Title: ANTI-TREM2 ANTIBODIES AND METHODS OF USE THEREOF

Abstract: The present disclosure is generally directed to compositions that include antibodies, e.g., monoclonal, chimeric, humanized antibodies, antibody fragments, etc., that specifically bind a TREM2 protein, e.g., a mammalian TREM2 or human TREM2, and use of such compositions in preventing, reducing risk, or treating an individual in need thereof.
<table>
<thead>
<tr>
<th>Box No.</th>
<th>Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:</td>
</tr>
<tr>
<td>a.</td>
<td>X forming part of the international application as filed:</td>
</tr>
<tr>
<td></td>
<td>✔ in the form of an Annex C/ST.25 text file.</td>
</tr>
<tr>
<td></td>
<td>□ on paper or in the form of an image file.</td>
</tr>
<tr>
<td>b.</td>
<td>□ furnished together with the international application under PCT Rule 13fer1 (a) for the purposes of international search only in the form of an Annex C/ST.25 text file.</td>
</tr>
<tr>
<td>c.</td>
<td>□ furnished subsequent to the international filing date for the purposes of international search only:</td>
</tr>
<tr>
<td></td>
<td>□ in the form of an Annex C/ST.25 text file (Rule 13fer1 (a)).</td>
</tr>
<tr>
<td></td>
<td>□ on paper or in the form of an image file (Rule 13fer1 (b) and Administrative Instructions, Section 713).</td>
</tr>
<tr>
<td>2.</td>
<td>□ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.</td>
</tr>
<tr>
<td>3.</td>
<td>Additional comments:</td>
</tr>
</tbody>
</table>
INTERNATIONAL SEARCH REPORT

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.: 9, 40-71 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:

see FURTHER INFORMATION sheet PCT/ISA/210

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, 10-47, 72-146(al l 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.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K16/28 A61K39/395

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, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category* Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No.


* 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 on a date of invention
"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
25 January 2017

Date of mailing of the international search report
31/03/2017

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
Wagner, Rene

Form PCT/ISA/210 (second sheet) (April 2005)
<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X,P</td>
<td>Wo 2016/023019 A2 (ALECTOR LLC [US])</td>
<td>1-5, 10-47, 72-146</td>
</tr>
</tbody>
</table>

The whole document
<table>
<thead>
<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
<th>Patent family member(s)</th>
<th>Publication date</th>
</tr>
</thead>
<tbody>
<tr>
<td>WO 2016023019 A2</td>
<td>11-02-2016</td>
<td>AU 2015300787 A1</td>
<td>02-02-2017</td>
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<td></td>
<td></td>
<td>CA 2955086 A1</td>
<td>11-02-2016</td>
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<tr>
<td></td>
<td></td>
<td>WO 2016023019 A2</td>
<td>11-02-2016</td>
</tr>
</tbody>
</table>
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 2F6.

2. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 11H5

3. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 2H8

4. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 1H7

5. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 3A7

6. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 3B10

7. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 7F8

8. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 7E5

9. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 8F8

10. claims: 1-5, 10-47, 72-146 (all partially)
   Anti body binding to TREM-2, referred to as 9F5

11. claims: 1-5, 10-47, 72-146 (all partially)
Anti body binding to TREM-2, referred to as 9G3

12. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 11A8

13. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 12D9

14. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 12F9

15. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 12G6

16. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 3C1

17. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 4D7

18. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 2C7

19. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 2F5

20. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 7B3

21. claims: 1-5, 10-47, 72-146 (all partly)
   Anti body binding to TREM-2, referred to as 9G1
Claims Nos.: 6-9, 48-71

The present application comprises 146 claims thereof 14 independent claims relating to an excessively large number of definitions of anti-TREM2 antibodies. Some of the dependent claims also include a very large number of independent possibilities, see e.g. claims 28, 37, 40, 48... According to Rule 6.1 (a) PCT, the number of claims shall be reasonable even considering the nature of the invention claimed, which is not the case here.

The applicant relates to anti-TREM2 antibodies, which according to claim 99 and the general summary of the disclosure (page 7) can be agonist, antagonist or inert. The antibodies are defined as binding to one or more amino acids of a very large number of fragments of TREM2 (claim 40) or by more than a hundred sequences of single CDRs. The examiner is unable to search high number of different features and combinations thereof without undue burden, furthermore, it is apparent that such a search would not be useful, since only an antibody defined by at least 6 CDRs (HCDR3, LCDR3) has any defined technical properties of binding.

After an informal clarification, the search was restricted to anti-TREM2 antibodies having agonist activity. The antibodies which are searched and examined are identified as 2F6, 11H5, 2H3, 1H7, 3A7, 3B10, 7F8, 7E5, 8F8, 9F5, 9G3, 11A8, 12D9, 12F9, 12G6, 3C1, 4D7, 2C7, 2F5, 7B3 and 9G1.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examination Authority is normally not to carry out a preliminary examination on a matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination on before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.