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[Continued on next page]

(54) Title: SYSTEM AND METHOD FOR MONITORING IN VIVO DRUG RELEASE USING OVERHAUSER-ENHANCED NMR

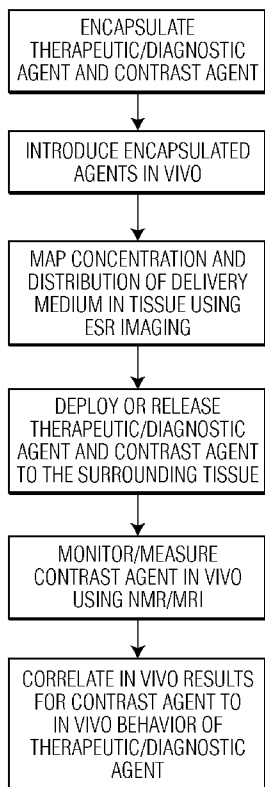


FIG. 1

(57) Abstract: Systems and methods for monitoring in vivo release of therapeutic and/or diagnostic agents, e.g., drugs, are provided. The disclosed systems and methods use a contrast agent and Overhauser-enhanced nuclear magnetic resonance (NMR) to monitor and/or measure the concentration and distribution of the contrast agent. Provided the contrast agent and the therapeutic/diagnostic agent have similar pharmacokinetics, the disclosed system/method may also be used to monitor and/or measure the concentration of such therapeutic/diagnostic agent (e.g., a drug), e.g., in the form of a volume-averaged signal and/or dynamic two-dimensional or three-dimensional images. In exemplary embodiments of the present disclosure, the therapeutic/diagnostic agent and the contrast agent are introduced to the body in an encapsulated form, e.g., within hollow nanoparticles.

WO 2007/066247 A3



ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

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21 August 2008

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2006/054273

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K49/00 A61K41/00 A61K49/06 A61K49/18
 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
 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, BIOSIS, MEDLINE, EMBASE, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2001/034483 A1 (PRINCE MARTIN R [US]) 25 October 2001 (2001-10-25)	1, 3-9, 11, 12, 14, 17-19
Y	paragraphs [0043], [0044] paragraph [0048] claims 1, 12	1-4, 11-21
X	US 5 362 478 A (DESAI NEIL P [US] ET AL) 8 November 1994 (1994-11-08) column 18; examples 15, 17	1-16, 18-20
X	US 6 311 086 B1 (ARDENKJAER-LARSEN JAN HENRIK [NO] ET AL) 30 October 2001 (2001-10-30)	1, 3-9, 11
Y	claim 1 column 6, paragraph 3	12-21
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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	*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
E earlier document but published on or after the international filing date	*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
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)	*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.
O document referring to an oral disclosure, use, exhibition or other means	*&* document member of the same patent family
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 24 June 2008	Date of mailing of the international search report 30/06/2008
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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 Bonzano, Camilla
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INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2006/054273

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 6 466 812 B1 (OVERWEG JOHANNES A [DE] ET AL) 15 October 2002 (2002-10-15) claims 1,2 column 2, paragraph 2	1, 3-9, 11, 12, 14, 17-21
X	GB 2 311 138 A (NYCOMED IMAGING AS [NO]) 17 September 1997 (1997-09-17) cited in the application page 4, paragraph 5 - page 5, paragraph 1 page 9; example 1	1-9, 11, 12, 18-21
Y	WO 99/52505 A (NYCOMED IMAGING AS [NO]; COCKBAIN JULIAN [GB]; FOSSHEIM SIGRID LISE [N]) 21 October 1999 (1999-10-21) page 11, paragraph 3 page 15, paragraph 4 page 24, paragraph 2 page 32, paragraph 2 example 31 claims 1,5,6	1-4, 11-15, 17-21
X	WO 96/28090 A (IMARX PHARMACEUTICAL CORP [US]) 19 September 1996 (1996-09-19) claims 1-3 examples 10,11 page 11, line 15 - line 21 page 13, line 7	1-21

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2006/054273

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:

Although claims 12-21 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 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:

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable 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.:
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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2006/054273

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2001034483	A1	25-10-2001	NONE
US 5362478	A	08-11-1994	US 5508021 A 16-04-1996
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