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(71) Applicants: JUNO THERAPEUTICS, INC. [US/US];

400 Dexter Avenue N., Suite 1200, Seattle, Washington

98109 (US). MEMORIAL SLOAN KETTERING CAN-

CER CENTER [US/US]; 1275 York Avenue, New York, New York 10065 (US).

(72) Inventors: SATHER, Blythe D.; 400 Dexter Avenue N.,

Suite 1200, Seattle, Washington 98109 (US). SMITH, Eric

L.; 1275 York Avenue, New York, New York 10065 (US).

TAREEN, Semih; 400 Dexter Ave. N, Suite 1200, Seattle,

Washington 98109 (US). CHEN, Aye; 400 Dexter Ave. N,

Suite 1200, Seattle, Washington 98109 (US). DE IMUS,

Cyr; 400 Dexter Ave. N, Suite 1200, Seattle, Washington

98109 (US). HESS, Erik; 400 Dexter Ave. N, Suite 1200,

Seattle, Washington 98109 (US). OLSHEFSKY, Audrey;

400 Dexter Ave. N, Suite 1200, Seattle, Washington 98109

(US). PONKO, Stefan; 400 Dexter Ave. N, Suite 1200,

Seattle, Washington 98109 (US). STIRNER, Mariana Co-

ta; 400 Dexter Ave. N, Suite 1200, Seattle, Washington

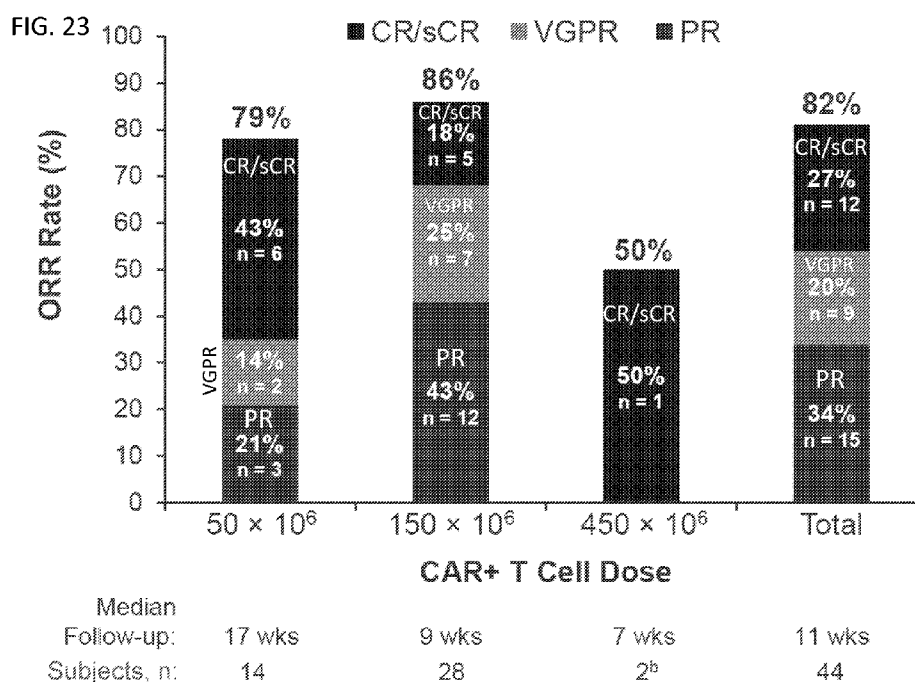
98109 (US).

(74) Agent: AHN, Sejin et al.; Morrison & Foerster LLP,

12531 High Bluff Drive, Suite 100, San Diego, California

92130-2040 (US).

(54) Title: METHODS FOR TREATMENT USING CHIMERIC ANTIGEN RECEPTORS SPECIFIC FOR B-CELL MATURATION ANTIGEN



(57) **Abstract:** Provided herein are adoptive cell therapy methods involving the administration of doses of cells for treating disease and conditions, including certain plasma cell malignancy. The cells generally express recombinant receptors such as chimeric antigen receptors (CARs) specific to B-cell maturation antigen (BCMA). In some embodiments, the methods are for treating subjects with multiple myeloma (MM). Also provided are genetically engineered cells containing such BCMA-binding receptors for uses in adoptive cell therapy.



(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, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, 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, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Declarations under Rule 4.17:

- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
- *of inventorship (Rule 4.17(iv))*

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))*

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27 August 2020 (27.08.2020)

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International application No
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A. CLASSIFICATION OF SUBJECT MATTER INV. C07K16/30 C07K16/28 A61P35/00 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		
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, 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.
Y	WO 2016/014565 A2 (NOVARTIS AG [CH]; UNIV PENNSYLVANIA [US] ET AL.) 28 January 2016 (2016-01-28) e.g. claims 25,33,35,36,39,51,54; example 13; page 270, paragraph 1; page 290, paragraph 2; page 324, lines 21-24; page 354, lines 18-20; the whole document	1,5-146, 150, 154-178
A	WO 2018/085690 A1 (BLUEBIRD BIO INC [US]) 11 May 2018 (2018-05-11) e.g. claims 1,32,40; example 2; the whole document ----- -/-	1,5-146, 150, 154-178
☒ 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 6 February 2020		Date of mailing of the international search report 08/07/2020
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 Gruber, Andreas

INTERNATIONAL SEARCH REPORT

International application No
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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.
A	WO 2018/175988 A1 (LENTIGEN TECH INC [US] ET AL.) 27 September 2018 (2018-09-27) e.g. page 8, paragraph 1; page 34, paragraph 4; SEQ ID NO: 86; the whole document -----	1,5-146, 150, 154-178
A	WO 2016/090327 A2 (SLOAN KETTERING INST CANCER [US]; EUREKA THERAPEUTICS INC [US]) 9 June 2016 (2016-06-09) e.g. example 1; claims 1,2; SEQ ID NO: 53, 54; the whole document -----	1,5-146, 150, 154-178
Y	WO 2016/090320 A1 (SLOAN KETTERING INST CANCER [US]; EUREKA THERAPEUTICS INC [US]) 9 June 2016 (2016-06-09) e.g. claims 1,5,12,72,104,105; example 8; SEQ ID NO 53, 54; the whole document -----	1,5-146, 150, 154-178
A	CN 107 827 989 A (YINFENG BIOLOGICAL GROUP CO LTD ET AL.) 23 March 2018 (2018-03-23) e.g. claims 1,5,6,10; the whole document -----	1,5-146, 150, 154-178

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/059271

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.:

1, 5-146, 150, 154-178(all 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: 1, 5-146, 150, 154-178(all partially)

method of claim 1, dose of claim 97, use of claim 146, use of claim 150, all comprising use of CAR with SEQ ID NO: 97,101,103 and 105,107,108 or SEQ ID NO: 116 and 119 and prior treatment with fludarabine and/or cyclophosphamide

1.1. claims: 1, 5-146, 150, 154-178(all partially)

method of claim 1, dose of claim 97, use of claim 146, use of claim 150, all comprising use of CAR with SEQ ID NO: 97,101,103 and 105,107,108 and prior treatment with fludarabine and/or cyclophosphamide

1.2. claims: 1, 5-146, 150, 154-178(all partially)

method of claim 1, dose of claim 97, use of claim 146, use of claim 150, all comprising use of CAR with SEQ ID NO: 116 and 119 and prior treatment with fludarabine and/or cyclophosphamide

2. claims: 1, 5-146, 150, 154-178(all partially)

method of claim 1, dose of claim 97, use of claim 146, use of claim 150, all comprising use of CAR with SEQ ID NO: 96,100,103 and 105,107,108 and prior treatment with fludarabine and/or cyclophosphamide

3. claims: 1, 5-146, 150, 154-178(all partially)

method of claim 1, dose of claim 97, use of claim 146, use of claim 150, all comprising use of CAR with SEQ ID NO:95,99,103 and 105,107,108 and prior treatment with fludarabine and/or cyclophosphamide

4. claims: 1, 5-146, 150, 154-178(all partially)

method of claim 1, dose of claim 97, use of claim 146, use of claim 150, all comprising use of CAR with SEQ ID NO:94,98,102 and 104,106,108 and prior treatment with fludarabine and/or cyclophosphamide

5. claims: 2, 147, 151(completely); 5-146, 154-178(partially)

method of claim 2, dose of claim 97, use of claim 147, use of claim 151, all comprising use of CAR with SEQ ID NOs specified in claim 2 and prior treatment with ASCT, immunomodulatory agent, proteasome inhibitor or anti-CD38

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

6. claims: 3, 148, 152(completely); 5-146, 154-178(partially)

method of claim 3, dose of claim 97, use of claim 148, use of claim 152, all comprising use of CAR with SEQ ID NO as specified in claim 3 and subject has not had active or history of PCL

7. claims: 4, 149, 153(completely); 5-146, 154-178(partially)

method of claim 4, dose of claim 97, use of claim 149, use of claim 153, all comprising use of CAR with SEQ ID NO as specified in claim 4 and the dose is as specified in claim 4, a certain ratio of CD4+ and CD8+ T cells is used or a certain percentage as specified in claim 4 express a marker of apoptosis

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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