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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:
29 September 2016

WO 2016/126858 A3

(54) Title: ANTIBODIES DIRECTED AGAINST LYMPHOCYTE ACTIVATION GENE 3 (LAG-3)

(57) Abstract: The invention relates to an isolated immunoglobulin heavy chain polypeptide and an isolated immunoglobulin light chain polypeptide that bind to a protein encoded by the Lymphocyte Activation Gene-3 (LAG-3). The invention provides a LAG-3-binding agent that comprises the aforementioned immunoglobulin heavy chain polypeptide and immunoglobulin light chain polypeptide. The invention also provides related vectors, compositions, and methods of using the LAG-3-binding agent to treat a disorder or disease that is responsive to LAG-3 inhibition, such as cancer or an infectious disease.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/16424

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07K 16/28, A61K 39/395, A61K 45/06, A61K 47/48 (2016.01)
CPC - A61K 39/3955, C07K 16/28, C07K 16/2803, C07K 16/2818, A61K 2039/507, C07K 2317/24

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) - C07K 16/28, A61K 39/395, A61K 45/06, A61K 47/48 (2016.01)
CPC - A61K 39/3955, C07K 16/28, C07K 16/2803, C07K 16/2818, A61K 2039/507, C07K 2317/24

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC- C07K 2317/33, C07K 2317/565, C07K 2317/76, C07K 2317/92, C07K 2317/94
USPC- 424/136.1, 424/139.1, 424/178.1, 530/387.3, 530/387.9, 530/391.7

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST(PGPB,USPT,USOC,EPAB,JPAB); PatBase, Google/Scholar: Intrabody, single domain, camelid, llama, VHH, sdAb, LAG3, LAG-3, CD223, CD-223, Lymphocyte activation gene 3 protein...
GenCore 6.4.1: 181, 190, 191

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2013/0224188 A1 (InhibRx LLC, et al.) 29 August 2013 (29.08.2013) claims 1, 7; SEQ ID NO: 6	1-3, 13, 14
A	WO 2014/089493 A1 (VANDERBILT UNIVERSITY, et al.) 12 June 2014 (12.06.2014) claim 7, SEQ ID NO: 17, amino acids 1-120	13, 14

☐ Further documents are listed in the continuation of Box C. ☐

* 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
20 June 2016	21 JUL 2016
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: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/16424

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.: 17, 19-28, 30-42
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:
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.

Group I+: claims 1-5, 13, 14, directed to a HC polypeptide. The HC polypeptide will be searched to the extent that it encompasses SEQ ID NO:181, 190-191. It is believed that claims 1-3, 13, 14 encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass first species of each variable, specifically, the first invention encompases SEQ ID NO: 181 wherein Xaa1 is Asn, Xaa2 is Lys, Xaa3 is Lys, Xaa4 is Ile, Xaa5 is Ala, Xaa6 is Glu, Xaa7 is Gly, Xaa8 is Glu, Xaa9 is Ala, Xaa10 is Glu, Xaa11 is Asp, Xaa12 is Glu, as represented in SEQ ID NO:190 and 191. Additional HC polypeptide will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected polypeptide. 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 HC polypeptide of SEQ ID NO:35.

********** See Supplemental Sheet to continue **********

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.:
1-3, 13, 14, restricted to SEQ ID NO:181, 190-191

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.

---- In Continuation of Box III. Observations where unity of invention is lacking: ----

Group II+: Claims 6-12, 15, 16, 18, directed to a LC polypeptide. The LC polypeptide may be searched, for example, to the extent that LC polypeptide encompasses SEQ ID NO:57, 196, 197 for an additional fee and election as such, i.e. claims 6, 7, 15, 16, 18(in part). Additional LC polypeptide will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected LC polypeptide. 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. Another exemplary election would be LC polypeptide of SEQ ID NO: 89, i.e., claims 8-12.

The inventions listed as Groups I+ and II+ 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:

Special Technical Features
The special technical feature of each invention of Group I+ is a HC polypeptide of a specified amino acid sequence, because no significant structural similarities can readily be ascertained among (SEQ ID Nos: 181, 190-191) and SEQ ID NO:35.

The special technical feature of each invention of Group II+ is a LC polypeptide of a specified amino acid sequence, because no significant structural similarities can readily be ascertained among (SEQ ID NO:57, 196, 197) and SEQ ID NO:89.

The inventions of Group I+ do not include the shared or common technical feature of a LC polypeptide, as required by Group II+.
The inventions of Group II+ do not include the shared or common technical feature of a HC polypeptide, as required by Group I+.

Common Technical Features
The inventions of Group I+ share the technical feature of an isolated HC polypeptide. However, this shared technical feature does not represent a contribution over prior art as being anticipated by US 2014/0056878 A1 (ANAPTYSBIO, INC) (hereinafter "Anaptysbio") discloses an isolated HC polypeptide (para [0009], "an isolated immunoglobulin heavy chain polypeptide which comprises an amino acid sequence that is at least 90% identical to any one of SEQ ID NOs: 2-5"). As said technical feature was known in the art at the time of the invention, this cannot be considered special technical feature that would otherwise unify the groups.

The inventions of Group II+ share the technical feature of an isolated LC polypeptide. However, this shared technical feature does not represent a contribution over prior art as being anticipated by Anaptysbio, as above, disclosing an isolated LC polypeptide (para [0011], "an isolated immunoglobulin light chain polypeptide which comprises an amino acid sequence that is at least 90% identical to any one of SEQ ID NOs: 7-24"). As said technical feature was known in the art at the time of the invention, this cannot be considered special technical feature that would otherwise unify the groups.

Groups I+ and II+ therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Note re item 4:
Claims 17, 19-28, 30-42 are not drafted in accordance with the second and third sentences of Rule 6.4 (a). These claims are improper multiple dependent claims.

Note, Claim 29 is absent.