF LESIONED SITES OF BODY VESSELS

(57) Abstract: Methods and compositions for inducing apoptosis of cells, such as macrophages, at a lesioned site of a body vessel are disclosed herein. Nitric oxide can be directly or indirectly delivered to a treatment site to increase macrophage apoptosis. Delivery can include site specific delivery of nitric oxide gas, nitric oxide in aqueous solution or a substance(s) which releases nitric oxide or causes nitric oxide to be generated from an endogenous source. Delivery can be achieved by a delivery system such as a catheter assembly, stent or other suitable device.



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## INTERNATIONAL SEARCH REPORT

International application No  
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
INV.	A61K31/198	A61L31/00
	A61M25/00	A61M29/00
		A61P9/10
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols)		
A61K A61L A61M 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		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 2007/097875 A (ADVANCED CARDIOVASCULAR SYSTEM [US]; GLAUSER THIERRY [US]; PACETTI STE) 30 August 2007 (2007-08-30) claims	1-40
X	WO 2005/070008 A2 (UNIV AKRON [US]; RENEKER DARRELL [US]) 4 August 2005 (2005-08-04) claims	1-40
X	US 2005/249777 A1 (MICHAL EUGENE T [US] ET AL) 10 November 2005 (2005-11-10) claims; examples	1-40
X	US 7 022 334 B1 (DING NI [US]) 4 April 2006 (2006-04-04) claims; examples	1-40
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<input checked="" type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> See patent family annex.
* Special categories of cited documents :		
<p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p>		<p>*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</p> <p>*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</p> <p>*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.</p> <p>*Z* document member of the same patent family</p>
Date of the actual completion of the international search		Date of mailing of the international search report
4 October 2007		30/10/2007
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  GIMENEZ MIRALLES, J

## 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	WO 00/62614 A (NITROSYSTEMS INC [US]) 26 October 2000 (2000-10-26) page 11, line 18 - page 12, line 14; claims; figures -----	1-40
X	WO 03/017989 A (SCIMED LIFE SYSTEMS INC [US]) 6 March 2003 (2003-03-06) paragraphs [0007], [0008], [0019], [0038], [0039], [0042], [0045]; claims 8,13 -----	1-40
X	US 2005/145258 A1 (DONG YONGHUA [US]) 7 July 2005 (2005-07-07) paragraphs [0032], [0044]; examples -----	1-40
X	US 2002/094985 A1 (HERRMANN ROBERT A [US] ET AL) 18 July 2002 (2002-07-18) paragraphs [0003], [0127], [0128]; claims -----	1-40
X	NIEBAUER, J. ET AL.: "Local L-arginine delivery after balloon angioplasty reduces monocyte binding and induces apoptosis" CIRCULATION, vol. 100, 1999, pages 1830-1835, XP002453636 See "Local drug delivery" the whole document -----	1-40
X	PULFER S K ET AL: "INCORPORATION OF NITRIC OXIDE-RELEASING CROSSLINKED POLYETHYLENEIMINE MICROSPHERES INTO VASCULAR GRAFTS" JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, WILEY, NEW YORK, NY, US, vol. 37, no. 2, November 1997 (1997-11), pages 182-189, XP000978327 ISSN: 0021-9304 the whole document -----	1-40

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2007/008934

## 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.: 17-29  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 17-29 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:

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.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/008934

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			US 2007196424 A1 23-08-2007
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