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Published:

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09 August 2018 (09.08.2018)

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

(57) Abstract: Anti-FGFR antibodies which bind to particular isoforms of FGFR1-4, therapeutic compositions comprising the anti-FGFR antibodies, and methods of using such antibodies and compositions in the treatment of FGFR-related disorders (e.g., cancer) are disclosed.



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/012791

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 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, 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 2005/066211 A2 (FIVE PRIME THERAPEUTICS INC [US]; ZENG CHANGJIANG [US]; HESTIR KEVIN []) 21 July 2005 (2005-07-21)	1-3, 12-49, 54,55, 73-86,98
Y	the whole document in particular, pages 15-28 ----- -/--	5,51-53



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

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2018/012791

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JOHNSTON ET AL: "Fibroblast Growth Factor Receptors (FGFRs) Localize in Different Cellular Compartments: A SPLICE VARIANT OF FGFR-3 LOCALIZES TO THE NUCLEUS", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 51, 22 December 1995 (1995-12-22), pages 30643-30650, XP055135615, ISSN: 0021-9258, DOI: 10.1074/jbc.270.51.30643 the whole document in particular, pages 30644-30645 -----	1
X	HUGHES ET AL: "Localisation and differential expression of the fibroblast growth factor receptor (FGFR) multigene family in normal and atherosclerotic human arteries", CARDIOVASCULAR RESE, OXFORD UNIVERSITY PRESS, GB, vol. 32, no. 3, 1 September 1996 (1996-09-01), pages 557-569, XP005819136, ISSN: 0008-6363, DOI: 10.1016/0008-6363(96)00102-2 the whole document in particular, page 559 -----	1
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X	SUN H D ET AL: "Monoclonal antibody antagonists of hypothalamic FGFR1 cause potent but reversible hypophagia and weight loss in rodents and monkeys", AMERICAN JOURNAL OF PHYSIOLOGY: ENDOCRINOLOGY AND METABOL, AMERICAN PHYSIOLOGICAL SOCIETY, BETHESDA, MD, US, vol. 292, no. 3, 1 March 2007 (2007-03-01), pages E964-E976, XP008085179, ISSN: 0193-1849, DOI: 10.1152/AJPENDO.00089.2006 the whole document in particular, E967-E968 -----	1-4, 8-11,55
A	----- -/--	12-48

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2018/012791

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WEI-MENG ZHAO ET AL: "Monoclonal Antibodies to Fibroblast Growth Factor Receptor 2 Effectively Inhibit Growth of Gastric Tumor Xenografts", CLINICAL CANCER RESEARCH, THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, US vol. 16, no. 23 1 December 2010 (2010-12-01), pages 5750-5758, XP002673994, ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-10-0531 Retrieved from the Internet: URL:http://clincancerres.aacrjournals.org/content/16/23/5750 [retrieved on 2010-07-29]	1-3, 8-11, 75-86
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X	US 2010/098696 A1 (SUN HAIJUN [US] ET AL) 22 April 2010 (2010-04-22)	1-3,6, 50,55, 56, 66-72, 74-86
Y	the whole document	5
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X	DOROTHY M. FRENCH ET AL: "Targeting FGFR4 Inhibits Hepatocellular Carcinoma in Preclinical Mouse Models", PLOS ONE, vol. 7, no. 5, 1 January 2012 (2012-01-01) , pages e36713-e36713, XP055028245, ISSN: 1932-6203, DOI: 10.1371/journal.pone.0036713	1-3,7, 75-86
Y	the whole document	5
A	in particular, pages 5 and 7, figures 2B and 3	12-48
Y	AN ZHIQIANG ET AL: "IgG2m4, an engineered antibody isotype with reduced Fc function", MABS, LANDES BIOSCIENCE, US, vol. 1, no. 6, 1 November 2009 (2009-11-01), pages 572-579, XP002665505, ISSN: 1942-0870, DOI: 10.4161/MABS.1.6.10185 the whole document	51-53
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2018/012791

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	C. LAU ET AL: "Chimeric Anti-CD14 IGG2/4 Hybrid Antibodies for Therapeutic Intervention in Pig and Human Models of Inflammation", THE JOURNAL OF IMMUNOLOGY, vol. 191, no. 9, 23 September 2013 (2013-09-23), pages 4769-4777, XP055148991, ISSN: 0022-1767, DOI: 10.4049/jimmunol.1301653 the whole document in particular, page 4776 -----	51-53

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/012791

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.:

1-56, 66-86, 98(all 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: 1-56, 66-86, 98(all partially)

directed to antibodies that bind to FGFR1c, FGFR2c, FGFR3c and/or FGFR4 and uses thereof, comprising certain sequences found within (or the complete sequence of, or certain percentage identity to) SEQ ID NO:29 and 30.

2-107. claims: 1-56, 66-86, 98(all partially)

directed to antibodies that bind to FGFR1c, FGFR2c, FGFR3c and/or FGFR4 and uses thereof, comprising certain sequences found within (or the complete sequence of, or certain percentage identity to) SEQ ID NO:40 and 41 (invention 2), SEQ ID NO:51 and 52 (invention 3), etc.

108. claims: 57(completely); 59-65(partially)

directed to a modified antibody that binds FGFR1c, wherein the antibody exhibits increased tolerability as compared to an antibody comprising identical VH and VL and an IgG1 constant region when administered to a mammal.

109. claims: 58(completely); 59-65(partially)

directed to a modified antibody that binds FGFR1c, wherein administration to a mammal does not result in significant weight loss.

110. claims: 87-97

directed to medical uses of an IgG2 antibody that binds FGFR1c.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2018/012791

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