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(54) Title: ANTI-CD117 ANTIBODY-DRUG CONJUGATES AND USES THEREOF

(57) Abstract: Anti-CD117 antibody-drug conjugates (ADCs) comprising calicheamicin and are provided, as well as compositions and methods of using the same. The compositions and methods provided herein can also be used to prepare a patient for hematopoietic stem cell transplant therapy and to improve the engraftment of hematopoietic stem cell transplants by selectively depleting endogenous hematopoietic stem cells prior to the transplant procedure. Methods and compositions for the treatment of various hematopoietic diseases, metabolic disorders, cancers, and autoimmune diseases, are provided.



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INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 39/395; 31/216; 47/68; C07K 16/28 (2020.01)

CPC - A61K 39/39541; 31/216; 47/6849; C07K 16/2896

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	WO 2017/219029 A1 (MAGENTA THERAPEUTICS, INC.) 21 December 2017; abstract; page 2, lines 1-2; page 2, lines 21-24; page 3, lines 9-12; page 34, lines 2-3; page 32, lines 9-23; page 22, lines 13-24	1, 4
A	US 2014/0065168 A1 (KOLLITAN PHARMACEUTICALS, INC.) 06 March 2014; abstract, paragraphs [0003], [0008], [0010], [0011] [0043], [0336], [0124], [0128]	1, 4
A	US 2017/0121409 A1 (JANSSEN BIOTECH, INC.) 04 May 2017; abstract, paragraph [0144]; SEQ ID NO: 44	1, 4
A	US 2011/0293618 A1 (ONO et al.) 01 December 2011; abstract, paragraph [0497]; SEQ ID NO: 50	1, 4
P,X	WO 2019/234694 A2 (MAGENTA THERAPEUTICS, INC) 12 December 2019; abstract, page 1, second paragraph; page 10; page 70, second paragraph; page 85, second paragraph-third paragraph; Sequence Table; SEQ ID NOS: 200, 201	1, 4
P,Y	US 2019/0144558 A1 (MAGENTA THERAPEUTICS, INC.) 16 May 2019; abstract, paragraphs [0013], [0026]; SEQ ID NOS: 19, 20	1, 4
P,Y	WO 2019/084067 A1 (MAGENTA THERAPEUTICS, INC) 02 May 2019; abstract, page 2, fifth paragraph; page 3, second paragraph; page 5, fifth paragraph; page 7, seventh paragraph - page 8, first paragraph; SEQ ID NOS: 19, 20	1, 4



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

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,Y	WO 2020/092655 A1 (MAGENTA THERAPEUTICS, INC) 7 May 2020; abstract, page 1, lines 30 - page 2, line 14; page 5, lines 8-16; page 39, lines 1-9; page 101, lines 6 - 19; SEQ ID NOs: 19, 20	1,4

INTERNATIONAL SEARCH REPORT

International application No.

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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.: 5-19
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 examined, the appropriate additional examination fees must be paid.

Groups I+, Claims 1-4, and Ab55 (antibody) are directed toward antibody-drug conjugates.

-Please See Extra 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 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 (in-part) and 4 (in-part)

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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-Continued from Box III: Observations where Unity of Invention is Lacking -

The conjugates will be searched to the extent they encompass Ab55 (first exemplary antibody). Applicant is invited to elect additional antibody(ies), with specified name thereof, and, where applicable, associated specified SEQ ID NOs: for each, such that the sequence of each elected species is fully specified (i.e. no optional or variable residues or substituents), where available as an option within at least one searchable claim, to be searched. Additional antibody(ies) and/or associated sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1 (in-part) and 4 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass Ab55 (antibody). Applicants must specify the searchable claims that encompass any additionally elected antibody(ies) and/or associated 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 Ab54 (antibody).

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

Additionally, even if Groups I+ were considered to share the technical features including: an antibody-drug conjugate (ADC) comprising an anti-CD117 antibody, or an antigen binding portion thereof (Ab), conjugated to a calicheamicin via a linker (L), and wherein the anti-CD117 antibody, or antigen binding portion thereof, comprises a heavy chain comprising a heavy chain variable region comprising a CDR1, CDR2, and CDR3; and a light chain comprising a light chain variable region comprising a CDR1, CDR2, and CDR3; however, these shared technical features are previously disclosed by US 2017/0360954 A1 to Magenta Therapeutics, Inc. (hereinafter 'Magenta') in view of US 2018/0339058 A1 to Wyeth Holdings LLC (hereinafter 'Wyeth').

Magenta discloses an antibody-drug conjugate (ADC) comprising an anti-CD117 antibody, conjugated to a cytotoxin (an antibody-drug conjugate (ADC) comprising an anti-CD117 antibody, conjugated to, amongst a list of drugs, a calicheamicin; paragraphs [0004], [0009]) via a linker (via a linker; paragraph [0032], [0276]), and wherein the anti-CD117 antibody, or antigen binding portion thereof, comprises a heavy chain comprising a heavy chain variable region comprising a CDR1, CDR2, and CDR3 (wherein the anti-CD117 antibody, or antigen binding portion thereof, comprises a heavy chain comprising a heavy chain variable region comprising a CDR1, CDR2, and CDR3; paragraph [0279]); and a light chain comprising a light chain variable region comprising a CDR1, CDR2, and CDR3 (a light chain comprising a light chain variable region comprising a CDR1, CDR2, and CDR3; paragraph [0279]).

Magenta does a single embodiment comprising the antibody conjugated to a calicheamicin.

Wyeth discloses an antibody-calicheamicin conjugate with decreased aggregation (an antibody-calicheamicin conjugate with decreased aggregation; abstract).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the disclosure of Magenta to have used a calicheamicin conjugate of an anti-CD117 antibody, in order to provide a conjugate with decreased aggregation, as disclosed by Wyeth.

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 a combination of the Magenta and Wyeth references, unity of invention is lacking.