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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))
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- with sequence listing part of description (Rule 5.2(a))
- in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE

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

30 June 2022 (30.06.2022)

(54) Title: ANTIBODY Fc VARIANTS

(57) Abstract: The present invention relates to antibodies comprising Fc variants and their uses. The Fc variants exhibit reduced or undetectable binding to Fc receptors, and reduced or undetectable effector functions. These variants are beneficial for a patient suffering from a disease which could be treated with an antibody for which it is desirable to reduce the effector functions induced by antibodies.



WO 2022/097065 A3

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2021/060228

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K16/28

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

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, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2017/029583 A2 (PFIZER [US]) 23 February 2017 (2017-02-23) page 140; table 33; sequence 64 -----	1-19
X	WO 2019/166596 A1 (ULTRAHUMAN TWELVE LTD [GB]) 6 September 2019 (2019-09-06) sequence 362 -----	1-19
X	WO 2015/200905 A2 (OLIGASIS LLC [US]) 30 December 2015 (2015-12-30) paragraph [00234]; claim 23 ----- -/--	8-10

☒ 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

16 May 2022

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20/05/2022

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/060228

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.:
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.:
1-19 (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.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/060228

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CARL U. BIALUCHA ET AL: "Discovery and Optimization of HKT288, a Cadherin-6-Targeting ADC for the Treatment of Ovarian and Renal Cancers", CANCER DISCOVERY, vol. 7, no. 9, 1 September 2017 (2017-09-01), pages 1030-1045, XP055484340, US ISSN: 2159-8274, DOI: 10.1158/2159-8290.CD-16-1414 figures 2F,2G -----	1-19
X	WO 2018/142322 A1 (NOVARTIS AG [CH]) 9 August 2018 (2018-08-09) paragraph [00368] -----	1-19
E	WO 2022/040586 A2 (NOVARTIS AG [CH]) 24 February 2022 (2022-02-24) sequences 885,886,889 -----	1-19
A	M. HEZAREH ET AL: "Effector Function Activities of a Panel of Mutants of a Broadly Neutralizing Antibody against Human Immunodeficiency Virus Type 1", JOURNAL OF VIROLOGY, vol. 75, no. 24, 15 December 2001 (2001-12-15), pages 12161-12168, XP055559941, US ISSN: 0022-538X, DOI: 10.1128/JVI.75.24.12161-12168.2001 figures 1-4; tables 1,2 -----	1-19
A	TILMAN SCHLOTHAUER ET AL: "Novel human IgG1 and IgG4 Fc-engineered antibodies with completely abolished immune effector functions", PROTEIN ENGINEERING, DESIGN AND SELECTION, vol. 29, no. 10, 29 August 2016 (2016-08-29), pages 457-466, XP055414310, GB ISSN: 1741-0126, DOI: 10.1093/protein/gzw040 page 462, left-hand column, paragraph 4-10; figures 1,3,5 page 464, right-hand column, paragraph 1 ----- -/--	1-19

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2021/060228

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GREGORY L. MOORE ET AL: "A robust heterodimeric Fc platform engineered for efficient development of bispecific antibodies of multiple formats", METHODS, vol. 154, 1 February 2019 (2019-02-01), pages 38-50, XP055625796, NL ISSN: 1046-2023, DOI: 10.1016/j.ymeth.2018.10.006 figures 7A,7B -----	1-19
A	SUSAN H. TAM: "Functional, Biophysical, and Structural Characterization of Human IgG1 and IgG4 Fc Variants with Ablated Immune Functionality", ANTIBODIES, vol. 6, no. 3, 1 January 2017 (2017-01-01), page 12, XP055703620, DOI: 10.3390/antib6030012 figures 5,6; tables 5,6 -----	1-19

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-19(partially)

A binding molecule comprising a human IgG1 Fc variant of a wild-type human IgG1 Fc region and one or more antigen binding domains, wherein the Fc variant comprises a combination of amino acid substitutions L234A, L235A, G237A (LALAGA) .

2-7. claims: 1-19(partially)

Idem as item 1, wherein the substitutions are
L234A, L235A, S267K, P329A (LALASKPA)
D265A, P329A, S267K (DAPASK)
G237A, D265A, P329A (GADAPA)
G237A, D265A, P329A, S267K (GADAPASK)
L234A, L235A, P329G (LALAPG)
L234A, L235A, P329A (LALAPA), respectively,
and wherein the amino acid residues are numbered according to the EU index of Kabat.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2021/060228

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