

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

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/US2020/066507

International filing date (day/month/year)
22.12.2020

Priority date (day/month/year)
23.12.2019

International Patent Classification (IPC) or both national classification and IPC
INV. C07D471/04 C07D487/04 A61K31/4375 A61K31/519 A61P35/00

Applicant
BRISTOL-MYERS SQUIBB COMPANY

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

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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. 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>4, 6, 7, 10, 11, 13-15</u>
	No: Claims	<u>1-3, 5, 8, 9, 12</u>
Inventive step (IS)	Yes: Claims	<u>4, 6, 7, 10, 11, 13-15</u>
	No: Claims	<u>1-3, 5, 8, 9, 12</u>
Industrial applicability (IA)	Yes: Claims	<u>1-15</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

re item V:

1. Prior art

Reference is made to the following documents:

- D1 WO 2012/142498 A2 (INNOVIMMUNE BIOTHERAPEUTICS INC [US];
GAWECO ANDERSON [US] ET AL.) 18 October 2012 (2012-10-18)
- D2 WO 2012/009649 A1 (GAWECO ANDERSON [US]; WALKER JOHN [US]
ET AL.) 19 January 2012 (2012-01-19)

2. Novelty

The thiazole carboxamide IIIc-9 on p. 84, the cyclopropane carboxamide IIIc-2 on p. 81, the pyrazolylamino and the pyrimidinylamino derivatives III-25 and III-27 on p. 72 and in claim 51 according to D1 destroy the novelty of present claims 1 to 3, 5, 8, 9 and 12. The piperidine carboxamides IIIc-1, IIIc-2, IIIc-4, IIIc-8 and IIIc-10 on p. 66 and example 3 according to D2 destroy the novelty of present claims 1 to 3, 5, 9 and 12. Therefore, the subject matter of these claims does not fulfil the requirements according to Art. 33 (2) PCT.

3. Inventive step

Documents D1 and D2 are concerned with 1-(quinolinonyl)-piperidine derivatives which act as macrophage migration inhibitors, whereas the present application is concerned with 1-(quinolinonyl, naphthyridinonyl and pyridopyrimidinonyl)-piperidine derivatives which are T-cell activators due to their ability to inhibit diacylglycerol kinase.

Therefore, the problem underlying the present application is to be seen in the provision of further diacylglycerol kinase inhibitors. As can be seen from the examples and tests as given in the specification, this problem has apparently been solved. The solution of this problem is considered to involve an inventive step with respect to the cited documents, since the skilled man, faced with said problem could not have been lead by documents D1 and D2 that the claimed compounds may show such a pharmaceutical activity. Therefore, the claimed subject matter of claims 1 to 15, presumed it were novel, can be considered to fulfil the requirement of Art. 33 (3) PCT.

4. Industrial applicability

Claims 13 to 15 in their present form are directed to methods for the treatment of the human or animal body (use of a compound for the treatment has to be considered as such). These claims relate to subject-matter considered by this Authority to be covered by the provisions 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.

re item VII:

Claim 15 is defined in functional terms that are not considered to be clear in the sense of Art. 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). The objection could be overcome by either introducing in the claims a list of pathological conditions (diseases) cited in the application or by showing that means are available which would allow the skilled person to recognise which additional conditions would fall within the functional definition.