(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 February 2007 (01.02.2007)

PCT

(10) International Publication Number
WO 2007/013041 A3

(51) International Patent Classification:
G01N 33/68 (2006.01) *G01N 33/74* (2006.01)

(21) International Application Number:
PCT/IB2006/052578

(22) International Filing Date: 27 July 2006 (27.07.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/703,928 29 July 2005 (29.07.2005) US

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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, 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, HN, 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.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, 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).

Declaration under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

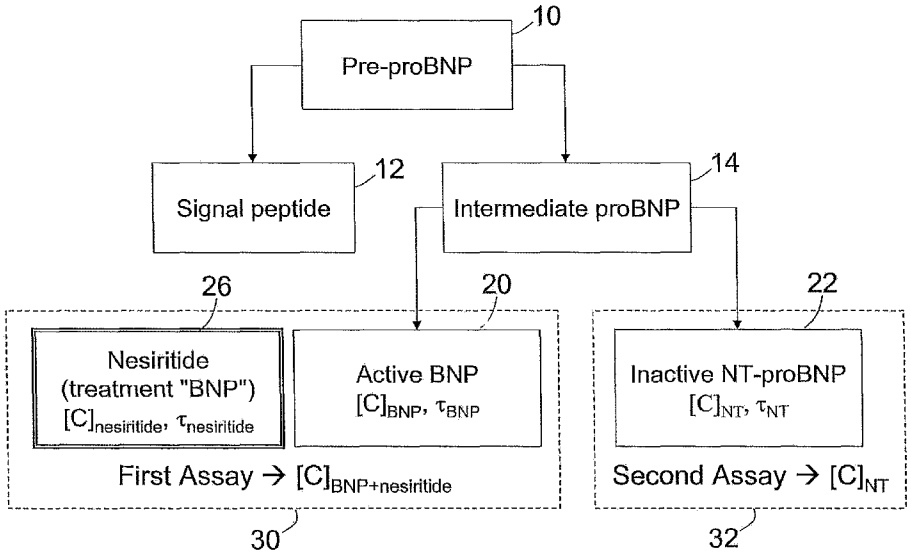
Published:

— *with international search report*

(88) Date of publication of the international search report:
11 October 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: MONITORING OF CARDIAC NATRIURETIC PEPTIDES DURING DIAGNOSIS, MANAGMENT, AND TREATMENT OF CARDIAC DISEASES



(57) Abstract: In a cardiac monitoring method, at least an inactive natriuretic peptide (22) and an active natriuretic peptide (20) are assayed in a biological sample taken from a patient. Both the inactive and active natriuretic peptides are produced in the patient responsive to cardiac stress. A therapeutic agent (26), such as a synthetic or mimetic natriuretic peptide, is administered to the patient. The administered therapeutic agent substantially interferes with the active natriuretic peptide assay but does not substantially interfere with the inactive natriuretic peptide assay. Kinetics of the administered therapeutic agent are determined based on at least the active natriuretic peptide assay. Cardiac diagnostic information is determined based on at least the inactive natriuretic peptide assay.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2006/052578

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/68 G01N33/74

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)
G01N

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GEGENHUBER ALFONS ET AL: "Time course of B-type natriuretic peptide (BNP) and N-terminal proBNP changes in patients with decompensated heart failure." CLINICAL CHEMISTRY FEB 2004, vol. 50, no. 2, February 2004 (2004-02), pages 454-456, XP002427032 ISSN: 0009-9147 the whole document	1-17

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[X] 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	Date of mailing of the international search report
28 March 2007	26/06/2007

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2006/052578

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	RADEMAKER M T ET AL: "CARDIAC NATRIURETIC PEPTIDES FOR CARDIAC HEALTH" CLINICAL SCIENCE, BIOCHEMICAL SOCIETY AND THE MEDICAL RESEARCH SOCIETY, LONDON,, GB, vol. 108, no. 1, January 2005 (2005-01), pages 23-36, XP009060567 ISSN: 0143-5221 whole document; in particular abstract, p. 31-33	1-17
A	RICHARDS MARK ET AL: "NT-proBNP in heart failure: therapy decisions and monitoring." EUROPEAN JOURNAL OF HEART FAILURE : JOURNAL OF THE WORKING GROUP ON HEART FAILURE OF THE EUROPEAN SOCIETY OF CARDIOLOGY 15 MAR 2004, vol. 6, no. 3, 15 March 2004 (2004-03-15), pages 351-354, XP002427033 ISSN: 1388-9842 the whole document	1-17
A	BURGER ANDREW J ET AL: "Effect of nesiritide (B-type natriuretic peptide) and dobutamine on ventricular arrhythmias in the treatment of patients with acutely decompensated congestive heart failure: The PRECEDENT study." AMERICAN HEART JOURNAL, vol. 144, no. 6, December 2002 (2002-12), pages 1102-1108, XP002427034 ISSN: 0002-8703 the whole document	1-17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2006/052578

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

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. [X] 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.:

1-17

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: 1-17

   A cardiac monitoring method comprising the steps according to independent claims 1 or 11.

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2. claims: 18-21

   Cardiac monitoring apparatus for performing the method of claim 11 or a cardiac monitoring apparatus comprising the devices according to claim 19.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 1-17 are directed to a diagnostic method practised on the human body, the search has been carried out and based on the alleged effects of the compound/composition. Although claims 1-17 are directed to a method of treatment of the human, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.1

Claims Nos.:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy