

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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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/US2022/051770	International filing date (day/month/year) 05.12.2022	Priority date (day/month/year) 07.12.2021
International Patent Classification (IPC) or both national classification and IPC INV. C07D491/16 C07D491/18 C07D491/22 A61K31/519 A61P33/06		
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 Fax: +49 89 2399 - 4465	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Fazzi, Raffaella Telephone No. +49 89 2399-0	
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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.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.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 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>1-36</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-36</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-36</u>
	No: Claims	

2. Citations and explanations

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

1 Reference is made to the following document:

D1 WO 2021/155791

2 **Item V**

2.1 Claims 25-32 and 35-36 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.

2.2 **Article 33(2) PCT**

D1 discloses general compounds of formula (I), which do not possess present X including ring (cf. for instance compounds 118 and 120A-120D on pages 149-150 of D1). In fact, substituents R³ and R⁴ in D1 cannot form a ring.

Thus, the subject-matter of present claims 1-36 can be considered new in the sense of Article 33(2) PCT.

2.3 **Article 33(3) PCT**

D1, which can be considered to represent the closest state of the art, discloses compounds of formula (I) useful in the treatment of *Plasmodium* infections such as malaria.

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

As mentioned above, the closest compounds of D1 are examples 118 and 120A-120D, which differ from present compounds of formula (I) in that the ring containing U-Z-X-Y is not further condensed.

The skilled person wishing to solve the mentioned technical problem would have had not hint from D1 in developing compounds with a further condensed ring (cf. present X including ring).

Experimental data showing that present compounds can be active in the treatment of malaria are given on pages 257-265 of the description.

The requirements of Article 33(3) PCT are therefore met.

3 Item VIII

- 3.1 Although claims 21-24 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter of claim 1. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.
- 3.2 It appears that claim 34 should be dependent on claim 33.
- 3.3 In claim 7 "heterocycloalkyl" should be replaced with "cycloalkyl".