

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 055920-553001WO		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US 22/11669	International filing date (day/month/year) 07 January 2022 (07.01.2022)	(Earliest) Priority Date (day/month/year) 08 January 2021 (08.01.2021)	
Applicant BRISTOL-MYERS SQUIBB COMPANY			

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 6 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. 20



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. 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 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).

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:

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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.: 7-13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35-57
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 for Box No. III Observations where unity of invention is lacking -

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.:
1-2, (5-6)(in part) limited to SEQ ID NOS: 1, 29, 52, 84

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 - C07K 16/36, C07K 16/42, A61P 7/02, A61K 31/4162 (2022.01)

CPC - A61P 7/02, C07K 16/36, C07K 16/4028, A61K 31/4162, A61K 31/506

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	US 2014/0186362 A1 (NOVIMMUNE S.A.) 03 July 2014 (03.07.2014) abstract, Fig. 6A, SEQ ID NO: 43	1-2, (5-6)/(1-2)
A	US 2008/0160035 A1 (STEVENS et al.) 03 July 2009 (03.07.2008) Claim 1, Claim 4, SEQ ID NO: 405	1-2, (5-6)/(1-2)
A	US 2018/0134787 A1 (EUREKA THERAPEUTICS, INC.) 17 May 2018 (17.05.2018) abstract, para [0061], SEQ ID NO:16	1-2, (5-6)/(1-2)

☐ 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 May 2022

Date of mailing of the international search report

MAY 23 2022

Name and mailing address of the ISA/US

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Continuation of:

Box No. III. Observations where unity of invention is lacking

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.

Groups I+: Claims 1-6, drawn to an isolated antigen binding peptide. The composition will be searched to the extent that the antibody encompassing VH-CDR1 and VL-CDR1 of SEQ ID NOs: 1 and 29, respectively, VH and VL of SEQ ID NOs: 52 and 84, respectively. It is believed that claims 1-2, (5-6)(in part) encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass SEQ ID NOs: 1, 29, 52 and 84. Additional antigen binding peptide(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected antigen binding peptide(s). 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. An exemplary election would be an antigen binding peptide encompassing VH-CDR1-3 and VL-CDR1-3 of SEQ ID NOs: 1, 14, 23, 29, 38 and 45, respectively; VH and VL of SEQ ID NOs: 53 and 85, respectively (Claims 1-6).

Groups II+: Claims 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, drawn to an isolated antibody Fab fragment that specifically binds to the compound of Formula (II). Group II+ will be searched upon payment of additional fees. The composition may be searched, for example, to the extent that the Fab fragment encompasses SEQ ID NOs: 106 and 164, for an additional fee and election as such. It is believed that claim 14 read on this exemplary invention. Additional Fab fragment(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected Fab fragment(s). 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. Another exemplary election would be a Fab fragment encompassing SEQ ID NOs: 180 and 164 (Claim 16).

The inventions listed as Groups I+ and II+ 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

Groups I+ include the special technical feature of an isolated antigen binding peptide comprising specific amino acid sequences for VH-CDRs, VL-CDRs, VH and VL, not required by Groups II+.

Groups II+ include the special technical feature of an isolated antibody Fab fragment that binds to the compound of Formula (II), not required by Groups I+.

No technical features are shared between the amino acid sequences of Groups I+ and II+, accordingly, these groups lack unity a priori.

Common Technical Features

Additionally, even if Groups I+ and II+ were considered to share the technical features of including: an isolated antibody, these shared technical features are previously disclosed by WO 2020/216379 A1 to (I-MAB).

I-MAB teaches (instant claim 1) an isolated antigen binding peptide comprising at least one heavy chain variable region (VH) and at least one light chain variable region (VL), wherein the at least one VH comprises at least one of:

(a) a VH complementarity-determining region 1 (VH-CDR1) comprising an amino acid sequence consisting of SEQ ID NO: 1; and wherein the at least one VL comprises at least one of:

(e) a VL-CDR2 comprising an amino acid sequence consisting of SEQ ID NO: 38 (abstract, Provided are full human anti-PD-L1 antibodies or fragments thereof. In various examples, the antibodies or fragments thereof include a VH CDR1, a VH CDR2, a VH CDR3, a VL CDR1, a VL CDR2, and a VL CDR3 which are selected from sequence groups of SEQ ID NO: 35-42, SEQ ID NO: 43-51, SEQ ID NO: 52-66, SEQ ID NO: 67-79, SEQ ID NO: 80-88 and SEQ ID NO: 89-102, respectively, para [0006]. In an example antibody or fragment, VH comprises the amino acid sequence of SEQ ID NO: 23, 124, 126, 127, 128, 130, 140, or 145, and the VL comprises the amino acid sequence of SEQ ID NO: 24 or 125, as well as their variants.; para [0037], Table A CDR sequence from antibodies B01-B17 (Kabat); HCDR1 SEQ ID NO: 42 (SNAMS); LCDR2 SEQ ID NO: 80 (AASSLQS).; Note, SEQ ID NOs: 42 and 80 are 100% match to SEQ ID NO: 1 and 38 of instant claim.).

The inventions of Groups II+ share the technical feature of an isolated antibody Fab fragment that specifically binds to the compound of Formula (II).

However, these shared technical features do not represent a contribution over prior art in view of the abstract "FEIBA and Novoseven Neutralize the Anticoagulant Effects of a Novel Small Molecule FXIa Inhibitor BMS-986177/JNJ-70033093 in Human Plasma and Whole Blood in Vitro" by Bunce et al. (hereinafter "Bunce") (Blood, 05 November 2020, 136, Supplement 1: 10) and WO 2020/089380 A1 to Bayer Aktiengesellschaft (hereinafter "Bayer").

----continued on next sheet----

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Continuation of:

Box No. III. Observations where unity of invention is lacking

Bunce teaches (instant claim 14) an isolated compound that specifically neutralizes to the compound of Formula (II) (abstract, Background: FXIa inhibition is a promising antithrombotic drug target. BMS-986177/JNJ-70033093 (BMS-177/JNJ-3093) is a novel small molecular inhibitor of FXIa currently in Phase II clinical trials with the potential for reduced bleeding risk.; Note, BMS-986177 corresponds to Formula (II) of instant claim.; Aim: To evaluate the ability of nonspecific reversal agents (NSRAs) FEIBA, NovoSeven, Kcentra, Profilnine, BeneFix, Novoeight, and Cyklokapron to neutralize the anticoagulation of BMS-177/JNJ-3093 in the activated partial thromboplastin time (aPTT), thromboelastography (TEG) and thrombin generation assay (TGA) in vitro using human plasma or whole blood.; Results: FEIBA effectively neutralized the anticoagulant effects of JNJ-3093 in aPTT, TEG and TGA.).

Bunce does not specifically teach an isolated antibody Fab fragment that binds to the compound of Formula (II). Bayer teaches an isolated antibody Fab fragment that binds to inhibitor of FXIa (abstract, The present invention relates to reversal agents, which specifically bind to the anti-FXIa antibody 076D-M007-H04-CDRL3-N110D as described in WO2013/167669, and neutralize the therapeutic activity of this anti-FXIa antibody, as well as to compositions comprising these reversal agents. Methods of obtaining the antibodies or antigen-binding fragments thereof (such as Fab fragments) and nucleic acids encoding the same, are also provided.). It would have been obvious to one of ordinary skill in the art to have developed an isolated antibody Fab fragment as a reversal agent, as taught by the Bayer, to counteract the compound of Formula (II), as taught by Bunce.

As said technical features were known in the art at the time of the invention, these cannot be considered special technical features that would otherwise unify the groups.

Groups I+ and II+ therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Item 4 (continued):

Claims 7-13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35-57 are held unsearchable because they are not drafted in accordance with the second and third sentences of Rule 6.4(a).