



(51) International Patent Classification:
C07K 16/28 (2006.01) C07K 16/18 (2006.01)

(21) International Application Number:
PCT/US2019/028987

(22) International Filing Date:
24 April 2019 (24.04.2019)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/662,605 25 April 2018 (25.04.2018) US
62/756,494 06 November 2018 (06.11.2018) US

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(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.

(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).



WO 2019/209995 A3

(54) Title: OPTIMIZED ANTI-TL1A ANTIBODIES

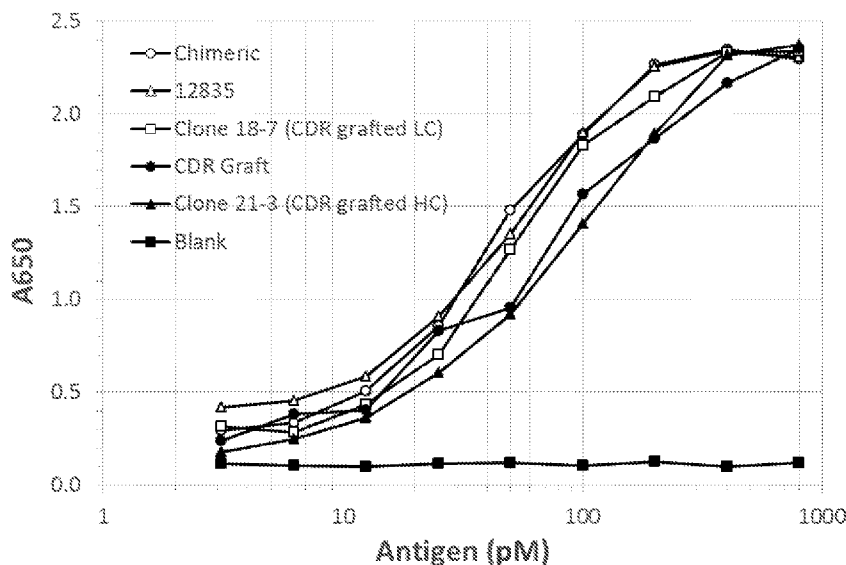


FIG. 5

(57) Abstract: Described herein are humanized anti-TL1A antibodies and pharmaceutical compositions for the treatment of inflammatory bowel disease (IBD), such as Crohns Disease (CD) and ulcerative colitis (UC).

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))*

(88) Date of publication of the international search report:

12 December 2019 (12.12.2019)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 19/28987

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(8) - C07K 16/28, C07K 16/18 (2019.01)
 CPC - C07K2317/76, C07K2317/565, C07K2317/56, C07K2317/24, G01N2800/065

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	US 2018/0064825 A1 (INSERM (INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE) et al.) 08 March 2018 (08.03.2018) Abstract, para [0055], SEQ ID NO: 18	1, 7, 8/(1,7), 11
A	US 7,700,739 B2 (LACY et al.) 20 April 2010 (20.04.2010) col 45, ln 24-29; SEQ ID NO: 49	1, 7, 8/(1,7), 11
A	US 2015/0299720 A1 (MONSANTO TECHNOLOGY LLC) 22 October 2015 (22.10.2015) Claim 1; SEQ ID NO 19998	1, 7, 8/(1,7), 11
A	WO 2006/017173 A1 (ALEXION PHARMACEUTICALS, INC.) 16 February 2006 (16.02.2006) Claim 14; SEQ ID NO 37	1, 7, 8/(1,7), 11
A	WO 2003/068821 A2 (IMMUNOMEDICS, INC.) 21 August 2003 (21.08.2003) Claim 6; Page 68	1, 7, 8/(1,7), 11
A	WO 2014/051109 A1 (KYOWA HAKKO KIRIN CO., LTD.) 03 April 2014 (03.04.2014) Claim 1; SEQ ID NO 65	1, 7, 8/(1,7), 11
A	WO 2017/076878 A1 (BIOUNIVERSA S.R.L.) 11 May 2017 (11.05.2017) Claim 1; SEQ ID NO 12	1, 7, 8/(1,7), 11
A	WO 2014/197849 A2 (IGENCIA BIOTHERAPEUTICS) 11 December 2014 (11.12.2014) Claim 29; SEQ ID NO 26	1, 7, 8/(1,7), 11
A	US 2014/0315250 A1 (TEVA BIOPHARMACEUTICALS USA INC.) 23 October 2014 (23.10.2015) Abstract	1, 7, 8/(1,7), 11

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

03 October 2019

Date of mailing of the international search report

29 OCT 2019

Name and mailing address of the ISA/US

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 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 19/28987

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.: 9-10, 22-48
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 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, 7, 8/(1,7) and 11

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.

continuation of Box 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 searched, the appropriate additional search fees must be paid.

Group I+: Claims 1-8 and 11-21 directed to an antibody or antigen-binding fragment that specifically binds TL1A and comprises a heavy chain variable region (VH) and VCDR1-3, and a light chain variable region (VL), and LCDR1-3, and heavy and light chain framework regions on either side of each CDR. The TL1A antibody will be searched to the extent that the antibody (clone L8) comprises a VH comprising the sequence SEQ ID NO: 491, the VH comprising HCDR1-HCDR3 comprising the sequences of SEQ ID NOS: 553, 554, and 565; and a light chain variable region (VL), comprising the sequence SEQ ID NO: 490, the VL comprising LCDR1-LCDR3 comprising the sequences of SEQ ID NOS: 569, 488 and 571. It is believed that claims 1, 7-8 and 11 limited to a TL1A antibody comprising VH and VL comprising SEQ ID Nos: 491 and 490, HCDR1-3 comprising SEQ ID Nos: 553, 554, 565; and LCDR1-3 comprising SEQ ID Nos: 569, 488 and 571 encompass this first named invention, and thus these claims will be searched without fee to the extent that the antibody encompasses said sequences. Additional TL1A antibodies will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected oligonucleotides. 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. An exemplary election would be a TL1A antibody comprising VH and VL comprising SEQ ID Nos: 503 and 502, respectively, the HCDR1-3 (within VH) comprising SEQ ID Nos: 553, 559, 567; and LCDR1-3 comprising SEQ ID Nos: 570, 488 and 573 (claims 1, 7-8, 11-13).

The inventions listed as Groups I+ do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Common Technical Features

No technical features are shared between the amino acid sequences of the antibodies (or fragments therein) of Groups I+ and, accordingly, these groups lack unity a priori.

Additionally, even if the inventions listed as Group I+ were considered to share technical features, these shared technical features are previously disclosed by the prior art, as further discussed below.

The inventions of Group I+ share the technical feature of an antibody or antigen-binding fragment that specifically binds TL1A and comprises a heavy chain variable region (VH) and VCDR1-3, and a light chain variable region (VL), and LCDR1-3, and heavy and light chain framework regions on either side of each CDR. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is anticipated by US 2018/0086840 A1 to Glenmark Pharmaceuticals S. A. (hereinafter 'Glenmark'). Glenmark teaches TL1A antibodies having said VH, VL, HCDR1-3, and LCDR1-3 (para [0010] "antibodies or fragments thereof that bind to TL1A, methods for their preparation and use, including methods for treating TL1A mediated disorders.", para [0012] "the present invention provides an antibody or fragment thereof that binds to TL1A comprising a heavy chain variable region", para [0013] "the present invention provides an antibody or fragment thereof comprising a heavy chain variable framework region", para [0015] "the present invention provides an antibody or fragment thereof that binds to TL1A comprising a light chain variable region sequence", para [0016] "the present invention provides an antibody or fragment thereof comprising a light chain variable framework region", para [0073] "All Complementarity Determining Regions (CDRs) discussed in the present invention, are defined preferably according to IMGT.RTM.. The variable domain residues for each of these CDRs are as follows (numbering according to Kabat E A, et al., supra): LCDR1: 27-32, LCDR2: 50-52, LCDR3: 89-97, HCDR1: 26-35, HCDR2: 51-57 and HCDR3: 93-102.").

As the technical feature was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the inventions.

The inventions of Group I+ therefore lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.