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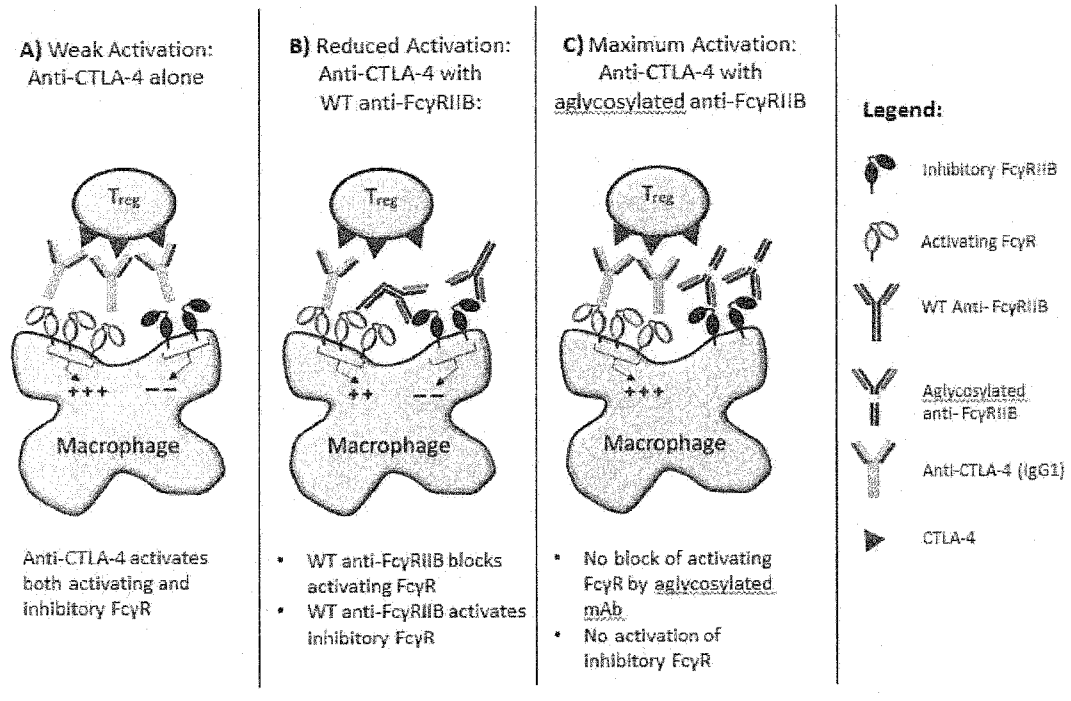



*Fig. 1*

(57) Abstract: Described is the use of a first antibody molecule that specifically binds FcγRIIb via its Fab region, but lacks Fc region or has reduced binding to Fcγ receptors via its Fc region, for use in combination with a second antibody molecule that specifically binds to a receptor present on an immune cell, wherein the immune cell is an immune cell that suppresses anti-cancer immunity, which second antibody molecule has an Fc region that binds to at least one activating Fcγ receptor, and wherein the binding of the second antibody molecule to the receptor on the immune cell causes depletion and/or deactivation of the immune cell in the treatment of an FcγRIIb-negative cancer in a patient, as well as pharmaceutical compositions and kits comprising these to antibody molecules, and methods of treating cancer using these two antibodies.

WO 2019/138005 A3

*[Continued on next page]*

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# INTERNATIONAL SEARCH REPORT

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
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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, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | WO 2017/174331 A1 (CANCER RES TECH LTD [GB]) 12 October 2017 (2017-10-12) | 1-33 |
| Y | page 6, line 31 - page 7, line 12; figures 4,5b<br>page 26, lines 28-37 | 1-33 |
| | ----- | |
| | -/-- | |

[X] Further documents are listed in the continuation of Box C.

[X] 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

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| Date of the actual completion of the international search | Date of mailing of the international search report |
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| Name and mailing address of the ISA/ | Authorized officer |
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| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016 | Cilensek, Zoran |

3

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | FREDERICK ARCE VARGAS ET AL: "Fc-Optimized Anti-CD25 Depletes Tumor-Infiltrating Regulatory T Cells and Synergizes with PD-1 Blockade to Eradicate Established Tumors", IMMUNITY., vol. 46, no. 4, 1 April 2017 (2017-04-01), pages 577-586, XP055487134, US ISSN: 1074-7613, DOI: 10.1016/j.immuni.2017.03.013 page 582, left-hand column, paragraph 1; figures 4B,4G | 1-33 |
| Y | M. J. SELBY ET AL: "Anti-CTLA-4 Antibodies of IgG2a Isotype Enhance Antitumor Activity through Reduction of Intratumoral Regulatory T Cells", CANCER IMMUNOLOGY RESEARCH, vol. 1, no. 1, 7 April 2013 (2013-04-07), pages 32-42, XP055100395, ISSN: 2326-6066, DOI: 10.1158/2326-6066.CIR-13-0013 figures 1-6 & M.J. SELBY: "Supplemental Tables Supplemental Table S1. Anti-CTLA-4 antibodies of IgG2a isotype enhance antitumor activity through reduction of intratumoral regulatory T cells.", , 1 July 2013 (2013-07-01), XP055583459, Retrieved from the Internet: URL:http://cancerimmunolres.aacrjournals.org/highwire/filestream/28860/field_highwire_adjunct_files/2/tab1-2.pdf [retrieved on 2019-04-25] table 1 | 1-33 |
| Y | WO 2017/103895 A1 (NOVARTIS AG [CH]) 22 June 2017 (2017-06-22) paragraph [0038]; examples 20-29 | 1-33 |
| Y | DAHAN RONY ET AL: "Fc[gamma]Rs Modulate the Anti-tumor Activity of Antibodies Targeting the PD-1/PD-L1 Axis", CANCER CELL,, vol. 28, no. 3, 14 September 2015 (2015-09-14), pages 285-295, XP002766294, ISSN: 1878-3686 page 293, left-hand column, paragraph 3 - right-hand column, line 1; figure 2 | 1-33 |

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| A | WO 2006/073921 A2 (UNIV ROCKEFELLER [US]; DHODAPKAR KAVITA M [US] ET AL.) 13 July 2006 (2006-07-13) the whole document | 1-33 |

3

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2019/050566

**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.: 34
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.:

1-33(partially)

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.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/** 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-33(partially)

A first antibody molecule that specifically binds FcyRllb via its Fab region, and that lacks an Fc region or has reduced binding to Fey receptors via its Fc region, for use in combination with
a second antibody molecule that specifically binds to a receptor present on an immune cell, wherein the immune cell is an immune cell that suppresses anti-cancer immunity, which second antibody molecule has an Fc region that binds to at least one activating Fey receptor, and wherein the binding of the second antibody molecule to the receptor on the immune cell causes depletion and/or deactivation of the immune cell;
in the treatment of an FcyRllb-negative cancer in a patient, wherein said receptor is CTLA-4.

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2-7. claims: 1-33(partially)

Idem as item 1, wherein said receptor is 4-1BB, OX-40, TNFR2, PD-L1, IL-2R or GITR, respectively.

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**FURTHER INFORMATION CONTINUED FROM PCT/ISA/** 210

Continuation of Box II.2

Claims Nos.: 34

Claim 34 cannot be searched since it is directed to an antibody molecule that specifically binds FcyRllb for use, a pharmaceutical composition for use, a kit, a use or a method, substantially as described herein in the accompanying claims, description, examples and/or figures.

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 Examining Authority is normally not to carry out a preliminary examination on 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 before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2019/050566

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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