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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, 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, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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[Continued on next page]

(54) Title: GLU-GLP-1 DUAL AGONIST SIGNALING-SELECTIVE COMPOUNDS

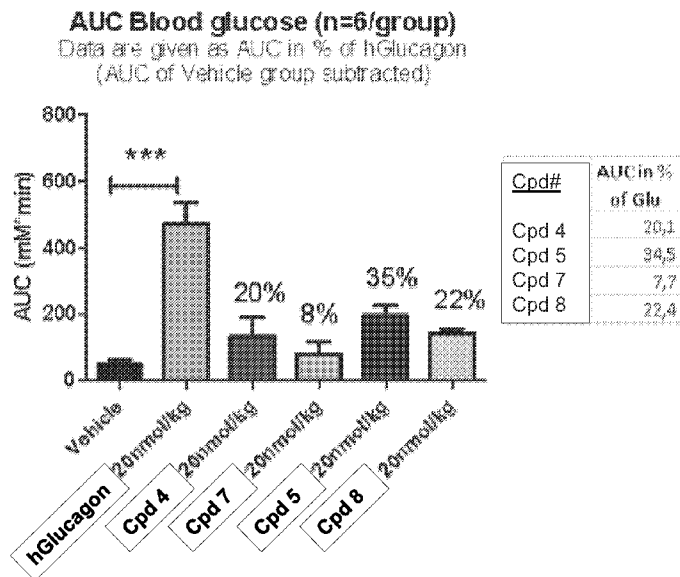


Figure 13

(57) Abstract: The present application relates to methods of screening Glu-GLP1 dual agonists (GGDAs) that activate alternative intracellular signalling pathways through the Glucagon receptor (Glu R). Compounds have been identified as partial agonists rather than full agonists, eliciting a sub-maximal response, presumably caused by generation of an alternative conformational state of the receptor induced by the ligand-receptor interaction. The compounds may be useful in the treatment of metabolic diseases, e.g., diabetes, obesity, and related glucose metabolism diseases, or other conditions characterized by excess body weight.

WO 2012/153196 A3



TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

Published:

— *with international search report (Art. 21(3))*

(88) Date of publication of the international search report:

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2012/001090

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K14/605 G01N33/50
ADD.
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 C07K

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)
EPO-Internal, BIOSIS, EMBASE, FSTA, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	A. POCAI ET AL: "Glucagon-Like Peptide 1/Glucagon Receptor Dual Agonism Reverses Obesity in Mice", DIABETES, vol. 58, no. 10, 1 October 2009 (2009-10-01), pages 2258-2266, XP055040607, ISSN: 0012-1797, DOI: 10.2337/db09-0278 abstract; figure 1b page 2259	1-29
X	WO 2010/096052 A1 (MERCK SHARP & DOHME [US]; ANGELETTI P IST RICHERCHE BIO [IT]; UNIV IND) 26 August 2010 (2010-08-26) pages 71-74; figure 1	1-29

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 13 November 2012	Date of mailing of the international search report 25/01/2013
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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, Fax: (+31-70) 340-3016	Authorized officer Lunter, Pim
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2012/001090

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:

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 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 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.:

1-29

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-29

Method of screening GGDA compounds

2. claim: 30

Method of treating or preventing a metabolic disease or condition

3. claims: 31-34

compounds 17, 18, 19 and 20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2012/001090

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010096052	A1	26-08-2010	
		AU 2009340439 A1	15-09-2011
		CA 2754350 A1	26-08-2010
		CN 102573872 A	11-07-2012
		EP 2398483 A1	28-12-2011
		JP 2012518035 A	09-08-2012
		PE 06212012 A1	08-06-2012
		SG 173791 A1	28-10-2011
		WO 2010096052 A1	26-08-2010
		WO 2010096142 A1	26-08-2010
