

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/IB2024/053554

International filing date (day/month/year)
11.04.2024

Priority date (day/month/year)
14.04.2023

International Patent Classification (IPC) or both national classification and IPC
INV. C07D207/16 C07D209/52 C07D401/12 C07D401/14 C07D403/12 A61P3/10 A61K31/4025

Applicant
PFIZER INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Bissmire, Stewart

Telephone No. -0



Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established 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)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)),
 - ☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
4. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established to the extent that a meaningful opinion could be formed without a WIPO Standard ST.26 compliant sequence listing.
5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>1-39</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>33, 34</u>
	No: Claims	<u>1-32, 35-39</u>
Industrial applicability (IA)	Yes: Claims	<u>1-39</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1 Claims 36, 37 and 39 relates to subject-matter considered by this Authority to be covered by the provision of Rule 39.1(iv)/67.1(iv) PCT. Patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions in a first or further medical treatment.
- 2 Reference is made to the following documents:
 - D1 WO 2011/005929 A1 (ARENA PHARM INC [US]; JONES ROBERT M [US]; LEHMANN JUERG [US]) 13 January 2011 (2011-01-13)
 - D2 WO 03/045912 A1 (WARNER LAMBERT CO [US]; BIGGE CHRISTOPHER FRANKLIN [US] ET AL.) 5 June 2003 (2003-06-05)
 - D3 WO 2007/131982 A2 (BOEHRINGER INGELHEIM INT [DE]; BOEHRINGER INGELHEIM PHARMA [DE] ET AL.) 22 November 2007 (2007-11-22)
- 3 The current application discloses 1,2-pyrrolidinedicarboxamide derivatives for use as glucose-dependent insulintropic polypeptide receptor (GIPR) inhibitors for the treatment of diabetes and related disorders. The compounds of the current application differ from those of D1 as they include the central 1,2-pyrrolidinedicarboxamide moiety. Despite the overlap between the generic disclosures of D2 and D3 (compare claim 1 of each with current claim 1), the currently claimed compounds can be differentiated from those of the prior art through the invariable presence of the Ra substituent. The compounds of D2 and D3 have completely different activity. The subject-matter of claim 1, dependent claims 2-33, claim 34 and claims 35-39 relating to compositions and use is therefore novel in the sense of Art. 33(2) PCT.
- 4 D1 is considered the most relevant state of the art. The problem to be solved by the current application is considered to be the provision of alternative glucose-dependent insulintropic polypeptide receptor (GIPR) inhibitors for the treatment of diabetes and related disorders. The currently claimed compounds are structurally far enough removed from those of D1, that they would not have been obvious to the person skilled in the art. As previously mentioned, the

structurally closest compounds of D2 and D3 have completely unrelated activity (both factor Xa inhibitors). The currently claimed activity could not have been anticipated. The data provided by the applicant (see table 3, pages 234-257) demonstrates that the compounds tested provide a solution to the above mentioned technical problem. However, in the compounds tested Ra is either COOH, CONH₂ or OH. The current scope of the claims is therefore not considered to be justified. It is therefore only possible to acknowledge an inventive step in the sense of Art. 33(3) PCT for the subject-matter of claims 33 and 34.

Re Item VII

Certain defects in the international application

- 1 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1-D3 is not mentioned in the description, nor is this document identified therein.
- 2 Claim 29 comprises all the features of claim 1 and is therefore not appropriately formulated as a claim dependent on the latter (Rule 6.4 PCT).

Re Item VIII

Certain observations on the international application

- 1 Claim 39 is defined in functional terms that are not considered to be clear in the sense of Article 6 PCT. The therapeutic application is defined by means of a mechanism of action which does not allow for a practical application in the treatment of a specific pathological condition (disease).