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BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME,
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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a
patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))

[Continued on next page]

(54) Title: CO-AGONISTS OF THE GLUCAGON AND GLP-1 RECEPTORS

	1	10	20	29
Glucagon	HSQGTFTSDYSKYLSRRAQDFVQWLMNT			
Libr 1	XXXXXXXXFTSDYSKYLSRRAQDFVQWLXXT			
Libr 2	XXXXXXXXSDYSKYLSRRAQDFVQWLXXT			
Libr 3	HSQGTFTXXXXXXXXLSRRAQDFVQWLXXT			
Libr 4	HSQGTFTSDYSKYXXXXXXXXDFVQWLXXT			
Libr 5	HSQGTFTSDYSKYLSRRAQXXXXXXXXXX			

FIG.1

(57) Abstract: Co-agonists of the glucagon and GLP-1 receptors are described.



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- *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))*
- *with sequence listing part of description (Rule 5.2(a))*
- (88) Date of publication of the international search report:**
17 August 2017

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/64882

A. CLASSIFICATION OF SUBJECT MATTER
 IPC - C07K 14/605, 14/575, 14/435 (2017.01)
 CPC - C07K 14/605, 14/575, 14/435

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2015/0307580 A1 (MERCK SHARP & DOHME CORP. et al.) October 29, 2015; paragraphs [0012], [0054]-[0056], [0058], [0063], [0091], [0140]	1-4
A	US 8,703,701 B2 (DIMARCHI) April 22, 2014; column 2, lines 43-44; column 4, lines 50-52; column 5, lines 50-52; column 29, lines 7-11; column 33, lines 36-39; column 34, lines 37-40; column 40, lines 22-25; column 69, lines 38-42	1-4
A	US 2011/0190200 A1 (DIMARCHI et al.) August 04, 2011; paragraphs [0018], [0021], [0118], [0121], [0161], [0291], [0293]; SEQ ID NO: 77	1-4
A	WO 2011/143208 A1 (INDIANA UNIVERSITY RESEARCH AND TECHNOLOGY CORPORATION et al.) November 17, 2011; paragraphs [0011], [00116], [00118], [00373], [00401], [00404]; SEQ ID NO: 877	1-4

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/64882

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

- a. ☒ forming part of the international application as filed:
 - ☒ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter. 1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter. 1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter. 1(b) and Administrative Instructions, Section 713).
2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/64882

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.: 6-23
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:

****-Please see supplemental page-****

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.:
Claims 1-4; SEQ ID NO: 1, wherein position 2 is Val (co-agonist peptide)

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/US16/64882

-Continued from Box No. III: Observations Where Unity of Invention Is Lacking-

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.

Groups I+, Claims 1-4 and SEQ ID NO: 1, wherein position 2 is Val, are directed toward a co-agonist peptide comprising a peptide wherein the residue at position 2 is replaced with Val, Ile, Asp, Glu, Met, Trp, Asn, D-Ala, D-Ser, or a-aminoisobutyric acid (aib), the residue at position 10 is replaced with a Lysine residue conjugated to a fatty acid or fatty diacid via a linking moiety.

The co-agonist peptide will be searched to the extent it encompasses SEQ ID NO: 1, wherein position 2 is Val (first exemplary co-agonist peptide). Applicant is invited to elect additional co-agonist peptide(s), with specified SEQ ID NO: for each, or with specified substitution(s) at specified site(s) of a SEQ ID NO: such that the complete sequence is fully specified (i.e. with no optional or variable residue(s) or substituent(s)), to be searched. Additional co-agonist peptide sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1 (in-part), 2 (in-part), 3 (in-part) and 4 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 1, wherein position 2 is Val (co-agonist peptide). Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be a co-agonist peptide encompassing SEQ ID NO: 2, wherein position 2 is Ile (first exemplary elected co-agonist peptide).

Groups II+, Claim 5 and SEQ ID NO: 44 are directed toward a co-agonist peptide optionally comprising one or more gamma-glutamic acid residues.

The co-agonist peptide can be searched to the extent it encompasses SEQ ID NO: 44 (first exemplary co-agonist peptide). Applicant is invited to elect additional co-agonist peptide(s), with specified SEQ ID NO: for each, to be searched. Additional co-agonist peptide sequence(s) can be searched upon the payment of additional fees. It is believed that claim 5 (in-part) encompasses this first named invention of Groups (II)+ and thus this claim can be searched with payment of a fee for the search of Groups (II)+, to the extent that it encompasses SEQ ID NO: 44 (co-agonist peptide). Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) can result in only the first claimed invention of groups (II)+ to be searched/examined. An exemplary election would be a co-agonist peptide encompassing SEQ ID NO: 45 (first exemplary elected co-agonist peptide).

No technical features are shared between the sequences of Groups I+ and, accordingly, these groups lack unity a priori. No technical features are shared between the sequences of Groups II+ and, accordingly, these groups lack unity a priori. No technical features are shared between the sequences of Groups I+ and II+, and, accordingly, these groups lack unity a priori.

The inventions listed as Groups I+ and II+ 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: the special technical features of Groups I+ include SEQ ID NO: 1, not present in any of Groups II+; the special technical features of Groups II+ include SEQ ID NO: 44, not present in any of Groups I+.

Groups I+ and II+ share the technical features including: co-agonist peptides comprising a C-terminal amide. Groups I+ share the technical features including: a co-agonist peptide comprising a peptide, wherein the residue at position 2 is replaced with Val, Ile, Asp, Glu, Met, Trp, Asn, D-Ala, D-Ser, or a-aminoisobutyric acid (aib), the residue at position 10 is replaced with a Lysine residue conjugated to a fatty acid or fatty diacid via a linking moiety, wherein the C-terminal amino acid carboxy group is amidated, and the peptide may comprise 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 additional amino acid substitutions. Groups II+ share the technical features including: a co-agonist peptide comprising a peptide, wherein the C-terminal amino acid carboxy group is amidated.

However, these shared technical features are previously disclosed by US 2015/0307580 A1 to Merck Sharp & Dohme Corp. et al. (hereinafter 'Merck').

Merck discloses co-agonist peptides (dual agonist (co-agonist) peptides; abstract) comprising a C-terminal amide (comprising a C-terminal amide; paragraph [0091]); wherein the residue at position 2 is replaced with a-aminoisobutyric acid (aib) (wherein X1 is a-aminoisobutyric acid (wherein the residue at position 2 is replaced with a-aminoisobutyric acid (aib)); paragraphs [0054]-[0056]), the residue at position 10 is replaced with a Lysine residue conjugated to a fatty acid or fatty diacid via a linking moiety (and M is a lysine residue covalently linked to a lipid moiety, including a fatty acid, by a spacer, and the lysine is at position X2 (the residue at position 10 is replaced with a Lysine residue conjugated to a fatty acid or fatty diacid via a linking moiety); paragraphs [0058], [0140]).

Since none of the special technical features of the Groups I+ and II+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Merck reference, unity of invention is lacking.