

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference BPX-04125	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US 19/26054	International filing date (<i>day/month/year</i>) 05 April 2019 (05.04.2019)	(Earliest) Priority Date (<i>day/month/year</i>) 06 April 2018 (06.04.2018)
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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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.: 5-42, 49-66, 68-79
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 supplemental page)

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.:
1-4 and 43-44
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.:

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.

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A. CLASSIFICATION OF SUBJECT MATTER
 IPC(8) - A61K 9/50 (2019.01)
 CPC - A61K 31/343; A61K 31/381; A61K 31/404

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.
	1st elected invention:	
A	WO 2017/136395 A1 (BIOCRYST PHARMACEUTICALS, INC.) 10 August 2017 (10.08.2017); pg. 24 - 55, pg. 56, ln 10-15	1-4, 43
A	Shagufta et al. "An insight into the therapeutic potential of quinazoline derivatives as anticancer agents" MedChemComm. 07 April 2017 (07.04.2017) vol 8, pg. 871-885; pg. 872, Fig. 1	1-4, 43
A	US 9,056,874 B2 (Adams et al.) 16 June 2015 (16.06.2015); col 1, ln 5-11, col 4, ln 5-15	1-4, 43
A	"Pubchem CID 14528241" Create Date: 09 February 2007 (09.02.2007) Date Accessed: 15 July 2019 (15.07.2019); pg. 2	1-4, 43
	2nd elected invention:	
A	WO 2017/136395 A1 (BIOCRYST PHARMACEUTICALS, INC.) 10 August 2017 (10.08.2017); pg. 24 - 55, pg. 56, ln 10-15	1-4, 43-44
A	US 9,056,874 B2 (Adams et al.) 16 June 2015 (16.06.2015); col 1, ln 5-11, col 4, ln 5-15	1-4, 43-44
A	US 7,442,808 B2 (Ge et al.) 28 October 2008 (28.10.2008); col 50, ln 30-50	1-4, 43-44
A	"Pubchem CID 14528241" Create Date: 09 February 2007 (09.02.2007) Date Accessed: 15 July 2019 (15.07.2019); pg. 2	1-4, 43-44

☐ 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

"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

15 July 2019

Date of mailing of the international search report

02 AUG 2019

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:

Lee W. Young

PCT Helpdesk: 571-272-4300
 PCT OSP: 571-272-7774

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International application No.

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--continued from Box No. III--

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 1-4, 43-48 and 67, directed to a compound of claim 1, Formula I. The compound of claim 1 will be searched to the extent that it encompasses the first species of claim 1, represented by a compound of formula I wherein ring A is aryl; B is aryl; C is aryl; R1 is NH2; n is 0; m is 0; p is 0; J is C(O); K is C(O); L is a bond; U is N; V is N; the stereochemical configuration at any chiral center is R, S. It is believed that claims 1-4 and 43 reads on this first named invention, and thus these claims will be searched without fee. Applicant is invited to elect additional compounds of claim 1 wherein each additional compound elected will require one additional invention fee. Applicants must specify the claims that encompass any additionally elected compound. Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the '+' group(s) will result in only the first claimed invention to be searched. Additionally, an exemplary election wherein different actual variables are selected is suggested. An exemplary election would be a compound of formula I wherein ring A is aryl; B is heteroaryl; C is aryl; R1 is CH2COOH; n is 0; m is 0; p is 0; J is C(O); K is NH; L is CH2; U is CR3; R3 is H; V is CH; the stereochemical configuration at any chiral center is R, S (i.e., claims 1-4, 43-48 and 67).

The group of inventions listed above 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+ includes the technical feature of a unique compound having the following formula I, which is not required by any other invention of Group I+.

Common technical features:

The inventions of Group I+ share the technical feature of a compound having the following formula I.

These shared technical features, however, do not provide a contribution over the prior art, as being obvious over a document entitled Pubchem CID 14528241 (hereinafter Pubchem-241) in view of US 3,377,387 A to Bachman et al. (hereinafter Bachman). Pubchem-241 discloses a compound of formula I wherein A is aryl; B is aryl; C is aryl; n is 0; m is 0; p is 0; J is C(O); K is NH; L is a bond; U is N; V is N (pg. 2, compound listed), but does not disclose wherein R1 is NH2 or wherein L is bound to an NH2. However, Pubchem-241 further discloses a compound wherein R1 is NO2 and wherein L is bound to an NO2. Additionally, Bachman discloses wherein nitro (NO2) groups are prepared from amine (NH2) groups (col 1, ln 10-15; col 2, ln 9-13). It would have been obvious to one with skill in the art to prepare the compound disclosed by Pubchem-231, comprising two nitro groups, from the corresponding di-amine compound (ie wherein R1 is NH2 and wherein L is bound to an NH2), as disclosed by Bachman, as a routine method for synthesis of nitro functional groups.

As said compound was known in the art at the time of the invention, these cannot be considered special technical features that would otherwise unify the inventions of Group I+. The inventions of Group I+ thus lack unity under PCT Rule 13.

Item 4 (contd.): Claims 5-42, 49-66, 68-79 have been found to be unsearchable because they are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Note: Regarding suggested claims of 1st elected invention listed in LOU response; the first elected invention of group I+ reads on claims 1-4 and 43, as claim 44 does not include a compound wherein J is C(O); K is C(O); and the compound of formula II in claim 45, does not include wherein RT3 and RT2 taken together with the intervening atoms, form an aryl ring.