

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference BPX-04925		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US 22/24805	International filing date (day/month/year) 14 April 2022 (14.04.2022)	(Earliest) Priority Date (day/month/year) 14 April 2021 (14.04.2021)	
Applicant BIOCRYST PHARMACEUTICALS, 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 4 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.

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International application No.

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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.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
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:
3. ☒ Claims Nos.: 4,14-22,26-35,40,54-69,73-81,86-102,104-111,116-118,122-126,128-136,140
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
(see extra sheet)

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-3,5-13,23-25,36

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 22/24805

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C07D 231/14; C07D 401/04; C07D 401/12 (2022.01)

CPC - A61K 31/415; A61K 31/4155; A61P 1/02; A61P 1/04

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ZHOU et al. "Structure-Activity Relationship Studies of Indole-Based Compounds as Small Molecule HIV-1 Fusion Inhibitors Targeting Glycoprotein 41", J. Med. Chem. 2014. 57, pp 5270-5281, especially: pg 5271, Scheme 1, formula 5.	1-3,5-13,23-25,36
A	US 2010/0256365 A1 (IBRAHIM et al.) 7 October 2010 (07.10.2010), especially: para [1236], [2,4-Difluoro-3-(5-pyridin-3-yl-1H-pyrrolo[2,3-b]pyridin-3-ylmethyl)-phenyl]-carbamic acid methyl ester (P-0257); pg 169, Table, formula P-0257.	1-3,5-13,23-25,36
A	RASSIAS et al. "Cell-active carbazole derivatives as inhibitors of the zika virus protease", European Journal of Medicinal Chemistry. 2019. 180, pp 536-545, especially: pg 539, Fig. 3a, formula 16.	1-3,5-13,23-25,36
P,A	WO 2021/072198 A1 (BIOCRYST PHARMACEUTICALS INC) 15 April 2021 (15.04.2021), entire document.	1-3,5-13,23-25,36

☐ 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

4 August 2022

Date of mailing of the international search report

SEP 01 2022

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer

Kari Rodríguez

Telephone No. PCT Helpdesk: 571-272-4300

--Box III - Lack of Unity--

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I: Claims 1-3, 5-13, 23-25 and 36, directed to a compound of formula (I), or a pharmaceutically acceptable salt thereof.

Group II: Claims 37-39, 41-53, 70-72 and 82, directed to a compound of formula (II), or a pharmaceutically acceptable salt thereof.

Group III: Claims 83-85, 103 and 112, directed to a compound of formula (III), or a pharmaceutically acceptable salt thereof.

Group IV: Claims 113-115, 119-121 and 127, directed to a compound of formula (IV), or a pharmaceutically acceptable salt thereof.

Group V: Claims 137-139 and 141-145, directed to a method of treating or preventing a disease or condition characterized by aberrant kallikrein activity, comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof; wherein the compound is selected from the group consisting of the formulas indicated in claim 137.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features

Group I requires a compound of formula (I), or a pharmaceutically acceptable salt thereof, which is not required by Groups II-V.

Group II requires a compound of formula (II), or a pharmaceutically acceptable salt thereof, which is not required by Groups I or III-V.

Group III requires a compound of formula (III), or a pharmaceutically acceptable salt thereof, which is not required by Groups I-II or IV-V.

Group IV requires a compound of formula (IV), or a pharmaceutically acceptable salt thereof, which is not required by Groups I-III or V.

Group V requires a method of treating or preventing a disease or condition characterized by aberrant kallikrein activity, comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, which is not required by Groups I-IV.

Shared Common Features

The only feature shared by Groups I-V that would otherwise unify the groups is a compound having the core structure of formula (I) (excepting the amindine moiety). However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is anticipated by the article entitled "Structure-Activity Relationship Studies of Indole-Based Compounds as Small Molecule HIV-1 Fusion Inhibitors Targeting Glycoprotein 41" by Zhou et al. (hereinafter 'Zhou').

Zhou teaches a compound having the core structure of formula (I) wherein ring A is arylene; ring B is heteroarylene; ring A is fused to ring B; ring C is heteroaryl; ring D is aryl; J represents -CH₂-; K represents a bond; LD represents a bond; R₁ represents unsubstituted alkyl; m, n, p and q are each 0 (pg 5271, Scheme 1, formula 5).

As the technical features were known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups. Groups I-V therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

*Item 4 (contd): Claims 4, 14-22, 26-35, 40, 54-69, 73-81, 86-102, 104-111, 116-118, 122-126, 128-136 and 140 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).