

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

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/US2024/015156

International filing date (day/month/year)
09.02.2024

Priority date (day/month/year)
13.02.2023

International Patent Classification (IPC) or both national classification and IPC
INV. A61P17/00 A61K31/4985 A61P19/00 A61P29/00 A61P37/00 C07D487/04

Applicant
DICE ALPHA, INC.

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

Authorized Officer

Goss, Ilaria

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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 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:

see separate sheet

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

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>1-171</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-171</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-171</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

Re Item I

Basis of the report

Independent compounds claims 1, 23, 150, 155 and 158 are the basis of the present report along with pharmaceutical compositions comprising such compounds and medical use claims.

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Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1 SABNIS RAM W.: "Imidazo[1,2- b]pyridazines as IL-17A Inhibitors for Treating Psoriasis, Rheumatoid Arthritis, and Multiple Sclerosis", ACS MEDICINAL CHEMISTRY LETTERS, vol. 12, no. 10, 13 September 2021 (2021-09-13), pages 1526-1527, XP055958394,
- D2 EP 3 943 495 A1 (LEO PHARMA AS [DK]) 26 January 2022 (2022-01-26)
- D3 WO 2020/146194 A1 (LILLY CO ELI [US]) 16 July 2020 (2020-07-16)
- D4 WO 2023/275301 A1 (UCB BIOPHARMA SRL [BE]) 5 January 2023 (2023-01-05)
- D5 WO 2024/017880 A1 (UCB BIOPHARMA SRL [BE]) 25 January 2024 (2024-01-25)

V.1 Rule 39 PCT

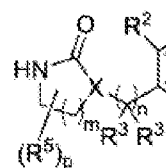
Claims 161 to 171 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 39(1)(iv) and Rule 67(1)(iv) PCT.

For the assessment of the present claims 161 to 171 on the question whether they are patentable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as patentable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first or further use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Consequently, and even if no opinion should be formulated with respect to the subject-matter of these claims (Article 34(4)(a)(I) PCT), this authority has decided to carry out and base the search and present opinion on the alleged effects of the compounds and/or compositions.

V.2 Novelty

The present compounds of formula (I') are novel over the compounds disclosed in D1-D5 on account of the present heterocyclic core, i.e. the present imidazotriazine ring, and



on account of the point of attachment of specific group combined with the right hand chain carrying the A group.

Novelty is acknowledged.

V.3 Inventive step

The present application relates to heterocyclic derivatives as IL-17 modulators.

3.1 D1-D4 can all be considered to represent the closest prior art as they disclose structurally similar compounds for the same use.

The present compounds differ from the compounds of D1-D4 on account of the present heterocyclic core, the point of attachment of specific group depicted above and the mandatory presence of the right hand chain containing A .

3.2 As these differences do not result in any additional effect, the objective problem to be solved can be seen in the provision of further heterocyclic derivatives as IL-17 modulators.

3.3 The solution of the applicant, i.e. the provision of compounds of formula (I') which have the desired activity as shown on page 572 ff (results according to tables 2 and 3) of the description, is considered to involve an inventive step. There was no hint in the prior art cited that the modification of the compounds of D1-D4 in order to arrive at the claimed derivatives would have led to compounds retaining the desired biological activity.

3.4 In this respect applicant's attention is drawn to the issue as to whether or not the breadth of a claim has a proper support in the application as filed. According to a generally accepted legal principle, the question is whether or not a specific technical effect can be reasonably ascribed to the whole spectrum of chemical structures, or only to a part of it even regardless the structural similarity that the claimed compound may or may not have with any known chemical compound.

3.4.1 It has been noticed that compounds have been provided wherein A/B are mostly cyclic elements better reflected in single dependent claims. Also the further, very few, meanings are specifically given in dependent claims.

The compounds provided show substituent R¹ always meaning H, substituent R² meaning either H, alkyl (optionally specifically substituted), NRR or a cyclic group according to claim 9.

This aspect will be closer considered once the application enters the regional phase before the EPO.

An inventive step can therefore at present be recognized.

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Re Item VI

Certain documents cited

The content of the PCT application D5 may be considered by the EPO authority, when entering the regional phase before the EPO, as comprised in the state of the art relevant to the question of novelty.

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Re Item VIII

Certain observations on the international application

Claim 23 (general formula (I)), claims 150, 155 and 158 relating to single compounds, each comprises all the features of claim 1 and they are therefore not appropriately formulated as claims dependent on the latter (Rule 6.4 PCT).