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1 September 2016

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(54) **Title**: MEANS AND METHODS FOR ASSESSING BONE DISORDERS

(57) **Abstract**: The present invention pertains to the field of diagnostics for bone disorders and toxicological assessments for risk stratification of chemical compounds. Specifically, it relates to a method for diagnosing a bone disorder, it also relates to a method for determining whether a compound is capable of inducing such a bone disorder in a subject and to a method of identifying a drug for treating a bone disorder. Furthermore, the present invention relates to a device and a kit for diagnosing a bone disorder.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2013/051228

A. CLASSIFICATION OF SUBJECT MATTER

See extra sheet
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: C07F;C07C

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 practicable, search terms used)

WPI, EPODOC, CNPAT, CNKI, Web of knowledge: bone, disease, disorder, marker, inositol, triglycer+, DPPC, heptadecanoic, dipalmitoyl, phosphatidylcholine

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO01/53477 A1(BAYLOR COLLEGE OF MEDICINE) 26 Jul. 2001 (26.07.2001). page 3 paragraph 4, page 4 paragraph 3, page 5 paragraphs 3 and 5, page 60 pagraph 3-page 61 pagraph 1, claims 13,32,37-42,56-60	1-20
A	WO01/60355 A1(UNIVERSITY OF SHEFFIELD) 23 Aug. 2001 (23.08.2001) the whole document	1-20
A	WO2011/063952A1(BRUZZESE, Tiberio) 03 Jun. 2011 (03.06.2011) the whole document	1-20
A	WO2006/102533A2(NEOPHARM, INC.) 28 Sep. 2006 (28.09.2006) the whole document	1-20

☐ 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 application or patent 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
01 Jul. 2013 (01.07.2013)	**18 Jul. 2013 (18.07.2013)**
Name and mailing address of the ISA/CN The State Intellectual Property Office, the P.R.China 6 Xitucheng Rd., Jimen Bridge, Haidian District, Beijing, China 100088 Facsimile No. 86-10-62019451	Authorized officer ZHONG,Hui Telephone No. (86-10)62414261

Form PCT/ISA /210 (second sheet) (July 2009)

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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.: 1-2,4-9(partially),16
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-2,4-9(partially),16 direct to a method for diagnosing bone disorder, the search has been carried out and based on the use of the agents for manufacturing of a diagnostic reagent.

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:

See extra 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 fees, this Authority did not invite payment of 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.:1-20 (all partially, relating to myo-Inositol-2-phosphate, Phosphatidylcholine (C16:0, C16:0), Heptadecanoic acid (C17:0), or TAG (C16:0, C18:0, C18:3)).
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

International application No.
PCT/IB2013/051228

Continuation of Box No. III of first sheet:

This Authority considers that there are 55 inventions covered by the claims indicated as follows:

Claims 1-15 direct to a method for diagnosing bone disorder, determining whether a compound is capable of inducing bone disorder, or identifying a substance for treating bone disorder, which method comprises determining the amount of at least one marker selected from any one of Tables 1a, 1b, 1c, 1d, 2a, 2b, 2c, or 2d. Claim 16 direct to use of at least one biomarker selected form any one of Tables 1a, 1b, 1c, 1d, 2a, 2b, 2c, or 2d for diagnosing bone disorder. Claims 17-20 direct to device or kit for diagnosing bone disorder, which comprises a detection agent for at least one biomarker selected form any one of Tables 1a, 1b, 1c, 1d, 2a, 2b, 2c, or 2d.

In Tables 1a, 1b, 1c, 1d, 2a, 2b, 2c, and 2d, there are 55 different biomarkers, which are myo-Inositol-2-phosphate, Eicosaenoic acid(C20:1)No 02, Phosphatidylcholine(C18:0,C20:4), Coenzyme Q10, Sphingomyelin(d18:2,C16:0), 3-Hydroxybutyrate, Urea, Phosphate(inorganic and organic phosphates), Phenylalanine, lysophosphatidylcholine(C17:0), Glucose, Threonic acid, 4-Hydroxyphenylpyruvate, Methionine, Creatine, Alanine, 18-Hydroxy-11-deoxycorticosterone, Creatinine, Phosphatidylcholine(C16:0,C16:0), Glycine, TAG No 07, Pyruvate, Heptadecanoic acid(C17:0), TAG(C18:1,C18:2), Hippuric acid, 5-Oxoproline, TAG No 01, Linoleic acid(C18:cis[9,12]2), TAG(C18:2,C18:3), Malate, Lactate, 16-Methylheptadecanoic acid, coenzyme Q9, Glycerol (lipid fraction), TAG(C18:2,C18:2), linolenic acid(C18:cis[9,12,15]3), 17-Methyloctadecanoic acid, TAG No 05, gamma-linolenic acid(C18:cis[6,9,12]3), DAG(C18:1,C18:2), TAG(DAG-Fragment), TAG No 059, Isoleucine, leucine, Dodecanol, ketoleucine, TAG (C16:0,C18:1,C18:3), Cholesterolester No 01, Threonine, TAG(C16:0,C18:2), alpha-Tocopherol, Ornithine, Oleic acid(C18:cis[9]1), 14-Methylhexadecanoic acid, and Glycerol (polar fraction).

Since the above-mentioned 55 biomarkers are involved, claims 1-20 cover 55 inventions. Each invention relates to one of the 55 biomarkers. The same or corresponding technical feature among the inventions above is as follows: a biomarker for bone disorder. However, the same or corresponding technical feature above is well known in the art.

It follows that the same or corresponding technical features of claims above do not make a contribution over the prior art and can not be considered as special technical features within the meaning of Rule 13.2 PCT. The application, hence does not meet the requirement of unity of invention as defined in Rule 13.1 PCT.

Continuation of column A: CLASSIFICATION OF SUBJECT MATTER of Second Sheet

C07F 9/117 (2006.01)i

C07F 9/10 (2006.01)i

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C07C 69/30 (2006.01)i

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2013/051228

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
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