

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/US2024/051975

International filing date (day/month/year)
18.10.2024

Priority date (day/month/year)
20.10.2023

International Patent Classification (IPC) or both national classification and IPC
INV. C07D519/00 A61P35/00 A61K31/553

Applicant
MERCK SHARP & DOHME LLC

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:



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

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Kleidermigg, Oliver

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>1-20</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. 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

ad Item V

Reference is made to the following documents:

- D1 WO 2023/046135 A1 (JACOBIO PHARMACEUTICALS CO LTD [CN]) 30
 March 2023 (2023-03-30)
- D2 WO 2018/206539 A1 (ASTRAZENECA AB [SE]) 15 November 2018
 (2018-11-15)

Novelty

Documents D1 (cf. passages indicated in the SR) as well as D2 (cf. passages indicated in the SR) differ from the subject matter of claim 1 in the 1H-benzo[f]indazol ring which is not present in the prior art documents.

Consequently, the subject matter of claim 1 is novel. Claims 2-20 directly or indirectly refer to claim 1 and are therefore considered to be novel by analogy.

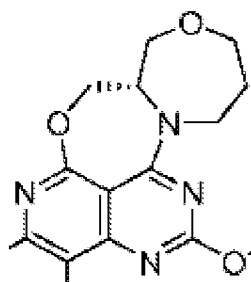
Inventive step

D1 is considered to represent the closest prior art.

In view of the distinguishing features as outlined above, the objective technical problem may be considered as the provision of alternative inhibitors of G12C, G12D, G12V, and/or G13D mutants of KRAS.

The solution is given in claim 1 and concerns the distinguishing features.

Starting from D1 the skilled person in the art gets no hint with respect to the 1H-benzo[f]indazol substituent attached to



ring system.

In addition the skilled person in the art is not motivated by D1 to modify the disclosure of D1 taken alone or in combination with D2 in order to arrive at the presently claimed subject matter.

Furthermore it is shown by means of biological tests (cf. paragraphs [0259] - [0268]) that the objective technical problem has been credibly solved.

Consequently, the subject matter of claim 1 is inventive. Claims 2-20 directly or indirectly refer to claim 1 and are therefore considered to be inventive by analogy.

Medical use

Claims 12, 13 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.

Patentability, in particular novelty and inventive step, of claims 12, 13 has been assessed on the basis of a purpose-limited product claim taking into account the alleged effects of the compound/composition.

ad Item VII

The phrase "incorporated by reference herein in their entirety" e.g. on page 1, paragraph [0001] contravenes Rule 9.1 iv) PCT.

ad Item VIII

Claims 8 to 11 are considered to contravene Article 6 PCT, because it is not clear if the contacting KRAS proteins with the compound of any one of claims 1-5 is performed "in vivo" or "in vitro".