

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 4547-017PC02		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/IB2022/055168	International filing date (<i>day/month/year</i>) 02 June 2022	(Earliest) Priority Date (<i>day/month/year</i>) 03 June 2021	
Applicant ORUM THERAPEUTICS, INC.			

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out 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)).

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (see Box No. II).

3. ☐ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____
☐ as suggested by the applicant.
☐ as selected by this Authority, because the applicant failed to suggest a figure.
☐ as selected by this Authority, because this figure better characterizes the invention.
- b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2022/055168

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out 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 13*ter*.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 13*ter*.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).
2. ☐ 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.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2022/055168

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **42-52**
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 42-52 pertain to methods for treatment of the human body therapy; as well as diagnostic methods, and thus relate to a subject matter which this International Search Authority is not required to search, under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv).
2. ☒ Claims Nos.: **9, 10, 13, 15-19, 21, 23, 25-27, 43-46, 50-52**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claims 9, 10, 13, 15-19, 21, 23, 25-27, 43-46 and 50-52 are regarded to be unclear because they refer to claims which do not comply with PCT Rule 6.4 (a).
3. ☒ Claims Nos.: **4-8, 11, 12, 14, 20, 22, 24, 28-36, 41, 42, 47-49, 56-61**
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2022/055168

A. CLASSIFICATION OF SUBJECT MATTER A61K 47/68(2017.01)i; A61K 31/454(2006.01)i; A61P 35/00(2006.01)i According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61K 47/68(2017.01); A61P 35/00(2006.01); C07D 401/04(2006.01); C07D 401/14(2006.01) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Korean utility models and applications for utility models Japanese utility models and applications for utility models Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) eKOMPASS(KIPO Internal), STN(Registry, Caplus), google & keyword: neodegrader conjugates, cancer, protein, binding moiety, linker		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2010-053732 A1 (CELGENE CORPORATION) 14 May 2010 (2010-05-14) paragraph [0251]; claims 1, 20, 21, 26, 27	1-3,37-40,53-55
A	ZHAO, M. et al., "Cereblon modulator CC-885 induces CRBN-dependent ubiquitination and degradation of CDK4 in multiple myeloma", Biochemical and biophysical research communications, 3 March 2021, Vol. 549, pages 150-156 abstract; page 152; figure 1A	1-3,37-40,53-55
A	HANSEN, J. D. et al., "Protein degradation via CRL4CRBN ubiquitin ligase: discovery and structure-activity relationships of novel glutarimide analogs that promote degradation of aiolos and/or GSPT1", Journal of medicinal chemistry, 2018, Vol. 61, No. 2, pages 492-503 abstract; page 492; figure 1	1-3,37-40,53-55
A	SPERLING, A. S. et al., "Patterns of substrate affinity, competition, and degradation kinetics underlie biological activity of thalidomide analogs", Blood commentaries, 2019, Vol. 134, No. 2, pages 160-170 page 161	1-3,37-40,53-55
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "D" document cited by the applicant in the international application "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 08 September 2022		Date of mailing of the international search report 08 September 2022
Name and mailing address of the ISA/KR Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon 35208, Republic of Korea Facsimile No. +82-42-481-8578		Authorized officer HEO, Joo Hyung Telephone No. +82-42-481-5373

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2022/055168**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HANSEN, J. D. et al., "Discovery of CRBN E3 ligase modulator CC-92480 for the treatment of relapsed and refractory multiple myeloma", Journal of medicinal chemistry, 2020, Vol. 63, No. 13, pages 6648-6676 abstract; page 6649; figure 1	1-3,37-40,53-55
PX	WO 2021-198965 A1 (ORUM THERAPEUTICS, INC.) 07 October 2021 (2021-10-07) paragraphs [0551], [0552]; claims 1-94	1-3,37-40,53-55

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/IB2022/055168

Patent document cited in search report			Publication date (day/month/year)	Patent family member(s)		Publication date (day/month/year)
WO	2010-053732	A1	14 May 2010	AR	074001 A1	15 December 2010
				AR	106942 A2	07 March 2018
				AR	106943 A2	07 March 2018
				AR	106944 A2	07 March 2018
				AR	106945 A2	07 March 2018
				AR	106963 A2	07 March 2018
				AU	2009-311477 A1	14 May 2010
				AU	2009-311477 B2	30 October 2014
				BR	PI0919942 A2	23 December 2014
				BR	PI0919942 B1	19 February 2019
				CA	2741299 A1	14 May 2010
				CA	2741299 C	28 March 2017
				CA	2957226 A1	14 May 2010
				CA	2957226 C	14 August 2018
				CL	2011000957 A1	16 September 2011
				CN	102264720 A	30 November 2011
				CN	102264720 B	25 March 2015
				CN	104744434 A	01 July 2015
				CO	6361916 A2	20 January 2012
				CY	1117088 T1	05 April 2017
				DK	2358697 T3	25 January 2016
				EP	2358697 A1	24 August 2011
				EP	2358697 B1	21 October 2015
				EP	2985281 A2	17 February 2016
				EP	2985281 A3	30 March 2016
				EP	2985281 B1	27 December 2017
				EP	3354646 A1	01 August 2018
				ES	2559388 T3	11 February 2016
				ES	2662407 T3	06 April 2018
				HK	1154859 A1	04 May 2012
				HR	P20151366 T1	15 January 2016
				HU	E026105 T2	30 May 2016
				IL	212435 A	30 June 2015
				IL	228597 A	31 January 2017
				IL	234162 A	30 June 2016
				IL	234163 A	30 June 2016
				IL	234164 A	31 July 2016
				IL	234165 A	31 August 2017
				IL	234166 B	30 April 2018
				IL	234167 A	28 September 2017
				IL	234168 A	31 July 2016
				JP	2012-507541 A	29 March 2012
				JP	2014-224119 A	04 December 2014
				JP	2015-227343 A	17 December 2015
				JP	5603876 B2	08 October 2014
				JP	5998179 B2	28 September 2016
				JP	6034924 B2	30 November 2016
				KR	10-1696938 B1	16 January 2017
				KR	10-2011-0089162 A	04 August 2011
				KR	10-2017-0007531 A	18 January 2017

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/IB2022/055168

Patent document cited in search report	Publication date (day/month/year)	Patent family member(s)	Publication date (day/month/year)
		KR 10-2018-0000750 A	03 January 2018
		MX 2011004470 A	31 May 2011
		MX 361467 B	06 December 2018
		NI 201100082 A	26 October 2011
		NZ 592425 A	26 April 2013
		PE 20110547 A1	04 August 2011
		PE 20140963 A1	06 August 2014
		PL 2358697 T3	29 April 2016
		PT 2358697 E	03 February 2016
		RU 2011121567 A	10 December 2012
		RU 2527952 C2	10 September 2014
		SG 10201703508 QA	29 June 2017
		SG 195613 A1	30 December 2013
		SI 2358697 T1	29 February 2016
		SM T201600025 B	25 February 2016
		TW 201022227 A	16 June 2010
		TW I469974 B	21 January 2015
		UA 107783 C2	25 February 2015
		US 2010-0204227 A1	12 August 2010
		US 2012-0122865 A1	17 May 2012
		US 2012-0252843 A1	04 October 2012
		US 2013-0045976 A1	21 February 2013
		US 2016-0115161 A1	28 April 2016
		US 2017-0088538 A1	30 March 2017
		US 8129375 B2	06 March 2012
		US 8222249 B2	17 July 2012
		US 8318773 B2	27 November 2012
		US 9227954 B2	05 January 2016
		US 9550766 B2	24 January 2017
		US 9796698 B2	24 October 2017
		ZA 201102941 B	25 July 2012
WO 2021-198965	A1	07 October 2021	None

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:

STEFFE, Eric K.

**Sterne, Kessler, Goldstein & Fox
P.L.L.C. 1100 New York Avenue, NW
Washington, District of Columbia 20005
USA**

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 4547-017PC02		Date of mailing (day/month/year) 08 September 2022
International application No. PCT/IB2022/055168		International filing date (day/month/year) 02 June 2022
Priority date (day/month/year) 03 June 2021		FOR FURTHER ACTION See paragraph 2 below
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		
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
Facsimile No. +82-42-481-8578		Telephone No. +82-42-481-5373

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB2022/055168

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(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 13*ter*.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 13*ter*.1(a)).
☐ on paper or in the form of an image file (Rule 13*ter*.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:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB2022/055168

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. 4-36, 41-52, 56-61

because:

- ☒ the said international application, or the said claims Nos. 42-52 relate to the following subject matter which does not require an international search (*specify*):

The subject matter of claims 42-52 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, 10, 13, 15-19, 21, 23, 25-27, 43-46, 50-52 are so unclear that no meaningful opinion could be formed (*specify*):

Claims 9, 10, 13, 15-19, 21, 23, 25-27, 43-46 and 50-52 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. 4-36, 41-52, 56-61

- ☐ 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	1-3,37-40,53-55	YES
	Claims	NONE	NO
Inventive step (IS)	Claims	1-3,37-40,53-55	YES
	Claims	NONE	NO
Industrial applicability (IA)	Claims	1-3,37-40,53-55	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

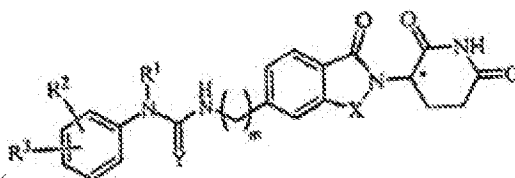
D3: HANSEN, J. D. et al., Journal of medicinal chemistry, 2018, Vol. 61, No. 2, pages 492-503

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

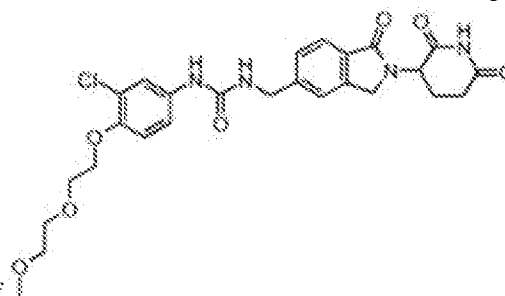
D5: HANSEN, J. D. et al., Journal of medicinal chemistry, 2020, Vol. 63, No. 13, pages 6648-6676

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

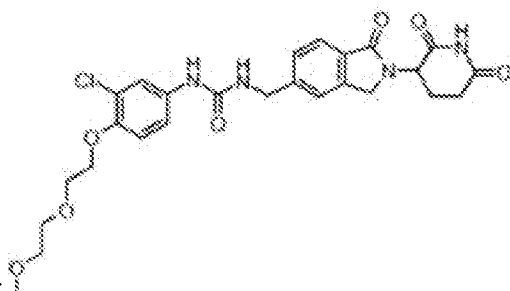
1. Claims 1-3, 37-40 and 53-55



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



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



The compound of formal (I) in D1, when U is NH; A is phenyl; R1 is halo (Cl).

in D1 corresponds to a compound of

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB2022/055168

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 1 differs from D1 in the compound comprising "X", "L" and "Bm", claim 37 differs from D1 in the compound of formula (V), claim 38 differs from D1 in the compound of formula (VI) and claim 39 differs from D1 in the conjugate of formula (VII).

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 and 3 are dependent on claim 1 and claim 40 is dependent on any one of claims 37-39.

Therefore, claims 1-3 and 37-40 are novel and involve an inventive step.

Claim 53 relates to a method of preparing the conjugate of claim 1, and claims 54 and 55 are dependent on claim 53.

Therefore, claims 53-55 are novel and involve an inventive step.

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

Claims 1-3, 37-40 and 53-55 are industrially applicable.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB2022/055168

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 1-3, 37-40, 53-55. 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>

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB2022/055168

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 4-8, 11, 12, 14, 20, 22, 24, 28-36, 41, 42, 47-49 and 56-61 which are multiple dependent claims, do not comply with PCT Rule 6.4(a) because the claims refer to another multiple dependent claims.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB2022/055168

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:

In claim 53, "the process" is not disclosed before itself. Therefore, claim 53 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".)