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(54) Title: CHIMERIC ANTIGEN RECEPTORS AND USE THEREOF

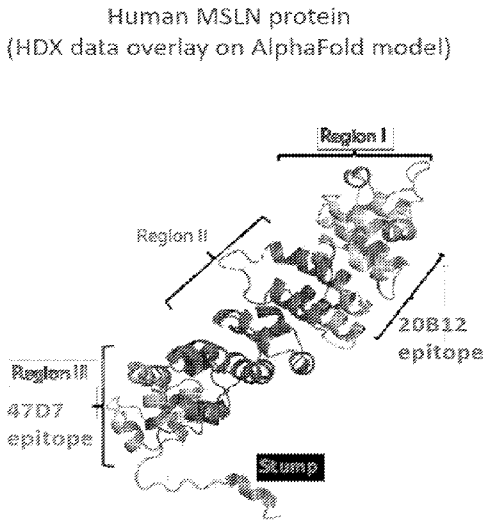

FIG. 1A

(57) Abstract: The present disclosure provides CARs comprising a human mesothelin (MSLN) binder, related polynucleotides and vectors, engineered cells, pharmaceutical compositions, and cell therapies.

[Continued on next page]

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— *with sequence listing part of description (Rule 5.2(a))*

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INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. A61K 39/00; A61K 35/17; C07K 14/705; C07K 16/30; C12N 5/0783 (2024.01)
ADD. A61P 35/00 (2024.01)

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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 database consulted during the international search (name of database 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 2021/0269537 A1 (NANJING LEGEND BIOTECH CO. LTD. (NANJING JIANGSU CN)) 02 September 2021; Abstract; paragraphs [0026], [0086]	1-2, 10, 14-16
A	WO 2021/207242 A2 (FRED HUTCHINSON CANCER RESEARCH CENTER (US)) 14 October 2021; Paragraphs [0006], [0180]; claim 1	1-2, 10, 14-16
A	US 2022/0370497 A1 (A2 BIOTHERAPEUTICS INC. (AGOURA HILLS US)) 24 November 2022; Abstract; paragraphs [0011], [0012]; Table 2	1-2, 10, 14-16

☐ 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
23 August 2024 (23.08.2024)	NOV 12 2024
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2024/033758

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:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2024/033758

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.: 17-75
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:

-***-Please 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.:

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.:

Group I+: claims 1-16, SEQ ID NO: 3 (VH chain sequence), SEQ ID NO: 4 (VL chain sequence), SEQ ID NO: 5 (VHCDR1 sequence), SEQ ID NO: 6 (VHCDR2 sequence), SEQ ID NO: 7 (VHCDR3 sequence), SEQ ID NO: 8 (VLCDR1 sequence), SEQ ID NO: 9 (VLCDR2 sequence), SEQ ID NO: 10 (VLCDR3 sequence).

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/US2024/033758

-***-Continued From 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 examined, the appropriate additional examination fees must be paid.

Group I+: claims 1-16, SEQ ID NO: 3 (VH chain sequence), SEQ ID NO: 4 (VL chain sequence), SEQ ID NO: 5 (VHCDR1 sequence), SEQ ID NO: 6 (VHCDR2 sequence), SEQ ID NO: 7 (VHCDR3 sequence), SEQ ID NO: 8 (VLCDR1 sequence), SEQ ID NO: 9 (VLCDR2 sequence), SEQ ID NO: 10 (VLCDR3 sequence), are directed to CAR comprising an extracellular binding domain for MSLN, transmembrane domain and an intracellular signaling domain.

The methods of Claims 1 (in part), 2, 10 (in part), and 14-16, are believed to encompass the first named invention of Groups I+ and are the claims that will be searched to the extent that they comprise a compound encompassing SEQ ID NO: 3 (first exemplary VH chain sequence), SEQ ID NO: 4 (first exemplary VL chain sequence), SEQ ID NO: 5 (first exemplary VHCDR1 sequence), SEQ ID NO: 6 (first exemplary VHCDR2 sequence), SEQ ID NO: 7 (first exemplary VHCDR3 sequence), SEQ ID NO: 8 (first exemplary VLCDR1 sequence), SEQ ID NO: 9 (first exemplary VLCDR2 sequence), SEQ ID NO: 10 (first exemplary VLCDR3 sequence). This first named invention of Group I+ has been selected to encompass the first species of each of the genera found in claims 1, 10, are based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines.

Applicant is invited to elect additional CDR sequences, where available as an option within at least one searchable claim, to be searched. Additional CDR sequence(s) will be searched upon the payment of additional fees. Applicants must specify the searchable claims that encompass any additionally elected CDR 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/examined. An exemplary election would be SEQ ID NO: 11 (VH chain sequence), SEQ ID NO: 12 (VL chain sequence), SEQ ID NO: 13 (VHCDR1 sequence), SEQ ID NO: 14 (VHCDR2 sequence), SEQ ID NO: 15 (VHCDR3 sequence), SEQ ID NO: 16 (VLCDR1 sequence), SEQ ID NO: 17 (VLCDR2 sequence), SEQ ID NO: 18 (VLCDR3 sequence)

Groups I+ share the technical features including: a chimeric antigen receptor "CAR" comprising a polypeptide comprising: a. an extracellular antigen binding domain comprising a human mesothelin MSLN. binder; b. a transmembrane domain; and c. an intracellular signaling domain; wherein the human MSLN binder comprises: VH and VL chain with CDR 1-3.

However, these shared technical features are previously disclosed by US 2021/0269537 A1 to Nanjing Legend Biotech Co. Ltd (hereinafter "Nanjing").

Nanjing discloses a chimeric antigen receptor "CAR" comprising a polypeptide comprising: a. an extracellular antigen binding domain comprising a human mesothelin "MSLN" binder (CAR designed in method against MSLN; abstract); b. a transmembrane domain; and c. an intracellular signaling domain (CAR comprises an extracellular domain, transmembrane domain and an intracellular signaling domain; paragraph [0086]); wherein the human MSLN binder comprises: VH and VL chain with CDR 1-3 (tumor antigen targeting body can have a VL and VH; paragraphs [0025], [0026]).

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Nanjing reference, unity of invention is lacking.