(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
06 May 2021 (06.05.2021)

WIPO | PCT

(10) International Publication Number
WO 2021/087368 A3

(51) International Patent Classification:
C07K 16/28 (2006.01) *A61P 35/00* (2006.01)
A61K 39/395 (2006.01)

(21) International Application Number:
PCT/US2020/058373

(22) International Filing Date:
30 October 2020 (30.10.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

62/929,137	01 November 2019 (01.11.2019)	US
62/929,194	01 November 2019 (01.11.2019)	US
62/929,207	01 November 2019 (01.11.2019)	US
62/929,283	01 November 2019 (01.11.2019)	US
62/929,288	01 November 2019 (01.11.2019)	US
62/929,347	01 November 2019 (01.11.2019)	US
62/929,601	01 November 2019 (01.11.2019)	US
62/940,742	26 November 2019 (26.11.2019)	US
62/978,147	18 February 2020 (18.02.2020)	US
63/015,348	24 April 2020 (24.04.2020)	US
63/046,046	30 June 2020 (30.06.2020)	US
63/046,164	30 June 2020 (30.06.2020)	US
63/084,903	29 September 2020 (29.09.2020)	US

(71) Applicant: **MAGENTA THERAPEUTICS, INC.** [US/US]; 100 Technology Square, 5th Floor, Cambridge, Massachusetts 02139 (US).

(72) Inventors: **BOITANO, Anthony**; 27 Evelyn Road, Newton, Massachusetts 02468 (US). **COOKE, Michael**; 1387 Washington St., Unit 202, Boston, Massachusetts 02118 (US). **MCDONAGH, Charlotte**; 27 Fells Road, Winchester, Massachusetts 01890 (US). **PALCHAUDHURI, Rahul**; 46 Springfield Street, Apt. 2, Somerville, Massachusetts 02143 (US). **PANWAR, Rajiv**; 11 Adeline Way, Acton, Massachusetts 01720 (US). **PEARSE, Bradley R.**; 18 Priest Road, Watertown, Massachusetts 02472 (US). **WIDBOOM, Paul Fredrick**; 3 Ledge Road, Hanover, New Hampshire 03755 (US). **CRUITE, Patricia Ann**; 197 Ashcroft Rd, Medford, Massachusetts 02155 (US).

(74) Agent: **ERICKSON, Briana M.** et al.; Womble Bond Dickinson (US) LLP, Independence Wharf, 470 Atlantic Avenue, Suite 600, Boston, Massachusetts 02210 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM,

(54) Title: ANTI-CD45 ANTIBODIES AND CONJUGATES THEREOF

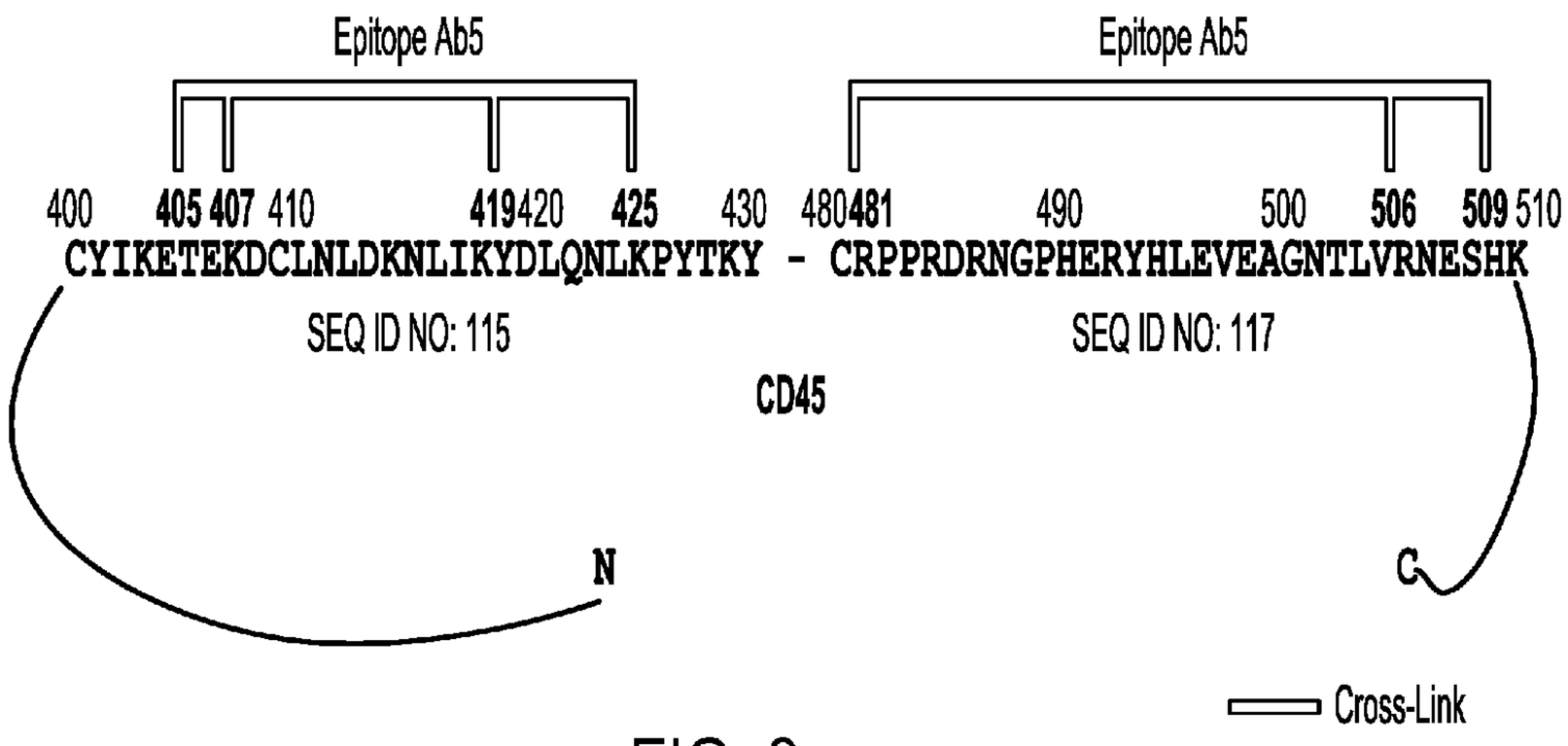

FIG. 3

(57) Abstract: Disclosed are anti-CD45 antibodies, antigen binding fragments thereof, and antibody drug conjugates (ADCs) that specifically bind to human CD45. Such antibodies and ADCs are useful in therapeutic methods, including methods of depleting CD45+ cells from a patient. The compositions and methods described herein can be used to treat a disorder directly, for instance, by depleting a population of CD45+ cancer cells or autoimmune cells. The compositions and methods described 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 CD45+ cells prior to the transplant procedure.

[Continued on next page]

WO 2021/087368 A3

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, IT, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

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

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

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))*

(88) Date of publication of the international search report:
10 June 2021 (10.06.2021)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US20/58373

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C07K 16/28; A61K 39/395; A61P 35/00 (2020.01)

CPC - C07K 16/289; C07K 16/28; A61K 39/3955; A61K 39/39558; A61K 39/395; A61P 35/00

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.
	-***-1ST INVENTION-***-	
X	(ATLAS ANTIBODIES AB) Anti-CD45 Product Datasheet Monoclonal Antibody. Product Datasheet (online). December 2012 [retrieved 16 March 2021]. Retrieved from the Internet: [URL: https://atlasantibodies.com/products/AMAb90519]; page 1	14-15
A	US 2014/0271617 A1 (CHUGAI SEIYAKU KABUSHIKI KAISHA) 18 September 2014; abstract; paragraphs [0054], [0112], [0201], [0471]-[0472]	1-5, 13
A	US 2018/0237521 A1 (UCB BIOPHARMA SPRL) 23 August 2018; Claim 1	1-5, 13
A	US 2012/0171223 A1 (SASS, PM et al.) 5 July 2012; abstract; paragraph [0015]	1
A	US 2008/0124345 A1 (ROTHE, M et al.) 29 May 2008; paragraph [0034]; claim 5	2
A	US 2007/0003554 A1 (MILLER, JL) 4 January 2007; abstract; Claim 8	3
A	US 2009/0117124 A1 (LIU, W et al.) 7 May 2009; Claims 2, 8	13
A	(SYMONS, A et al.) Domain organization of the extracellular region of CD45. Protein Engineering. 1999, Vol. 12, No. 10; pages 885-892; DOI: 10.1093/protein/12.10.885	1-5, 13-15

☒ 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
16 March 2021 (16.03.2021)	APR 22 2021
Name and mailing address of the ISA/US 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/US20/58373

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-***-2ND INVENTION-***-	
A	US 2014/0271617 A1 (CHUGAI SEIYAKU KABUSHIKI KAISHA) 18 September 2014; abstract; paragraphs [0054], [0112], [0201], [0471]-[0472]	1-5, 13
A	US 2018/0237521 A1 (UCB BIOPHARMA SPRL) 23 August 2018; Claim 1	1-5, 13-15
A	US 2015/0030600 A1 (MARKS, JD et al.) 29 January 2015; page 185, sequence 326	1-2
A	US 2007/0003554 A1 (MILLER, JL) 4 January 2007; abstract; Claim 8	3
A	US 2009/0117124 A1 (LIU, W et al.) 7 May 2009; Claims 2, 8	13
A	(ATLAS ANTIBODIES AB) Anti-CD45 Product Datasheet Monoclonal Antibody. Product Datasheet (online). December 2012 [retrieved 16 March 2021]. Retrieved from the Internet: [URL: https://atlasantibodies.com/products/AMAb90519]; page 1	14-15
A	US 2007/0161081 A1 (JIN, P et al.) 12 July 2007; Table 5; paragraph [0541]	14-15
A	(SYMONS, A et al.) Domain organization of the extracellular region of CD45. Protein Engineering. 1999, Vol. 12, No. 10; pages 885-892; DOI: 10.1093/protein/12.10.885	1-5, 13-15
P, X	WO 2020/092654 A1 (MAGENTA THERAPEUTICS, INC.) 7 May 2020; entire document	14-15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US20/58373

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.: 6-12, 17-89
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.:
-***-Please See Supplemental Page-***-

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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US20/58373

-***-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.

Groups I+, Claims 1-5, 13-16, and an anti-CD45 antibody encompassing a heavy chain encompassing SEQ ID NO: 9 (heavy chain), a heavy chain variable region encompassing SEQ ID NO: 1 (HCVR), a CDR1 encompassing SEQ ID NO: 2 (HCDR1) a CDR2 encompassing SEQ ID NO: 3 (HCDR2), and a CDR3 encompassing SEQ ID NO: 4 (HCDR3), and a light chain encompassing SEQ ID NO: 10 (light chain), a light chain variable region encompassing SEQ ID NO: 5 (LCVR), a CDR1 encompassing SEQ ID NO: 6 (LCDR1), a CDR2 encompassing SEQ ID NO: 7 (LCDR2), and a CDR3 encompassing SEQ ID NO: 8 (LCDR3); and an epitope within SEQ ID NO: 114 (epitope) are directed toward anti-CD45 antibodies.

The antibodies will be searched to the extent they encompass an anti-CD45 antibody encompassing a heavy chain encompassing SEQ ID NO: 9 (first exemplary heavy chain), a heavy chain variable region encompassing SEQ ID NO: 1 (first exemplary HCVR), a CDR1 encompassing SEQ ID NO: 2 (first exemplary HCDR1) a CDR2 encompassing SEQ ID NO: 3 (first exemplary HCDR2), and a CDR3 encompassing SEQ ID NO: 4 (first exemplary HCDR3), and a light chain encompassing SEQ ID NO: 10 (first exemplary light chain), a light chain variable region encompassing SEQ ID NO: 5 (first exemplary LCVR), a CDR1 encompassing SEQ ID NO: 6 (first exemplary LCDR1), a CDR2 encompassing SEQ ID NO: 7 (first exemplary LCDR2), and a CDR3 encompassing SEQ ID NO: 8 (first exemplary LCDR3); and an epitope within SEQ ID NO: 114 (first exemplary epitope) Applicant is invited to elect additional antibody(ies), with specified set(s) of sequence(s) thereof, and corresponding epitope(s) bound by said antibody(ies), with specified SEQ ID NO: for each elected species, or with specified substitution(s) at specified site(s) of a SEQ ID NO:, such that the sequence of each elected species is fully specified (i.e. no optional or variable residues or substituents), and where available as an option within at least one searchable claim, to be searched. Additional set(s) of antibody and/or epitope sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1-5 (each in-part), and 13-15 (each in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass an anti-CD45 antibody encompassing a heavy chain encompassing SEQ ID NO: 9 (heavy chain), a heavy chain variable region encompassing SEQ ID NO: 1 (HCVR), a CDR1 encompassing SEQ ID NO: 2 (HCDR1) a CDR2 encompassing SEQ ID NO: 3 (HCDR2), and a CDR3 encompassing SEQ ID NO: 4 (HCDR3), and a light chain encompassing SEQ ID NO: 10 (light chain), a light chain variable region encompassing SEQ ID NO: 5 (LCVR), a CDR1 encompassing SEQ ID NO: 6 (LCDR1), a CDR2 encompassing SEQ ID NO: 7 (LCDR2), and a CDR3 encompassing SEQ ID NO: 8 (LCDR3); and an epitope within SEQ ID NO: 114 (epitope). Applicants must specify the searchable claims that encompass any additionally elected 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 an anti-CD45 antibody encompassing a heavy chain encompassing SEQ ID NO: 19 (heavy chain), a heavy chain variable region encompassing SEQ ID NO: 11 (HCVR), a CDR1 encompassing SEQ ID NO: 12 (HCDR1) a CDR2 encompassing SEQ ID NO: 13 (HCDR2), and a CDR3 encompassing SEQ ID NO: 14 (HCDR3), and a light chain encompassing SEQ ID NO: 20 (light chain), a light chain variable region encompassing SEQ ID NO: 15 (LCVR), a CDR1 encompassing SEQ ID NO: 16 (LCDR1), a CDR2 encompassing SEQ ID NO: 17 (LCDR2), and a CDR3 encompassing SEQ ID NO: 18 (LCDR3).

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

Groups I+ share the technical features including: an isolated anti-CD45 antibody, or antigen binding portion thereof, comprising: (a) a heavy chain variable region comprising a CDR1 domain, a CDR2 domain, and a CDR3 domain; and a light chain variable region comprising a CDR1 domain, a CDR2 domain, and a CDR3 domain; and an isolated anti-CD45 antibody comprising (a) a heavy chain amino acid sequence, and a light chain amino acid sequence.

However, these shared technical features are previously disclosed by US 2018/0237521 A1 to UCB Biopharma SPRL (hereinafter 'UCB').

UCB discloses an isolated anti-CD45 antibody, or antigen binding portion thereof (an isolated anti-CD45 antibody, or antigen binding portion thereof; paragraphs [0010], [0019]), comprising: (a) a heavy chain variable region (a heavy chain variable region; paragraph [0019]) comprising a CDR1 domain (comprising a CDR1 domain; paragraph [0019]), a CDR2 domain (a CDR2 domain; paragraph [0019]), and a CDR3 domain (a CDR3 domain; paragraph [0019]); and a light chain variable region (a light chain variable region; paragraph [0026]) comprising a CDR1 domain (comprising a CDR1 domain; paragraph [0026]), a CDR2 domain (a CDR2 domain; paragraph [0026]), and a CDR3 domain (a CDR3 domain; paragraph [0026]); and comprising (a) a heavy chain amino acid sequence (comprising (a) a heavy chain amino acid sequence; paragraph [0019]), and a light chain amino acid sequence (a light chain amino acid sequence; paragraph [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 UCB reference, unity of invention is lacking.

-***-Continued From Box III: Item III-***-

Claims 1-5, 13-15; 1st invention) anti-CD45 antibody encompassing a heavy chain encompassing SEQ ID NO: 9 (heavy chain), a heavy chain variable region encompassing SEQ ID NO: 1 (HCVR), a CDR1 encompassing SEQ ID NO: 2 (HCDR1) a CDR2 encompassing SEQ ID NO: 3 (HCDR2), and a CDR3 encompassing SEQ ID NO: 4 (HCDR3), and a light chain encompassing SEQ ID NO: 10 (light chain), a light chain variable region encompassing SEQ ID NO: 5 (LCVR), a CDR1 encompassing SEQ ID NO: 6 (LCDR1), a CDR2 encompassing SEQ ID NO: 7 (LCDR2), and a CDR3 encompassing SEQ ID NO: 8 (LCDR3); and an epitope within SEQ ID NO: 114 (epitope); 2nd invention) anti-CD45 antibody that encompasses a heavy chain comprising SEQ ID NO: 49 (heavy chain), a heavy chain variable region comprising SEQ ID NO: 41 (HCDR), a CDR1 comprising SEQ ID NO: 42 (HCDR1) a CDR2 comprising SEQ ID NO: 43 (HCDR2), and a CDR3 comprising SEQ ID NO: 44 (HCDR3), and a light chain comprising SEQ ID NO: 50 (light chain), a light chain variable region comprising SEQ ID NO: 45 (LCDR), a CDR1 comprising SEQ ID NO: 46 (LCDR1), a CDR2 comprising SEQ ID NO: 47 (LCDR2), and a CDR3 comprising SEQ ID NO: 48 (LCDR3), and an epitope within SEQ ID NO: 116