

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

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Date of mailing
(day/month/year)

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Applicant's or agent's file reference
2206689.00151WO1

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US 22/22230

International filing date (day/month/year)

29 March 2022 (29.03.2022)

Priority date (day/month/year)

30 March 2021 (30.03.2021)

International Patent Classification (IPC) or both national classification and IPC

IPC - A61P 35/00; C07D 213/75; C07D 401/12 (2022.01)

CPC - A61P 13/12; A61P 17/06; A61P 25/28

Applicant

D. E. SHAW RESEARCH, 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 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/US
Mail Stop PCT, Attn: ISA/US
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Facsimile No. 571-273-8300

Date of completion of this opinion

31 May 2022 (31.05.2022)

Authorized officer

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WRITTEN OPINION OF THE
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Box No. I Basis of this 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(b)).

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:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 7-20,22-68,76-82,85-98

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 7-20,22-68,76-82,85-98 are so unclear that no meaningful opinion could be formed (*specify*):

Claims 7-20, 22-68, 76-82 and 85-98 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 7-20,22-68,76-82,85-98

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE
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International application No.

PCT/US 22/22230

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

1. Statement

Novelty (N)	Claims	1-6,21,69-75,83-84	YES
	Claims	None	NO
Inventive step (IS)	Claims	1-6,21,69-75,83-84	YES
	Claims	None	NO
Industrial applicability (IA)	Claims	1-6,21,69-75,83-84	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1-6, 21, 69-75 and 83-84 meet the criteria set out under PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed invention.

Regarding claim 1, the document entitled PubChem-SID-310740648 (hereinafter 'PubChem-648') teaches an analog of Formula I' wherein Z is ORa, Ra is alkyl; X1 is H; X2 is halogenated alkyl; X3 is H; R3 is halogen; R1 and R2 are H; R5 is alkyl; R9 is H; m is 1; and n1 is 0 (pg 2, figure, this is a purchasable chemical), but PubChem-648 does not teach the -C(=O)R10 moiety, thus PubChem-648 does not teach wherein R10 is independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl. Furthermore, PubChem-648 does not teach any of the other compounds listed in the instant claim.

The document entitled PubChem-SID-282566420 (hereinafter 'PubChem-420') teaches an analog of Formula II' wherein Z is ORa, Ra is alkyl; X1 is H; X2 is alkyl; X3 is H; R3 is H; R1 and R2 are H; R5 is (C=O)Ra, Ra is alkyl; R9 is H; m is 1; and n1 is 0 (pg 2, figure, this is a purchasable chemical), but PubChem-420 does not teach the -C(=O)R10 moiety, thus PubChem-420 does not teach wherein R10 is independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl. Furthermore, PubChem-420 does not teach any of the other compounds listed in the instant claim.

WO 2020/108500 A1 to Hinova Pharmaceuticals Inc (hereinafter 'Hinova') teaches an analog of Formula II wherein Z is ORa, Ra is alkyl; X1 is halogen; X2 is H; X3 is H; R1 and R2 are H; R3 is H; R5 is H; m is 1 and n1 is 0 (pg 120, top, formula Int 337-3), but Hinova does not teach the -C(=O)NR6R7 moiety, thus Hinova does not teach wherein each occurrence of R6 is alkylaryl, or alkylheteroaryl; each occurrence of R7 is alkylaryl, or alkylheteroaryl; independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, or alternatively R6 and R7 taken together with the nitrogen atom they are connected to form a heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S; wherein the heterocycle is optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, OR8, -(CH2)0-2OR8, N(R8)2, (C=O)R8, (C=O)N(R8)2, NR8(C=O)R8, and oxo where valence permits. Furthermore, Hinova does not teach any of the other compounds listed in the instant claim. Therefore the prior art does not teach or fairly suggest the claimed invention.

Regarding claims 2-6, 21, 69-75 and 83-84, these claims are dependent on claim 1, thus these claims also meet the criteria set out under PCT Article 33(2)-(3).

Claims 1-6, 21, 69-75 and 83-84 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used by industry.