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

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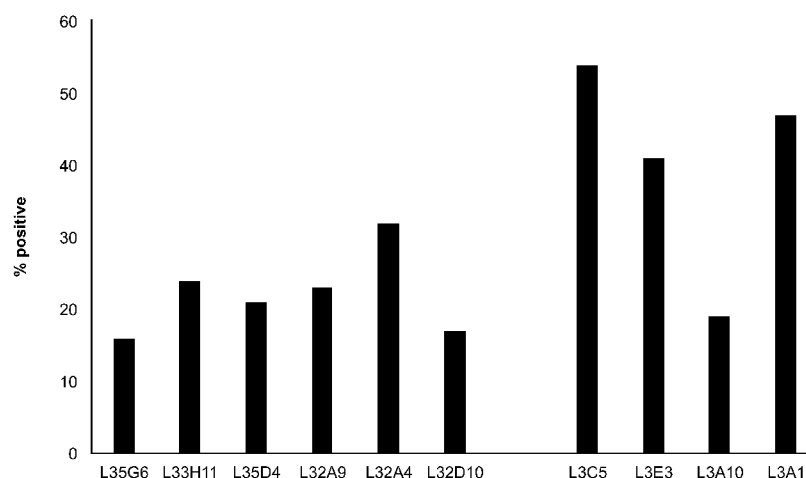
— with sequence listing part of description (Rule 5.2(a))

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

2 March 2017

(54) Title: ANTIBODY THERAPEUTICS THAT BIND LAG3

Figure 1



(57) Abstract: There is disclosed compositions and methods relating to or derived from anti-LAG3 antibodies. More specifically, there is disclosed fully human antibodies that bind LAG3, LAG3-antibody binding fragments and derivatives of such antibodies, and LAG3-binding polypeptides comprising such fragments. Further still, there is disclosed nucleic acids encoding such antibodies, antibody fragments and derivatives and polypeptides, cells comprising such polynucleotides, methods of making such antibodies, antibody fragments and derivatives and polypeptides, and methods of using such antibodies, antibody fragments and derivatives and polypeptides, including methods of treating a disease.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/43562

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/395; 45/06; C07K 16/18 (2016.01)

CPC - A61K 39/395; 45/06; C07K 16/18

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)

IPC(8): A61K 39/00, 39/395; 45/00, 45/06; C07K 16/00, 16/18 (2016.01)

CPC: A61K 39/00, 39/395; 45/00, 45/06; C07K 16/00, 16/18

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)

PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); EBSCO Discovery; PubMed; Google Scholar; The Lens; ENA; NCBI Blast; KEYWORDS: LAG3, antibody, heavy chain, light chain, linker

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2014/0093511 A1 (BRISTOL-MYERS SQUIBB COMPANY) April 3, 2014; abstract; paragraphs [0007], [0009], [0053], [0056]	1-2, 3/1-2, 4-5, 6/4-5, 7-8, 9/7-8, 18-21, 22/18-21, 23/22/18-21, 24/18-21
A	US 2013/0323248A1 (SORRENTO THERAPEUTICS INC.) December 5, 2013; paragraphs [0008], [0015]	1-2, 3/1-2, 4-5, 6/4-5, 7-8, 9/7-8, 18-21, 22/18-21, 23/22/18-21, 24/18-21
A	US 2009/0104204 A1 (THROSBY, M et al.) April 23, 2009; claim 1	1-2, 3/1-2, 4-5, 6/4-5, 7-8, 9/7-8
A	US 2004/0142382 A1 (VELDMAN, G et al.) July 22, 2004; claim 1	18-21, 22/18-21, 23/22/18-21, 24/18-21
A	US 2014/0294827 A1 (GASTWIRT, R et al.) October 2, 2014; paragraph [0012]	18-21, 22/18-21, 23/22/18-21, 24/18-21
A	US 2005/0220795 A1 (WITTRUP, K et al.) October 6, 2005; paragraph [0089]	18-21, 22/18-21, 23/22/18-21, 24/18-21
A	US 2014/0349349 A1 (BUTAMAX ADVANCED BIOFUELS LLC) November 27, 2014; paragraph [0036]	18-21, 22/18-21, 23/22/18-21, 24/18-21
A	US 2013/0011406A1 (HADARI, Y et al.) January 10, 2013; Table 1C	18-21, 22/18-21, 23/22/18-21, 24/18-21

☐ 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

07 November 2016 (07.11.2016)

Date of mailing of the international search report

12 January 2017

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/43562

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.: 10-17, 25-28
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.:

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.:

1-2, 3/1-2, 4-5, 6/4-5, 7-8, 9/7-8, 18-21, 22/18-21, 23/22/18-21, 24/18-21

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
Information on patent family members

International application No.

PCT/US16/43562

-Continued from Box III-

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 1-9, 18-24 and SEQ ID NOs: 1, 2, 15, 16, 17, 18, 19 and 20 are directed toward an isolated antibody or fragment thereof that binds to a LAG3 epitope.

The antibody and fragments thereof will be searched to the extent it encompasses a heavy chain variable domain encompassing SEQ ID NO: 1 (first exemplary VH), an HCDR1 encompassing SEQ ID NO: 15 (first exemplary HCDR1), an HCDR2 encompassing SEQ ID NO: 16 (first exemplary HCDR2), and an HCDR3 encompassing SEQ ID NO: 17 (first exemplary HCDR3) and a light chain variable domain encompassing SEQ ID NO: 2 (first exemplary VL), an LCDR1 encompassing SEQ ID NO: 18 (first exemplary LCDR1), an LCDR2 encompassing SEQ ID NO: 19 (first exemplary LCDR2) and an LCDR3 encompassing SEQ ID NO: 20 (first exemplary LCDR3). Applicant is invited to elect additional light and/or heavy chain variable region sequence(s) and corresponding CDR(s) with specified SEQ ID NOs: for each, to be searched. Additional light and/or heavy chain variable region sequence(s) and associated CDR(s) will be searched upon the payment of additional fees. It is believed that claims 1 (in-part), 2 (in-part), 3 (in-part), 4 (in-part), 5 (in-part), 6 (in-part), 7 (in-part), 8 (in-part), 9 (in-part), 18 (in-part), 19 (in-part), 20 (in-part), 21 (in-part), 22 (in-part), 23 (in-part) and 24 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 1 (VH), SEQ ID NO: 15 (HCDR1), SEQ ID NO: 16 (HCDR2), SEQ ID NO: 17 (HCDR3), SEQ ID NO: 2 (VL), SEQ ID NO: 18 (LCDR1), SEQ ID NO: 19 (LCDR2) and SEQ ID NO: 20 (LCDR3). 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 a heavy chain variable domain encompassing SEQ ID NO: 8 (first exemplary elected VH), an HCDR1 encompassing SEQ ID NO: 36 (first exemplary elected HCDR1), an HCDR2 encompassing SEQ ID NO: 37 (first exemplary elected HCDR2), and an HCDR3 encompassing SEQ ID NO: 38 (first exemplary elected HCDR3).

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

Groups I+ share the technical features including: an isolated fully human antibody of an IgG class that binds to a LAG3 epitope, said antibody comprising a heavy chain variable domain sequence; and a light chain variable domain sequence; an anti-LAG3 fully human antibody Fab fragment comprising a heavy chain variable domain sequence and comprising a light chain variable domain sequence; an anti-LAG3 single chain human antibody comprising a heavy chain variable domain and a light chain variable domain which are connected by a peptide linker; and an isolated anti-human LAG3 (hLAG3) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain comprising a heavy chain CDR set (CDR1, CDR2, and CDR3); and a light chain variable domain comprising a light chain CDR set (CDR1, CDR2, and CDR3).

However, these shared technical features are previously disclosed by US 2014/0093511 A1 to Bristol-Myers Squibb Company (hereinafter 'BMS').

BMS discloses an isolated (isolated; abstract) fully human (human (fully human); paragraph [0056]) antibody (antibody; abstract, paragraphs [0007], [0056]) of an IgG class (of an IgG class; paragraph [0022]) that binds to a LAG3 epitope (that binds to LAG-3 (a LAG3 epitope); abstract, paragraph [0007]), said antibody comprising a heavy chain variable domain sequence (said antibody comprising a heavy chain variable domain sequence; paragraph [0009]); and a light chain variable domain sequence (and a light chain variable domain sequence; paragraph [0009]); an anti-LAG3 (an anti-LAG3; abstract, paragraph [0007]) fully human (human (fully human); paragraph [0056]) antibody Fab fragment (antibody Fab fragment; paragraph [0022]) comprising a heavy chain variable domain sequence (comprising a heavy chain variable domain sequence; paragraph [0009]) and comprising a light chain variable domain sequence (a light chain variable domain sequence; paragraph [0009]); an anti-LAG3 (anti-LAG3; abstract, paragraph [0007]) single chain (single chain; paragraphs [0022], [0053]) human antibody (human antibody; paragraph [0056]) comprising a heavy chain variable domain (comprising a heavy chain variable domain; paragraph [0009]) and a light chain variable domain (a light chain variable domain; paragraph [0009]) which are connected by a peptide linker (which are connected by a peptide linker; paragraph [0053]); and an isolated (isolated; abstract) anti-human LAG3 (hLAG3) antibody (anti-human LAG3 antibody; abstract, paragraph [0007]), comprising a heavy chain variable domain (comprising a heavy chain variable domain; paragraph [0009]) comprising a heavy chain CDR set (CDR1, CDR2, and CDR3) (comprising a heavy chain CDR set (CDR1, CDR2, and CDR3); paragraph [0009]); and a light chain variable domain (a light chain variable domain; paragraph [0009]) comprising a light chain CDR set (CDR1, CDR2, and CDR3) (comprising a light chain CDR set (CDR1, CDR2, and CDR3); paragraph [0009]).

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 BMS reference, unity of invention is lacking.