

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.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/IB2020/055589

International filing date (day/month/year)
16.06.2020

Priority date (day/month/year)
18.06.2019

International Patent Classification (IPC) or both national classification and IPC
INV. C07D413/06 A61K31/41 A61K31/4192 A61K31/4402 A61K31/497 A61K31/506 A61P35/00

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 43bis.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 66.1bis(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:



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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Gettins, Marc

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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 43bis.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:
 - ☒ 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).
4. ☐ 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.
5. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43bis.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>1-34</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-34</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-34</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

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:

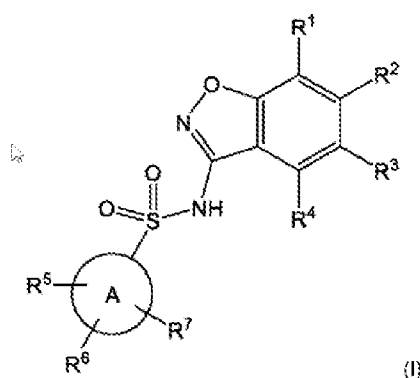
see separate sheet

Re Item V

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

- 1 Relevant prior art is provided by:
- D1 WO 2019/243491
- D2 WO 2018/102419
- D3 STEIN P D ET AL: "Discovery and structure-activity relationships of sulfonamide ETA-selective antagonists", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 38, no. 8, 1 January 1995 (1995-01-01), pages 1344-1354, XP002314442, ISSN: 0022-2623, DOI: 10.1021/JM00008A013
- 1.1 On the assumption that the current application is entitled to the priority date of 18.06.2019 D1 has not been taken into account for the PCT examination. For the sake of completeness and since it may become relevant at the national phase it is pointed out that the current application falls within the scope of D1 and that specific compounds in D1 (see e.g. examples 125-126 and 130-131) appear to fall within the scope of compounds (I) of the current application.
- 1.2 The Applicant should explain the reason for the provisos found in claim 1 relating to R¹ and R². If they are intended to exclude some unacknowledged prior art known to the Applicant the said prior art should be cited (Rule 5.1 (a) (ii) PCT).
- 2 Claims 27-29 relate to a subject-matter considered by this Authority to be covered by the provision of Rule 39.1(iv) /67.1(iv) PCT. The 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 for use in a first or further medical treatment. The patentability can be dependent upon the formulation of the claims.

- 3 The current application is directed to compounds (I)



where one of R^1 and R^2 is hydrogen and the other contains a heteroaryl group.

- 4 The current application is novel vis-à-vis D2 on account of the sulfonamide group - the equivalent L group in D2 is a linker with at least 3 atoms. The current application is novel vis-à-vis D3, see compound 87, on account of the R^1 and R^2 groups.
- 5 The current application addresses the problem of providing further KAT inhibitors of the MYST family. The given problem appears to have been solved by a representative range of claimed compounds as shown by data in e.g. Tables 1-2 on pages 172-179. The closest prior art can be seen as D2 which also discloses KAT inhibitors. The skilled person starting from D2 and seeking to modify the compounds therein did not have an explicit or implicit indication that the known compounds should be replaced by sulfonamide derivatives. The solution as given in claim 1 is considered to be inventive.

Re Item VI

Certain documents cited

Application No	Publication date	Filing date	Priority date (<i>valid claim</i>)
Patent No	(<i>day/month/year</i>)	(<i>day/month/year</i>)	(<i>day/month/year</i>)

WO2019/243491	26.12.2019	20.06.2019	20.06.2018
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Re Item VIII

Certain observations on the international application

- 1 Independent claim 34 appears to fall fully within the scope of claim 23 and should therefore be rewritten as a dependent claim (Rule 6.4 (a) PCT).
- 2 Prodrugs of compounds (I) are not claimed, but are said to be part of the invention (page 29, line 30). There is therefore a discrepancy in scope between the claims and the description (Art. 6 PCT). The term "prodrugs" is a functional definition which attempts to define a chemical compound in terms of a result to be achieved. This is not allowable. The precise scope of the term is not ascertainable and it should be deleted. "Prodrugs" is a functional definition without a specific technical guidance for the selection of the suitable derivatives in the description and without proven general knowledge to show which derivatives are suitable prodrugs. This would require an equally unquantifiable and thus unreasonable amount of experimentation, imposing a severe and undue burden on all those wishing to ascertain the scope of the invention, which is not in compliance with the clarity requirement of Article 6 PCT. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search (PCT Guidelines, 9.19 and 9.24). The said term was therefore not searched and will not be examined.
- 3 The prior art documents D1-D3 should be cited (Rule 5.1 (a) (ii) PCT).
- 4 "A" and "an" only have a singular meaning and never have a plural meaning. Page 23, lines 16-18 should be deleted.