

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
see form PCT/ISA/220

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/US2019/051592

International filing date (day/month/year)
17.09.2019

Priority date (day/month/year)
18.09.2018

International Patent Classification (IPC) or both national classification and IPC
INV. C07D519/00 A61P35/00 A61K31/5383

Applicant
NIKANG 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 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

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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:
 - ☐ 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:

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>1-49</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>43</u>
	No: Claims	<u>1-42, 44-49</u>
Industrial applicability (IA)	Yes: Claims	<u>1-49</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

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

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

Re Item V

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

1 Claims 46-49 relate to a 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 a first or further medical treatment.

2 Reference is made to the following documents.

D1 WO 2018/013597 A1, 18 January 2018.

D2 WO 2016/203405 A1, 22 December 2016.

3 Novelty

D1 and D2 relate to SHP2 inhibitors. The present claims are novel over D1 and D2 on account of the tricyclic heterocyclic ring system shown in formula (I).

4 Inventive step

The application describes the synthesis of certain compounds (I) and shows that they inhibit SHP2 (cf. pages 174-182, table 4). In view of D1 as closest prior art, the problem to be solved is the provision of further SHP2 inhibitors. This problem has been solved by the tested examples as evident from table 4. In the position of the present tricyclic heterocyclic ring, the compounds of D1 may have a polycyclic 5-12 membered heteroaryl ring. The examples of D1 show however only bicyclic ring systems and the compounds of D2 have a monocyclic ring in the corresponding position. None of the cited documents hints or suggests to employ the specific tricyclic ring systems of the present compounds, whilst maintaining the desired SHP2 inhibiting activity. Hence, an inventive step may be acknowledged for the tested examples and a plausible generalisation thereof. However, most terms in the claims are open-ended (without

being limitative see inter alia alkyl, haloalkyl, cycloalkyl, heterocyclyl, heteroaryl, aryl, aralkyl, optionally substituted) and thus likely to solve no relevant technical problem. Hence, the present claims 1-42 and 45-49 do at present not comply with the criterion of inventive step.

Re Item VII

Certain defects in the international application

It would appear that D1 is not cited in the description (Rule 5.1(a)(ii) PCT).

Re Item VIII

Certain observations on the international application

Claim 46 does not comply with Article 6 PCT, because the therapeutic application is functionally defined by a mechanism of action which does not allow any practical application in the form of a defined, real treatment of a pathological condition. This objection may be overcome by introducing in the claims a list of pathological conditions cited in the application.