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(54) Title: CHEMOSENSORY RECEPTOR LIGAND-BASED THERAPIES

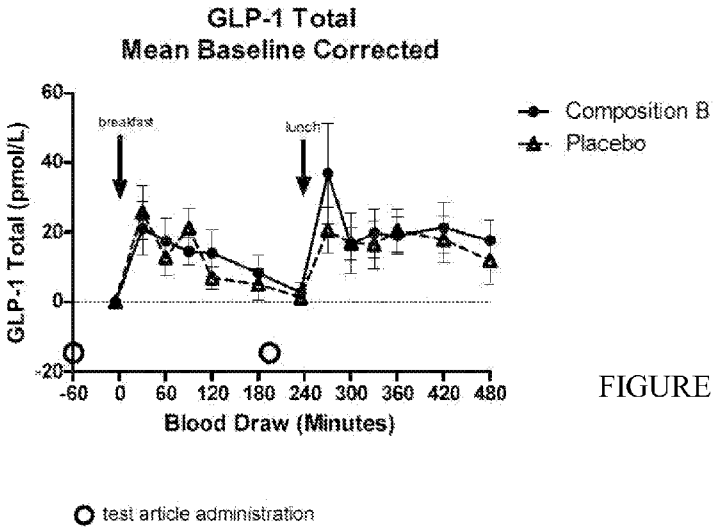

FIGURE 2 E

(57) Abstract: Methods of modulating hormone concentrations in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, wherein the composition is adapted to deliver the ligand to one or more regions of the intestine of said subject. Methods are directed to the modulation of circulating concentrations of one or more ofGLP-1 (total), GLP-I (active), GLP-2, oxyntomodulin, PYY (total), PYY 3-36, CCK, GIP, insulin, C-peptide, glycentin, uroguanylin amylin, and ghrelin (total), ghrelin (active) and glucagon.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/56766

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - G01N 33/53 (2012.01)
USPC - 435/7.1
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(8)- G01N 33/53 (2012.01);
USPC- 435/7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Patents and NPL (classification, keyword; search terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWest (US Pat, PgPub, EPO, JPO), GoogleScholar (PL, NPL), FreePatentsOnline (US Pat, PgPub, EPO, JPO, WIPO, NPL); search terms: modulate, concentrate, administer, treat, regulate, metabolic, stimulate, activate, release, hormone, glucose, PYY, GLP, glucagon, chemosensory, receptor, ligand, peptide, circulate, control, amount

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2008/0306093 A1 (SERVANT et al.) 11 December 2008 (11.12.2008), para [0013], [0078], [0200]-[0207], [0206], [0207], [0456]	1, 2, 97-100, 104-109 --- 3-78, 110-116
Y	WO 03/57235 A2 (COWLEY et al.) 17 July 2003 (17.07.2003), Figs. 9c, 10; pg 2, ln 28-31; pg 112, ln 19 to pg 114, ln 32	3-78, 110-116
Y	US 2009/0181887 A1 (HANSEN et al.) 16 July 2009 (16.07.2009), para [0008]-[0455]	1-78, 97-100, 104-116
Y	US 7,396,809 B1 (LU et al.) 08 July 2008 (08.07.2008), col 4-40	1-78, 97-100, 104-116
Y	US 5,159,928 A (KEPPEL) 03 November 1992 (03.11.1992), col 2-17	1-78, 97-100, 104-116

☐ Further documents are listed in the continuation of Box C. ☐

* 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
02 May 2012 (02.05.2012)	08 JUN 2012
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 11/56766

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.: 86-96
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:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: claims: 1-78, 97-100, and 104-116: directed to a method of modulating the concentration of one or more hormones in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject.

Group II: claims: 79-85: directed to a method of modulating the Tmax of the concentration of one or more hormones in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject.

-- Please 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 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.:

1-78, 97-100, and 104-116

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.

Continued from Box No. III, Observations where unity of invention is lacking:

Group III: claims: 101-103: directed to a method of modulating the concentration of one or more hormones in a subject comprising the administration of a chemosensory receptor antagonist and a chemosensory receptor agonist.

Group IV: claims: 117-123. A method of modulating glucose concentration in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject.

Group V: claims: 124-130: directed to a method of modulating concentration of triglycerides in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject.

Group VI: claims: 131-137. A method of modulating low-density lipoprotein concentration in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject.

Group VII: claims: 138-144: directed to a method of modulating apolipoprotein B concentration in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject.

Group VIII: claims: 145-151: directed to a method of modulating high-density lipoprotein concentration in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups II-VIII do not include the inventive concept of a method of modulating the concentration of one or more hormones in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject, as required by Group I.

Groups I and III-VIII do not include the inventive concept of modulating the Tmax of the concentration of one or more hormones in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject, as required by Group II.

Groups I, II, and IV-VIII do not include the inventive concept of modulating the concentration of one or more hormones in a subject comprising the administration of a chemosensory receptor antagonist and a chemosensory receptor agonist, as required by Group III.

Groups I-III and V-VIII do not include the inventive concept of modulating glucose concentration in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject, as required by Group IV.

Groups I-IV and VI-VIII do not include the inventive concept of a method of modulating concentration of triglycerides in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject, as required by Group V.

Groups I-V, VII, and VIII do not include the inventive concept of a method of modulating low-density lipoprotein concentration in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject, as required by Group VI.

Groups I-VI and VIII do not include the inventive concept of a method of modulating apolipoprotein B concentration in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject, as required by Group VII.

Groups I-VII do not include the inventive concept of a method of modulating high-density lipoprotein concentration in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject, as required by Group VIII.

Groups I-VIII share the technical features of a method of modulating the concentration of one or more hormones in a subject comprising the administration of a composition comprising a chemosensory receptor ligand, said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject. However, this shared technical feature does not represent a contribution over the prior art of US 2008/0306093 A1 to Servant et al. (11 December 2008) which teaches modulating the concentration of one or more hormones in a subject (para [0207]: "the method of the present invention includes modulating the expression, secretion, and/or activity level of hormones or peptides produced by T1R expressing cells or gastrointestinal hormone producing cells") comprising the administration of a composition comprising a chemosensory receptor ligand (para [0013]: "a suitable target for compounds or other entities to modulate the chemosensory receptor and/or its ligands") said composition being adapted to deliver said ligand to one or more regions of the intestine of said subject, (para [0200]: "the method of the present invention, e.g., modulating a chemosensory receptor and/or its ligand includes modulation, treatment, and/or prophylactic measure of a condition associated with gastrointestinal system including [...] diseases of the digestive tract [...] irritable bowel syndrome, inflammatory bowel disease, complications of inflammatory bowel disease, extraintestinal manifestations of inflammatory bowel disease, disorders of intestinal motility, vascular disorders of the intestine, anorectial disorders (e.g., hemorrhoids, anal inflammation, etc.), colorectal cancer, tumors of the small intestine"). As the above method was known at the time, as evidenced by the teaching of Servant, this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I-VIII therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.