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(54) Title: BINDING MOLECULES AGAINST BCMA AND USES THEREOF

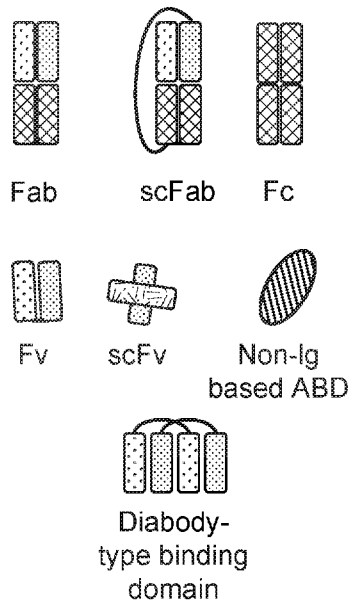


FIG. 1A

(57) Abstract: The present disclosure provides BCMA binding molecules that specifically bind to human BCMA, conjugates comprising the BCMA binding molecules, and pharmaceutical compositions comprising the BCMA binding molecules and the conjugates. The disclosure further provides methods of using the BCMA binding molecules to treat cancers that express cell surface BCMA. The disclosure yet further provides recombinant host cells engineered to express the BCMA binding molecules and methods of producing the BCMA binding molecules by culturing the host cells under conditions in which the BCMA binding molecules are expressed.

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[Continued on next page]

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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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))*
— *in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE*

(88) Date of publication of the international search report:
13 February 2020 (13.02.2020)

INTERNATIONAL SEARCH REPORT

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PCT/IB2019/054500

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61K39/395 A61P35/00
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)
A61P A61K C07K

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, WPI Data, BIOSIS, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2017/031104 A1 (JANSSEN PHARMACEUTICA NV [BE]; PILLARISETTI KODANDARAM [US]) 23 February 2017 (2017-02-23) page 3, 7-9; examples 5, 8-22; figures	1-16,19, 20, 23-43, 45-57

X	WO 2014/089335 A2 (AMGEN INC [US]) 12 June 2014 (2014-06-12)	1-16,19, 20, 23-42, 45-57
Y	page 6-7, figure 1, example 2, table 5	43

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[X] Further documents are listed in the continuation of Box C.

[X] 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
25 September 2019	18/12/2019

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Bernhardt, Wiebke

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	S HIPP ET AL: "A novel BCMA/CD3 bispecific T-cell engager for the treatment of multiple myeloma induces selective lysis in vitro and in vivo", LEUKEMIA, vol. 31, no. 8, 27 December 2016 (2016-12-27), pages 1743-1751, XP055547607, London ISSN: 0887-6924, DOI: 10.1038/leu.2016.388 abstract, figures, supplementary figure S2	1-16,19, 20, 23-43, 45-57
Y	BUELOW BEN ET AL: "T Cell Engagement without Cytokine Storm: A Novel Bcma x CD3 Antibody Killing Myeloma Cells with Minimal Cytokine Secretion", BLOOD, vol. 130, no. Suppl. 1, 7 December 2017 (2017-12-07), page 501, XP009516261, & 59TH ANNUAL MEETING OF THE AMERICAN-SOCIETY-OF-HEMATOLOGY (ASH); ATLANTA, GA, USA; DECEMBER 09 -12, 2017 abstract	43
Y	Ben Buelow ET AL: "Development of a fully human T cell engaging bispecific antibody for the treatment of multiple myeloma", , 2 June 2017 (2017-06-02), page 1, XP055476656, Retrieved from the Internet: URL:http://www.teneobio.com/wp-content/uploads/2018/01/Poster_1.pdf [retrieved on 2018-05-18] abstract	43
Y	GIRGIS SUZETTE ET AL: "Exploratory Pharmacokinetic/Pharmacodynamic and Tolerability Study of BCMAxCD3 in Cynomolgus Monkeys", BLOOD, vol. 128, no. 22, 2 December 2016 (2016-12-02), page 5668, XP009516262, & 58TH ANNUAL MEETING AND EXPOSITION OF THE AMERICAN-SOCIETY-OF-HEMATOLOGY (ASH); SAN DIEGO, CA, USA; DECEMBER 03 -06, 2016 abstract	43

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2019/054500

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2014/122144 A1 (ENGMAB AG [CH]) 14 August 2014 (2014-08-14) examples, claims -----	1-16,19, 20, 23-43, 45-57
Y	WO 2016/086196 A2 (XENCOR INC [US]) 2 June 2016 (2016-06-02) figure 3; sequence 18 -----	43
A	RUDIKOFF S ET AL: "Single amino acid substitution altering antigen-binding specificity", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (PNAS), US, vol. 79, no. 6, 1 March 1982 (1982-03-01), pages 1979-1983, XP002683593, ISSN: 0027-8424, DOI: 10.1073/PNAS.79.6.1979 abstract -----	1-16,19, 20, 23-43, 45-57

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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.:
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.:

16, 20(completely); 1-15, 19, 23-43, 45-57(partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 16, 20(completely); 1-15, 19, 23-43, 45-57(partially)

A BCMA binding molecule binding to human BCMA comprising the 6 CDRs of "AB1" according to table 1C to 1H; a BCMA binding molecule according to claim 43 comprising three polypeptides; medical use of said BCMA binding molecule; a conjugate comprising said BCMA binding molecule; a pharmaceutical composition comprising said BCMA binding molecule; a nucleic acid encoding said BCMA binding molecule; a cell engineered to express said BCMA binding molecule; a method of producing said BCMA binding molecule

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2. claims: 17, 21(completely); 1-15, 19, 23-43, 45-57(partially)

A BCMA binding molecule binding to human BCMA comprising the 6 CDRs of "AB2" according to table 1C to 1H; a BCMA binding molecule according to claim 43 comprising three polypeptides; medical use of said BCMA binding molecule; a conjugate comprising said BCMA binding molecule; a pharmaceutical composition comprising said BCMA binding molecule; a nucleic acid encoding said BCMA binding molecule; a cell engineered to express said BCMA binding molecule; a method of producing said BCMA binding molecule

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3-19. claims: 1-15, 19, 23-42, 45-57(all partially)

A BCMA binding molecule binding to human BCMA comprising the 6 CDRs of "R1F2" to "PALF20", respectively, according to table 1C to 1H; medical use of said BCMA binding molecule; a conjugate comprising said BCMA binding molecule; a pharmaceutical composition comprising said BCMA binding molecule; a nucleic acid encoding said BCMA binding molecule; a cell engineered to express said BCMA binding molecule; a method of producing said BCMA binding molecule

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20. claims: 18, 22, 44(completely); 1-15, 19, 23-43, 45-57(partially)

A BCMA binding molecule binding to human BCMA comprising the 6 CDRs of "AB3" according to table 1I to 1N; a BCMA binding molecule according to claims 43 and 44 comprising three polypeptides; medical use of said BCMA binding molecule; a conjugate comprising said BCMA binding molecule; a pharmaceutical composition comprising said BCMA binding molecule; a nucleic acid encoding said BCMA binding molecule; a cell engineered to express said BCMA binding molecule; a method of producing said BCMA binding molecule

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

21-46. claims: 1-15, 19, 23-42, 45-57(all partially)

A BCMA binding molecule binding to human BCMA comprising the 6 CDRs of "PI-61" to "H3-15", respectively, according to table 1I to 1N; medical use of said BCMA binding molecule; a conjugate comprising said BCMA binding molecule; a pharmaceutical composition comprising said BCMA binding molecule; a nucleic acid encoding said BCMA binding molecule; a cell engineered to express said BCMA binding molecule; a method of producing said BCMA binding molecule

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2019/054500

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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