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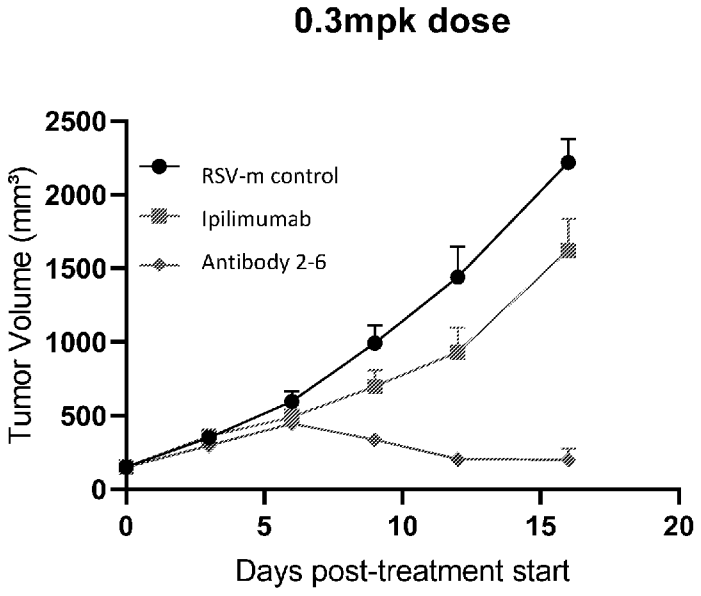
Declarations under Rule 4.17:
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

(54) Title: ANTI-CTLA4 ANTIBODIES AND METHODS OF USE THEREOF

FIG. 8D



(57) Abstract: The invention provides anti-CTLA4 binding proteins (e.g., antibodies, bispecific antibodies, and chimeric receptors) and their use in treating and preventing cancer, as well as compositions and kits comprising the anti-CTLA4 binding proteins.

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[Continued on next page]

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:
06 August 2020 (06.08.2020)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/068548

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.:

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.:

5, 14(completely); 1-4, 7-13, 16-19, 39-55(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

International application No
PCT/US2019/068548

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61P35/00
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 A61P

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.
X	WO 2018/209701 A1 (WUXI BIOLOGICS SHANGHAI CO LTD [CN]) 22 November 2018 (2018-11-22) the whole document, in particular example 4 and SEQ ID NOs: 6 and 13 -----	1-5, 7-14, 16-19, 39-55
A	US 2009/215991 A1 (LAZAR GREGORY ALAN [US] ET AL) 27 August 2009 (2009-08-27) paragraphs [0020], [0025], [0026], [0069], [0074], [0084], [0100], [0103] paragraphs [0113], [0131], [0165], [0199]; figure 41; examples 1-5,7,9,12,13; table 8 -----	1-5, 7-14, 16-19, 39-55

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[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

"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
11 March 2020	23/06/2020

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Bayer, Annette

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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.
A	MATHIEU DONDELINGER ET AL: "Understanding the Significance and Implications of Antibody Numbering and Antigen-Binding Surface/Residue Definition", FRONTIERS IN IMMUNOLOGY, vol. 9, 16 October 2018 (2018-10-16), pages 1-15, XP055572450, DOI: 10.3389/fimmu.2018.02278 the whole document -----	1-5, 7-13, 16-19, 39-55

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2019/068548

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2018209701 A1	22-11-2018	AU 2017414149 A1	07-11-2019
		CA 3060618 A1	22-11-2018
		EA 201992755 A1	22-04-2020
		EP 3625255 A1	25-03-2020
		TW 201900679 A	01-01-2019
		WO 2018209701 A1	22-11-2018
US 2009215991 A1	27-08-2009	US 2008051563 A1	28-02-2008
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		US 2015232567 A1	20-08-2015
		US 2018208668 A1	26-07-2018
		US 2019071512 A1	07-03-2019

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 5, 14(completely); 1-4, 7-13, 16-19, 39-55(partially)

An anti-CTLA4 antibody or antigen-binding fragment thereof comprising a light chain variable (VL) domain and a heavy chain variable (VH) domain, wherein:
a) the VL domain comprises (i) a CDR-L1 comprising the amino acid sequence of SEQID NO: 1, (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 2, and (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 3; and/or the VH domain comprises (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 4, (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 5, and (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 6; or
b) the VL domain comprises (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 7, (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 8, and (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 9; and/or the VH domain comprises (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 10, (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 11, and (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 12; and related subject-matter.

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2. claims: 6, 15, 25, 34(completely); 1-4, 7-13, 16-23, 26-32, 35-55(partially)

An anti-CTLA4 antibody or antigen-binding fragment thereof comprising a light chain variable (VL) domain and a heavy chain variable (VH) domain, wherein:
a) the VL domain comprises (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 13, (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 14, and (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 15; and/or the VH domain comprises (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 16, (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 17, and (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 18; or
b) the VL domain comprises (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 19, (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 20, and (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 21; and/or the VH domain comprises (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 22, (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 23, and (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 24; and related subject-matter.

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3. claims: 24, 33(completely); 20-23, 26-32, 35-55(partially)

A bispecific antibody or an antigen-binding fragment

thereof, comprising
1) a light chain and a heavy chain of a first pair that specifically binds to CTLA4;
2) a light chain and a heavy chain of a second pair that specifically binds to an antigen; wherein the light chain of the first pair comprises a VL domain, and the heavy chain of the first pair comprises a VH domain and wherein:
a) the VL domain comprises (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 1, (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 2,and (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 3; and/or theVH domain comprises (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 4, (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 5, and (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 6; or
b) the VL domain comprises (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 7, (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 8,and (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 9; and/or the VH domain comprises (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 10, (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 11, and (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 12; and related subject-matter.
