

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 25565	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2023/029676	International filing date (<i>day/month/year</i>) 8 August 2023 (08-08-2023)	(Earliest) Priority Date (<i>day/month/year</i>) 10 August 2022 (10-08-2022)
Applicant MERCK SHARP & DOHME LLC		

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 8 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. 1
☒ 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.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.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:

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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.:
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 additional 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 an 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.:

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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International application No
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A. CLASSIFICATION OF SUBJECT MATTER INV. C07K16/30 C07K16/28 A61K39/00 ADD.		
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) C07K A61K A61P		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, Sequence Search, BIOSIS, EMBASE, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2018/157147 A1 (DRAGONFLY THERAPEUTICS INC [US]) 30 August 2018 (2018-08-30) claims 1-61 -----	1-91
X	WO 2022/031965 A1 (DRAGONFLY THERAPEUTICS INC [US]) 10 February 2022 (2022-02-10) claim 66; sequences 164, 165 -----	35-40, 42-52
X	EP 3 981 793 A1 (BIOTHEUS INC [CN]) 13 April 2022 (2022-04-13) claims 1-25 -----	53-91
☐ 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		Date of mailing of the international search report
11 April 2024		18/04/2024
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Klee, Barbara

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Information on patent family members

International application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2018157147 A1	30-08-2018	AU 2018224319 A1	12-09-2019
		AU 2020267226 A1	10-12-2020
		BR 112019017758 A2	07-04-2020
		CA 3054738 A1	30-08-2018
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		IL 268888 A	31-10-2019
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		KR 20200130514 A	18-11-2020
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		KR 20220016943 A	10-02-2022
		TW 202100560 A	01-01-2021
		TW 202110895 A	16-03-2021
		US 2022235142 A1	28-07-2022
		US 2022242968 A1	04-08-2022
		WO 2020244526 A1	10-12-2020
		WO 2020244528 A1	10-12-2020

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-91 (partially)

1. A protein comprising:

- (a) a first antigen-binding site that binds NKG2D;
- (b) a second antigen-binding site that binds CEACAM5; and
- (c) a third antigen-binding site, or an antibody Fc domain or a portion thereof, that binds CD 16, wherein: the second antigen-binding site that binds CEACAM5 comprises a heavy-chain variable domain (VH) comprising a complementarity-determining region (CDR) 1 (CDRH1), CDRH2, and CDRH3, and a light-chain variable domain (VL) comprising a CDR 1 (CDL1), CDRL2, and CDRL3, wherein:
 - (a) the CDRH1, CDRH2, and CDRH3 of the second antigen-binding site are:
 - (i) SEQ ID NOs: 3, 37, and 38, respectively; and
 - b) the CDRL1, CDRL2, and CDRL3 of the second antigen-binding site are:
 - (i) SEQ ID NOs: 7, 8, and 9, respectively;

OR

2. A protein comprising:

- (a) a first polypeptide comprising the amino acid sequence of SEQ ID NO:549;
- (b) a second polypeptide comprising the amino acid sequence of SEQ ID NO:550; and
- (c) a third polypeptide comprising an amino acid sequence selected from the group consisting of: SEQ ID NOs:702.

3. OR: A protein comprising an antigen-binding site that binds CEACAM5, wherein the antigen-binding site comprises a heavy-chain variable domain (VH) comprising a complementarity-determining region (CDR) 1 (CDRH1), CDRH2, and CDRH3, and a light-chain variable domain (VL) comprising a CDR 1 (CDL1), CDRL2, and CDRL3, wherein:

- (a) the CDRH1, CDRH2, and CDRH3 of the second antigen-binding site are:
 - (i) SEQ ID NOs: 3, 37, and 38, respectively; and
- b) the CDRL1, CDRL2, and CDRL3 of the second antigen-binding site are:
 - (i) SEQ ID NOs: 7, 8, and 9.

2. claims: 1-91 (partially)

1. A protein comprising:

- (a) a first antigen-binding site that binds NKG2D;
- (b) a second antigen-binding site that binds CEACAM5; and
- (c) a third antigen-binding site, or an antibody Fc domain or a portion thereof, that binds CD 16, wherein: the second antigen-binding site that binds CEACAM5 comprises a heavy-chain variable domain (VH) comprising a complementarity-determining region (CDR) 1 (CDRH1), CDRH2, and CDRH3, and a light-chain variable domain (VL) comprising a CDR 1 (CDL1), CDRL2, and CDRL3, wherein:

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- (a) the CDRH1, CDRH2, and CDRH3 of the second antigen-binding site are:
 - (ii) SEQ ID NOs: 3, 718, and 6, respectively; and
- (b) the CDRL1, CDRL2, and CDRL3 of the second antigen-binding site are:
 - (ii) SEQ ID NOs: 40, 41, and 42;
- 2. OR: A protein comprising:
 - (a) a first polypeptide comprising the amino acid sequence of SEQ ID NO:549;
 - (b) a second polypeptide comprising the amino acid sequence of SEQ ID NO:550; and
 - (c) a third polypeptide comprising an amino acid sequence selected from the group consisting of: SEQ ID NOs: 706,
- 3. OR: A protein comprising an antigen-binding site that binds CEACAM5, wherein the antigen-binding site comprises a heavy-chain variable domain (VH) comprising a complementarity-determining region (CDR) 1 (CDRH1), CDRH2, and CDRH3, and a light-chain variable domain (VL) comprising a CDR 1 (CDL1), CDRL2, and CDRL3, wherein:
 - (a) the CDRH1, CDRH2, and CDRH3 of the second antigen-binding site are:
 - (i) SEQ ID NOs: 3, 718, and 6, respectively; and
 - b) the CDRL1, CDRL2, and CDRL3 of the second antigen-binding site are:
 - (i) SEQ ID NOs: 40, 41, and 42.

3. claims: 1-91 (partially)

- 1. A protein comprising:
 - (a) a first antigen-binding site that binds NKG2D;
 - (b) a second antigen-binding site that binds CEACAM5; and
 - (c) a third antigen-binding site, or an antibody Fc domain or a portion thereof, that binds CD 16, wherein: the second antigen-binding site that binds CEACAM5 comprises a heavy-chain variable domain (VH) comprising a complementarity-determining region (CDR) 1 (CDRH1), CDRH2, and CDRH3, and a light-chain variable domain (VL) comprising a CDR 1 (CDL1), CDRL2, and CDRL3, wherein:
 - (a) the CDRH1, CDRH2, and CDRH3 of the second antigen-binding site are:
 - (iii) SEQ ID NOs: 102, 104, and 105 and
 - (b) the CDRL1, CDRL2, and CDRL3 of the second antigen-binding site are:
 - (iii) SEQ ID NOs: 107, 108, and 109.
- 2. OR: A protein comprising:
 - (a) a first polypeptide comprising the amino acid sequence of SEQ ID NO:549;
 - (b) a second polypeptide comprising the amino acid sequence of SEQ ID NO:550; and
 - (c) a third polypeptide comprising an amino acid sequence selected from the group consisting of: SEQ ID NOs: 709 or 713.
- 3. OR: A protein comprising an antigen-binding site that binds CEACAM5, wherein the antigen-binding site comprises a

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

heavy-chain variable domain (VH) comprising a complementarity-determining region (CDR) 1 (CDRH1), CDRH2, and CDRH3, and a light-chain variable domain (VL) comprising a CDR 1 (CDL1), CDRL2, and CDRL3, wherein:

(a) the CDRH1, CDRH2, and CDRH3 of the second antigen-binding site are:

(i) SEQ ID NOS: 102, 104, and 105; and

b) the CDRL1, CDRL2, and CDRL3 of the second antigen-binding site are:

(i) SEQ ID NOS:107, 108 and 109.
