(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 March 2024 (21.03.2024)

WIPO | PCT

(10) International Publication Number
WO 2024/059677 A3

(51) International Patent Classification:
C07K 16/28 (2006.01) *A61K 39/395* (2006.01)
A61K 39/00 (2006.01) *A61P 35/00* (2006.01)

(21) International Application Number:
PCT/US2023/074133

(22) International Filing Date:
14 September 2023 (14.09.2023)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/375,676 14 September 2022 (14.09.2022) US
63/515,448 25 July 2023 (25.07.2023) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ,

(54) Title: PD-1 AGONIST ANTIBODIES

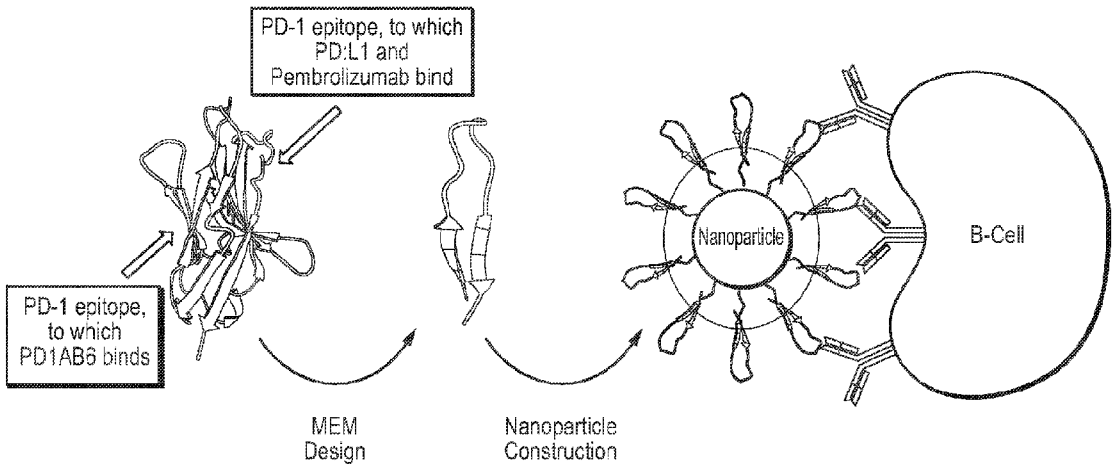

FIG. 1A

(57) Abstract: Provided herein are PD-1 agonist antibodies which bind PD-1. The PD-1 agonist antibodies of the disclosure are useful for the treatment of autoimmune and inflammatory diseases through the promotion of PD-1 signaling. Also provided herein are methods of use for the PD-1 agonist antibodies.

[Continued on next page]

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DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
16 May 2024 (16.05.2024)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 23/74133

A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. C07K 16/28, A61K 39/00, A61K 39/395 (2023.01)
ADD. A61P 35/00 (2023.01)

CPC - INV. C07K 16/28, A61K 39/0011, A61K 39/39558
ADD. A61K 2039/505, A61P 35/00, C07K 2317/56, C07K 2317/75

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.
X	US 2020/0190193 A1 (INHIBRX, INC.) 18 June 2020 (18.06.2020) para [0190], para [0202], para [0222]	11
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Y		12-13
–		1-3
A	US 2021/0253698 A1 (AFFIMED GMBH) 19 August 2021 (19.08.2021) para [0040], para [0403]	12-13
Y	US 2019/0263909 A1 (XENCOR, INC.) 29 August 2019 (29.08.2019) para [0012]	13
Y	WO 2021/076930 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 22 April 2021 (22.04.2021) abstract; para [0494]; Table 6; SEQ ID NO: 174	1-3, 14-15
A	WO 2022/054029 A1 (CELROS BIOTECH) 17 March 2022 (17.03.2022) abstract; claim 8; SEQ ID NO: 57	1-3, 14-15
A		

☐ 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	Date of mailing of the international search report
04 February 2024	MAR 13 2024
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 Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 23/74133

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 fi led.

   b. ☐ furnished subsequent to the international fi ling date for the purposes of international search (Rule 13ter.1(a)),

      ☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 23/74133

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.: 4-10, 16-24
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:
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, 11-15, directed to a PD-1 agonist antibody. The method will be searched to the extent that the PD-1 agonist antibody comprises the following variable sequences: VH SEQ ID NO: 1 (comprising CDR sequences SEQ ID NOs: 10-12), and VL SEQ ID NO: 6 (comprising CDR sequences SEQ ID NOs: 13-15). The first named invention was determined based on these being the first listed PD-1 agonist antibody sequences (claims 1 and 2, and see instant application specification para [0115], Table 4). This first named invention has been selected based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines. It is believed that claims 1-3, 11-15 encompass this first named invention, and thus these claims will be searched without fee to the extent that the PD-1 agonist antibody variable sequences are SEQ ID NOs: 1 and 6 (and corresponding CDR sequences SEQ ID NOs: 10-15).

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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, 11-15, limited to variable sequences SEQ ID NOs: 1, 6

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.

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

Additional PD-1 agonist antibody variable sequence(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected PD-1 agonist antibody variable sequence(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 where the PD-1 agonist antibody variable sequences are SEQ ID NOs: 2 and 7, respectively (and corresponding CDR sequences SEQ ID NOs: 16-21), (claims 1-3, 11-15).

The inventions listed as Group I+ do not relate to a single special technical feature 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

The inventions of Group I+ each include the special technical feature of a unique variable and CDR sequences, and is considered a distinct technical feature.

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

Common technical features

Additionally, even if the inventions listed as Group I+ were considered to share the technical features of including: a PD-1 agonist antibody, wherein the antibody comprises a heavy chain variable domain (VH) comprising three complementarily determining region (CDRs) and a light chain variable domain (VL) comprising three CDRs; and a tandem scFv-Fc PD-1 agonist antibody wherein said antibody comprises a scFv1 and a scFv2 binding site in tandem on each antibody arm and wherein said scFv1 and scFv2 are linked by a linker, optionally a flexible linker, these shared technical features are previously disclosed by US 2020/0190193 A1 to InhibRx Inc. (hereinafter "InhibRx").

InhibRx discloses a PD-1 agonist antibody (claim 17 - "An isolated single domain antibody that binds PD-1"), wherein the antibody comprises a heavy chain variable domain (VH) comprising three complementarily determining regions (CDRs) and a light chain variable domain (VL) comprising three CDRs (para [0197] - "In some embodiments, the CD3-binding domain contains a CDRH1, CDRH2 and CDRH3 of the variable heavy (VH) chain set forth in SEQ ID NO:27 and a CDRL1, CDRL2 and CDRL3 variable light chain set forth in SEQ ID NO:28. In some embodiments, the CD3-binding domain contains a CDRH1, CDRH2 and CDRH3 set forth in SEQ ID NOs:29, 30 and 31, respectively and a CDRL1, CDRL2 and CDRL3 variable light chain set forth in SEQ ID NO:32, 33, and 34, respectively.").

InhibRx further discloses a tandem scFv-Fc PD-1 agonist antibody wherein said antibody comprises an scFv1 and an scFv2 binding site in tandem on each antibody arm and wherein said scFv1 and scFv2 are linked by a linker, optionally a flexible linker (para [0190]-[0191] - "Among bispecific antibody T cell-engagers are bispecific T cell engager (BiTE) molecules, which contain tandem scFv molecules fused by a flexible linker (see e.g. Nagorsen and Bauerle, Exp Cell Res 317, 1255-1260 (2011); tandem scFv molecules fused to each other via, e.g. a flexible linker, and that further contain an Fc domain composed of a first and a second subunit capable of stable association.").

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

Therefore, Group I+ inventions lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.

**Continuation of item 4 above: claims 4-10, 16-24 are held unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).