

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)

Applicant's or agent's file reference 4547-016PC02		Date of mailing (day/month/year) 08 September 2022
FOR FURTHER ACTION See paragraph 2 below		
International application No. PCT/IB2022/055167	International filing date (day/month/year) 02 June 2022	Priority date (day/month/year) 03 June 2021
International Patent Classification (IPC) or both national classification and IPC A61K 47/68(2017.01)i; A61K 31/454(2006.01)i; A61P 35/00(2006.01)i; C07H 19/23(2006.01)i		
Applicant ORUM THERAPEUTICS, 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 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/KR Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon, 35208	Date of completion of this opinion 08 September 2022	Authorized officer HEO, Joo Hyung
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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(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. 5-13, 19, 20, 24, 26-36, 41-48

because:

- ☒ the said international application, or the said claims Nos. 27-36 relate to the following subject matter which does not require an international search (*specify*):

The subject matter of claims 27-36 does not require a written opinion as it is directed to method for treatment of the human body by surgery or therapy, as well as diagnostic method (PCT Rules 43 2.1(b) and 67.1 (iv)).

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 9-13, 24, 28-30, 34-36, 43-48 are so unclear that no meaningful opinion could be formed (*specify*):

Claims 9-13, 24, 28-30, 34-36 and 43-48 are regarded to be unclear because they refer to claims which do not comply with PCT 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. 5-13, 19, 20, 24, 26-36, 41-48

- ☐ 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 13^{ter}.1(a) or (b).

- ☐ See Supplemental Box for further details.

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	1-4,14-18,21-23,25,37-40	YES
	Claims	NONE	NO
Inventive step (IS)	Claims	1-4,14-18,21-23,25,37-40	YES
	Claims	NONE	NO
Industrial applicability (IA)	Claims	1-4,14-18,21-23,25,37-40	YES
	Claims	NONE	NO

2. Citations and explanations :

Reference is made to the following documents:

D1: WO 2010-053732 A1 (CELGENE CORPORATION) 14 May 2010

D2: ZHAO, M. et al., Biochemical and biophysical research communications, 3 March 2021(E-pub), Vol. 549, pages 150-156

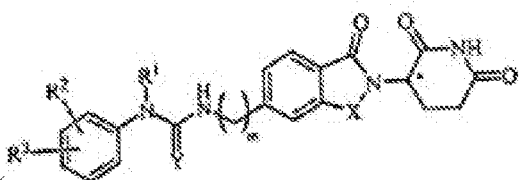
D3: HANSEN, J. D. et al., Journal of medicinal chemistry, 2018, Vol. 61, No. 2, pages 492-503

D4: SPERLING, A. S. et al., Blood commentaries, 2019, Vol. 134, No. 2, pages 160-170

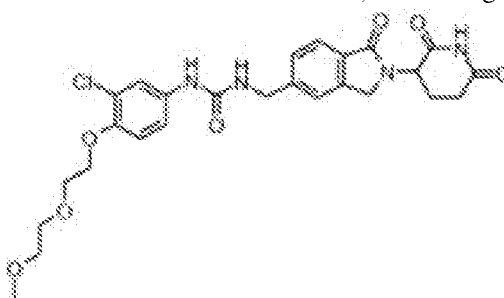
D5: HANSEN, J. D. et al., Journal of medicinal chemistry, 2020, Vol. 63, No. 13, pages 6648-6676

I. Novelty and Inventive Step (PCT Article 33(2) and (3))

1. Claims 1-4, 14-18, 21-23, 25 and 37-40



D1 discloses a compound of formula (I) () for treating



cancer, wherein the compound comprises the compound of (see claims 1, 20, 21, 26, 27).

Claim 1 differs from D1 in the compound comprising "-(CH₂)₂-N(CH₃)-", "L" and "Bm", claim 14 differs from D1 in the compound of formula (II), claim 15 differs from D1 in the compound of formula (III), claim 16 differs from D1 in the compound of formula (IV) and claim 17 differs from D1 in the conjugate of formula (V).

None of the cited documents discloses the different features. And they are not obvious to a person skilled in the art from the cited documents, when taken individually or in any combination.

Claims 2-4 are dependent on claim 1 and claims 18, 21-23 and 25 are dependent on claim 16 or 17.

Therefore, claims 1-4, 14-18, 21-23 and 25 are novel and involve an inventive step.

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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**

Claim 37 relates to a method of preparing the conjugate of claim 1, and claims 38-40 are dependent on claim 37.

Therefore, claims 37-40 are novel and involve an inventive step.

II. Industrial Applicability (PCT Article 33(4))

Claims 1-4, 14-18, 21-23, 25 and 37-40 are industrially applicable.

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Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

	<u>Application No. Patent No.</u>	<u>Publication date (day/month/year)</u>	<u>Filing date (day/month/year)</u>	<u>Priority date (valid claim) (day/month/year)</u>
PX	PCT/IB2021/052713	07/10/2021	31/03/2021	31/03/2020

Application No. PCT/IB2021/052713(publication WO 2021-198965 A1) does not constitute prior art within the meaning of PCT Rule 64.3, but appears to disclose all the feature of claims 1-4, 14-18, 21-23, 25, 37-40. In case the priority of the present application is not valid, this document is relevant for assessing novelty and inventive step.

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

<u>Kind of non-written disclosure</u>	<u>Date of non-written disclosure (day/month/year)</u>	<u>Date of written disclosure referring to non-written disclosure (day/month/year)</u>

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claims 5-8, 19, 20, 26, 27, 31-33, 41 and 42 which are multiple dependent claims, do not comply with PCT Rule 6.4(a) because the claims refer to another multiple dependent claims.

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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:

1. Claim 12 is referring to itself, thereby rendering the definition of the subject matter of said claim unclear (PCT Article 6).

2. In claim 37, "the process" is not disclosed before itself. Therefore, claim 37 is not clear, contrary to the requirement of PCT Article 6.

(Note: These international search report and written opinion have been established on the assumption that "the process" is a typo of "the method".)