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EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to the identity of the inventor (Rule 4.17(i))
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

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))

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

15 November 2018 (15.11.2018)

(54) Title: ANTI-CD137 ANTIBODIES AND METHODS OF USE THEREOF

(57) Abstract: The instant disclosure provides antibodies that specifically bind to CD137 (e.g., human CD137) and increases CD137 function. Also provided are pharmaceutical compositions comprising these antibodies, nucleic acids encoding these antibodies, expression vectors and host cells for making these antibodies, and methods of treating a subject using these antibodies.



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INTERNATIONAL SEARCH REPORT

International application No PCT/US2018/027310

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, BIOSIS, Sequence Search, WPI Data				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
Y	US 2016/244528 A1 (GRAY JOHN DIXON [US] ET AL) 25 August 2016 (2016-08-25) abstract	1-52, 57-60, 62,63, 65-72, 74-76, 78-83, 85-110		
Y	WO 2005/035584 A1 (SQUIBB BRISTOL MYERS CO [US]; JURE-KUNKEL MARIA [US]; HEFTA LAURA J [U] 21 April 2005 (2005-04-21) claims 1-10	1-52, 57-60, 62,63, 65-72, 74-76, 78-83, 85-110		
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"><input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.</td> <td style="width: 50%; border: none;"><input checked="" type="checkbox"/> See patent family annex.</td> </tr> </table>			<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> See patent family annex.
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/> 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			
16 July 2018	15/10/2018			
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 Scheffzyk, Irmgard			

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/027310

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>W. LIN ET AL: "Fc-dependent expression of CD137 on human NK cells: insights into "agonistic" effects of anti-CD137 monoclonal antibodies", BLOOD, vol. 112, no. 3, 1 August 2008 (2008-08-01), pages 699-707, XP055037053, ISSN: 0006-4971, DOI: 10.1182/blood-2007-11-122465 the whole document</p>	<p>1-52, 57-60, 62,63, 65-72, 74-76, 78-83, 85-110</p>
Y	<p>----- SIAW-LIN CHAN ET AL: "Epitope mapping of a chimeric CD137 mAb: a necessary step for assessing the biologic relevance of non-human primate models", JOURNAL OF MOLECULAR RECOGNITION, vol. 22, no. 3, 1 May 2009 (2009-05-01), pages 242-249, XP055070506, ISSN: 0952-3499, DOI: 10.1002/jmr.937 the whole document</p>	<p>1-52, 57-60, 62,63, 65-72, 74-76, 78-83, 85-110</p>
X	<p>----- WO 2014/143909 A1 (BAYER HEALTHCARE LLC [US]; MA XINGHANG [US]; NIU JIANJIE [US]) 18 September 2014 (2014-09-18) sequence 12</p>	<p>37</p>
X	<p>----- WO 2017/040790 A1 (AGENUS INC [US]; LUDWIG INST FOR CANCER RES LTD [CH]; MEMORIAL SLOAN K) 9 March 2017 (2017-03-09) sequences 57,59,61</p>	<p>31,33,35</p>

INTERNATIONAL SEARCH REPORT

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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, 7, 10, 12, 14, 18, 20, 49, 50(completely); 1-4, 6, 8, 9, 11, 13, 15-17
19, 21-48, 51, 52, 57-60, 62, 63, 65-72, 74-76, 78-83, 85-110(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.

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, 7, 10, 12, 14, 18, 20, 49, 50(completely); 1-4, 6, 8, 9, 11, 13, 15-17, 19, 21-48, 51, 52, 57-60, 62, 63, 65-72, 74-76, 78-83, 85-110(partially)

Antibody called BA001

2. claims: 1-4, 6, 8, 9, 13, 15, 16, 19, 21-25, 27, 29-48, 51, 52, 57-60, 62, 63, 65-72, 74-76, 78-83, 85-110(all partially)

Antibody called BA0049

3. claims: 1-4, 6, 8, 9, 11, 13, 15-17, 19, 21-23, 25-48, 51, 52, 57-60, 62, 63, 65-72, 74-76, 78-83, 85-110(all partially)

Antibody called BA0050

4. claims: 1-4, 11, 17, 19, 21-23, 25-48, 51, 52, 57-60, 62, 63, 65-72, 74-76, 78-83, 85-110(all partially)

Antibody called BA0051

5. claims: 1-4, 6, 8, 9, 11, 13, 15-17, 19, 21-23, 25-48, 51, 52, 57-60, 62, 63, 65-72, 74-76, 78-83, 85-110(all partially)

Antibody called BA0052

6. claims: 53-56(completely); 57-60, 62, 63, 65-72, 74-76, 78-83, 85-110(partially)

Antibody according to claim 53

7. claims: 64(completely); 65-72, 74-76, 78-83, 85-110(partially)

Antibody according to claim 64

8. claims: 73(completely); 74-76, 78-83, 85-110(partially)

Antibody according to claim 73

9. claims: 77, 79-83, 85-110(all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Antibody binding to an epitope consisting of SEQ.ID.NO. 26

10. claims: 77, 79-83, 85-110(all partially)

Antibody binding to an epitope consisting of SEQ.ID.NO. 27

11. claims: 77, 79-83, 85-110(all partially)

Antibody binding to an epitope consisting of SEQ.ID.NO. 28

12. claims: 77, 79-83, 85-110(all partially)

Antibody binding to an epitope consisting of SEQ.ID.No. 29

13. claims: 77, 79-83, 85-110(all partially)

Antibody binding to an epitope consisting of SEQ.ID.NO. 30

14. claims: 77, 79-83, 85-110(all partially)

Antibody binding to an epitope consisting of SEQ.ID.NO. 31

15. claims: 77-83, 85-110(all partially)

Antibody binding to an epitope consisting of SEQ.ID.NO. 43

16. claims: 84(completely); 85-110(partially)

Antibody according to claim 84

17. claims: 61(completely); 62, 63, 65-72, 74-76, 78-83,
85-110(partially)

Antibody according to claim 61

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2018/027310

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
US 2016244528 A1	25-08-2016	AR 105313 A1	27-09-2017	
		AU 2016219772 A1	21-09-2017	
		CA 2977257 A1	25-08-2016	
		CN 107921104 A	17-04-2018	
		EP 3258959 A1	27-12-2017	
		JP 2018508509 A	29-03-2018	
		KR 20180016972 A	20-02-2018	
		TW 201632559 A	16-09-2016	
		US 2016244528 A1	25-08-2016	
		US 2017226215 A1	10-08-2017	
WO 2016134358 A1	25-08-2016			

WO 2005035584 A1	21-04-2005	AU 2004279877 A1	21-04-2005	
		BR PI0415195 A	28-11-2006	
		CA 2542044 A1	21-04-2005	
		DK 1670828 T3	02-12-2013	
		EP 1670828 A1	21-06-2006	
		ES 2432357 T3	02-12-2013	
		HK 1085226 A1	17-04-2014	
		HR P20130922 T1	08-11-2013	
		IL 174460 A	28-06-2012	
		IS 8401 A	06-04-2006	
		JP 4616838 B2	19-01-2011	
		JP 2007532095 A	15-11-2007	
		KR 20060126455 A	07-12-2006	
		MX PA06003788 A	14-06-2006	
		NO 338685 B1	26-09-2016	
		PT 1670828 E	04-11-2013	
		RS 20060234 A	29-09-2008	
		RU 2376316 C2	20-12-2009	
		SI 1670828 T1	31-03-2014	
		US 2005095244 A1	05-05-2005	
		US 2009068192 A1	12-03-2009	
		US 2010183621 A1	22-07-2010	
		US 2012141494 A1	07-06-2012	
		US 2014193422 A1	10-07-2014	
		US 2016368998 A1	22-12-2016	
		WO 2005035584 A1	21-04-2005	

WO 2014143909 A1	18-09-2014	AR 095496 A1	21-10-2015	
		CA 2906101 A1	18-09-2014	
		CN 105025925 A	04-11-2015	
		EP 2968538 A1	20-01-2016	
		HK 1215175 A1	19-08-2016	
		JP 2016515515 A	30-05-2016	
		TW 201513882 A	16-04-2015	
		US 2014271659 A1	18-09-2014	
		US 2016002342 A1	07-01-2016	
		UY 35460 A	31-10-2014	
WO 2014143909 A1	18-09-2014			

WO 2017040790 A1	09-03-2017	AU 2016317915 A1	01-03-2018	
		BR 112018003186 A2	25-09-2018	
		CA 2993432 A1	09-03-2017	
		CN 107949573 A	20-04-2018	
		EP 3344656 A1	11-07-2018	
		JP 2018527952 A	27-09-2018	
		KR 20180042326 A	25-04-2018	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2018/027310

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		PE 13222018 A1	14-08-2018
		US 2017081409 A1	23-03-2017
		WO 2017040790 A1	09-03-2017