

PATENT COOPERATION TREATY

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APR 17 2019

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

ELI LILLY AND COMPANY
PATENT DIVISION

To:

Cholewa, Brian C.
Eli Lilly and Company
P.O. Box 6288
Indianapolis, IN 46206-6288
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference X21606	Date of mailing (day/month/year) 8 April 2019 (08-04-2019)
International application No. PCT/US2018/065663	International filing date (day/month/year) 14 December 2018 (14-12-2018)
Applicant ELI LILLY AND COMPANY	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.

How? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Fascimile No.: (41-22) 338 82 70

For more detailed instructions, see *PCT Applicant's Guide*, International Phase, paragraphs 9.004 - 9.011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ With regard to any protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis* 3).

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

Within 22 months from the priority date, the applicant may request that a supplementary international search be carried out by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040 Fax: (+31-70) 340-3016	Authorized officer FERNANDES SIMÃO, Iolanda Tel: +49 (0)89 2399-8637
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference X21606	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2018/065663	International filing date (<i>day/month/year</i>) 14 December 2018 (14-12-2018)	(Earliest) Priority Date (<i>day/month/year</i>) 21 December 2017 (21-12-2017)
Applicant ELI LILLY AND COMPANY		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☒ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box No. II)

3. ☐ Unity of invention is lacking (see Box No III)

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. _____
☐ as suggested by the applicant
☐ as selected by this Authority, because the applicant failed to suggest a figure
☐ as selected by this Authority, because this figure better characterizes the invention
- b. ☐ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/065663

Box No. I 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/US2018/065663

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K38/26 C07K14/605 A61P3/00
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)

A61K 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, INSPEC, CHEM ABS Data, EMBASE, 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	WO 2015/067716 A1 (ZEALAND PHARMA AS [DK]; JUST RASMUS [DK]; RIBER DITTE [DK]; SHELTON AN) 14 May 2015 (2015-05-14) cited in the application the whole document claims; examples; sequences	1-30
Y	PIA K. NØRREGAARD ET AL: "A novel GIP analogue, ZP4165, enhances glucagon-like peptide-1-induced body weight loss and improves glycaemic control in rodents", DIABETES, OBESITY AND METABOLISM, vol. 20, no. 1, 9 June 2017 (2017-06-09), pages 60-68, XP055568531, ISSN: 1462-8902, DOI: 10.1111/dom.13034 the whole document compound ZP4165	1-30

☒ 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

Z document member of the same patent family

Date of the actual completion of the international search

14 March 2019

Date of mailing of the international search report

08/04/2019

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

Orlando, Michele

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Anonymous: "BACHEM - Peptide Trends October 2017", 1 October 2017 (2017-10-01), XP055568606, Retrieved from the Internet: URL: http://www.bachem.com/service-support/newsletter/peptide-trends-october-2017/ [retrieved on 2019-03-13] the whole document table 3; compound LY3298176	1-30
Y	WO 2015/067715 A2 (ZEALAND PHARMA AS [DK]) 14 May 2015 (2015-05-14) the whole document claims; examples	1-30
A	JENSEN LENE ET AL: "Absorption, metabolism and excretion of the GLP-1 analogue semaglutide in humans and nonclinical species", EUROPEAN JOURNAL OF PHARMACEUTICAL SCIENCES, ELSEVIER, AMSTERDAM, NL, vol. 104, 16 March 2017 (2017-03-16), pages 31-41, XP085093781, ISSN: 0928-0987, DOI: 10.1016/J.EJPS.2017.03.020 the whole document	1-30
T	TAMER COSKUN ET AL: "LY3298176, a novel dual GIP and GLP-1 receptor agonist for the treatment of type 2 diabetes mellitus: From discovery to clinical proof of concept", MOLECULAR METABOLISM, vol. 18, 3 October 2018 (2018-10-03), pages 3-14, XP055567725, ISSN: 2212-8778, DOI: 10.1016/j.molmet.2018.09.009 the whole document	1-30
T	JUAN PABLO FRIAS ET AL: "Efficacy and safety of LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes: a randomised, placebo-controlled and active comparator-controlled phase 2 trial", LANCET, vol. 392, no. 10160, 4 October 2018 (2018-10-04), pages 2180-2193, XP055567738, AMSTERDAM, NL ISSN: 0140-6736, DOI: 10.1016/S0140-6736(18)32260-8 the whole document	1-30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2018/065663

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2015067716 A1	14-05-2015	AU 2014345570 A1 BR 112016009995 A2 CA 2929107 A1 CN 105829339 A EA 201690629 A1 EP 3066117 A1 JP 2017503474 A KR 20160074008 A US 2016257729 A1 WO 2015067716 A1	12-05-2016 05-12-2017 14-05-2015 03-08-2016 31-10-2016 14-09-2016 02-02-2017 27-06-2016 08-09-2016 14-05-2015
WO 2015067715 A2	14-05-2015	BR 112016009889 A2 CA 2929459 A1 CN 105849122 A EA 201690660 A1 EP 3065767 A2 JP 2016540741 A KR 20160079875 A TW 201605888 A US 2016280754 A1 WO 2015067715 A2	05-12-2017 14-05-2015 10-08-2016 31-03-2017 14-09-2016 28-12-2016 06-07-2016 16-02-2016 29-09-2016 14-05-2015

TITLE: INCRETIN ANALOGS AND USES THEREOF

APPLICANT: ELI LILLY AND COMPANY

IPC CLASSIFICATION: A61K38/26, C07K14/605, A61P3/00

EXAMINER: Orlando, Michele

CONSULTED DATABASES: NPL, BIOSIS, INET, INSPEC

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61K38/26, C07K14/605

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:

It discloses incretin analogs falling under general sequence ID NO 5, with triple agonist activity as well as their use in the treatment of type II diabetes mellitus (T2DM), obesity, fatty liver disease, NASH, dyslipidemia and metabolic syndrome.