

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/US2022/023387

International filing date (day/month/year)
05.04.2022

Priority date (day/month/year)
06.04.2021

International Patent Classification (IPC) or both national classification and IPC
INV. C07D401/14 A61P31/12 A61P35/00 A61K31/444

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 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:



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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>1-20</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-20</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-20</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

1 Reference is made to the following documents:

D1 WO 2021/194914

D2 WO 2019/191112

D3 WO 2020/165834

D4 WO 2020/165833

2 **Item VI**

D1, published on 30 September 2021, is not taken into consideration in the present Written Opinion. However, its content could become relevant after the entrance into the European Phase, if the present priority were found invalid.

Exemplified compounds of D1 seem to be disclaimed from the subject-matter of present claim 1 (cf. proviso at the end of this claim).

3 **Item V**

3.1 Claims 15-20 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.

3.2 **Article 33(2) PCT**

Present compounds of formula (I) differ from compounds of D2-D4 in that the oxoisindoline ring is substituted by a pyridine. In D2 the same position is covered by a methylaminopyrazole, in D3 and D4 by a piperidine.

Thus, the subject-matter of present claims 1-20 can be considered to meet the requirements of Article 33(2) PCT:

3.3 **Article 33(3) PCT**

Each of the documents D2, D3 and D4 can be considered to represent the closest state of the art as they disclose oxoisindoline derivatives useful in the treatment of cancer.

The problem to be solved by the present application may be regarded as the provision of alternative compounds for the same therapeutic use.

As mentioned in paragraph 3.2 above, none of the mentioned documents discloses that the oxoisindoline should be substituted by a pyridine ring. Rather, the presence of a methylaminopyrazole in D2 and of a piperidine in D3 and D4 seems mandatory.

Thus, the skilled person wishing to solve the mentioned technical problem would have not arrived at the present subject-matter starting from the teaching of D2-D4 or from a combination thereof.

Experimental data showing that the technical problem has been solved are present in the description.

Thus, the subject-matter of present claims 1-20 can be considered to meet the requirements of Article 33(3) PCT.

4 Item VIII

The vague and imprecise statement in the description on page 15, lines 17-19 implies that the subject-matter for which protection is sought may be different from what has been defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.