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*A61K 45/06* (2006.01)    *C07K 16/28* (2006.01)
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- (81) **Designated States (unless otherwise indicated, for every kind of national protection available):** AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) **Designated States (unless otherwise indicated, for every kind of regional protection available):** ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, 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).
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26 November 2015



WO 2014/163714 A3

(54) **Title:** ANTIBODY DRUG CONJUGATES

(57) **Abstract:** The present invention relates to anti-FGFR2 antibodies, antibody fragments, antibody drug conjugates, and their uses for the treatment of cancer.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/00052

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(8) - A61K 47/48, 45/06, 51/10; C07K 16/28 (2014.01) CPC - A61K 51/103, 45/06; C07K 16/2863 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC(8): A61K49/00, 47/48, 45/06, 51/10; C07K 16/28 (2014.01) CPC: A61K51/103, 45/06, 47/48561, 49/0004; C07K 16/2863 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) MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google; Google Scholar; PubMed; ProQuest; NCBI BLAST; 'fibroblast growth factor receptor 2,' 'FGFR2,' 'cluster of differentiation 332,' 'CD332,' 'Maytansinoid,' 'Mertansine,' antibody, conjugate		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2012/074757 A1 (FLYGARE, J et al.) June 7, 2012; page 44, line 10; page 45, lines 1-10	1-6, 13, 17/13
Y --- A	WO 2007/134210 A2 (CHANT, J et al.) November 22, 2007; abstract; page 3, lines 17-27; page 5, lines 17-24; page 13, lines 12-14; page 17, lines 7-12; page 18, lines 12-16; page 23, lines 3-15, 22-26; page 26, lines 22-26; page 27, line 27	1-6, 13, 17/13 --- 14, 15, 17/14, 17/15, 19, 20, 43, 44, 46/43, 46/44
A	US 2012/0039915 A1 (LIU, B et al.) February 16, 2012; paragraphs [0022], [0041]; Claim 1	43, 45, 46/43
A	WO 2007/008547 A2 (MI, S et al.) January 18, 2007; paragraph [0013]; abstract; Table 1; Claim 58	43, 45, 46/43
A	WO 2006/124451 A2 (HEAVNER, GA et al.) November 23, 2006; paragraphs [9], [20], [21], [45], Claim 2	43, 45, 46/43
A	WO 2012/021841 A2 (CHANG, XJ et al.) February 16, 2012; abstract	1-6, 13, 17/13
A	ABUSEDRA, A, et al. Selective Usage Of IGLV Segments (IgV-Lambda) In CLL Igl Rearrangements. NCBI GenBank Accession No. AAD29349.1, immunoglobulin lambda light chain variable region, partial [Homo sapiens]. 09 May 1999; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/4761418?report=genbank&amp;log\$=proalign">http://www.ncbi.nlm.nih.gov/protein/4761418?report=genbank&amp;log\$=proalign</a> .	14
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* Special categories of cited documents:	"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	
"A" document defining the general state of the art which is not considered to be of particular relevance	"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	
"E" earlier application or patent but published on or after the international filing date	"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	
"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)	"&" document member of the same patent family	
"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		
Date of the actual completion of the international search 05 November 2014 (05.11.2014)	Date of mailing of the international search report <b>13 NOV 2014</b>	
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774	

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/00052

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BRIDGES, SL. Immunoglobulin Lambda Light Chain Expression In Normal Individuals And Rheumatoid Arthritis Patients: Frequent N Region Addition, Oligoclonal B Lymphocyte Expansion, And Evidence Of Polymorphism Of The Lambda Locus. NCBI GenBank Accession No. AAC16822, Immunoglobulin Lambda Light Chain Variable Region, Partial [Homo sapiens]. 20 May 1998. Submitted 05 May 1998; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/3142546?report=genbank&amp;log">\$=protalign&amp;blast_rank=3&amp;RID=558YZEGP013</a> > on 30 October 2014, page 1.	14
A	JACOBIN, MJ et al. Human IgG Monoclonal Anti-Alpha(IIb)-Beta(3)-Binding Fragments Derived From Immunized Donors Using Phage Display. NCBI GenBank Accession No. CAC28922.1, Immunoglobulin Lambda Light Chain Variable Region, Partial [Homo sapiens]. 06 February 2002. Submitted 06 February 2001; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/12734074?report=genbank&amp;log">\$=protalign&amp;blast_rank=5&amp;RID=558YZEGP013</a> > on 30 October 2014, page 1.	14
A	KRAMER, RA et al. The Human Antibody Repertoire Specific For Rabies Virus Glycoprotein As Selected From Immune Libraries. European Journal of Immunology. 2005, Vol. 35, pages 2131-2145; figures 5, 7. DOI 10.1002/eji.200526134.	14, 17/14
A	BAXENDALE, HE et al. Immunogenetic Analysis Of The Immune Response To Pneumococcal Polysaccharide. European Journal of Immunology. 2000, Vol. 30, pages 1214-1223; figure 2.	15, 17/15, 44, 46/44
A	GIOMARELLI, B et al. Inhibition Of Thrombin-Induced Platelet Aggregation Using Human Single-Chain Fv Antibodies Specific For TREM-Like Transcript-1. Thrombosis and Haemostasis. 03 May 2007, Vol. 97, No. 6; pages 955-963; Table 1. DOI 10.1160/TH06-08-0456.	11, 15, 17/15, 44, 46/44
A	LANTTO, J et al. Capturing the natural diversity of the human antibody response against vaccinia virus. NCBI GenBank Accession No. ADU57665.1, anti-vaccinia virus immunoglobulin heavy chain variable region, partial [Homo sapiens]. 14 February 2011. Submitted 06 October 2010; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/316925257?report=genbank&amp;log">\$=protalign&amp;blast_rank=99&amp;RID=562BJHG2015</a> > on 30 October 2014, page 1.	15, 17/15, 44, 46/44
A	LANTTO, J et al. Capturing The Natural Diversity Of The Human Antibody Response Against Vaccinia Virus. NCBI GenBank Accession No. ADU57810.1, Anti-Vaccinia Virus Immunoglobulin Light Chain Variable Region, Partial [Homo sapiens]. 14 February 2011. Submitted 06 October 2010; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/316925547?report=genbank&amp;log">\$=protalign&amp;blast_rank=7&amp;RID=565WER54013</a> > on 30 October 2014, page 1.	12
A	HUNT, AR et al. A Humanized Murine Monoclonal Antibody Protects Mice Either Before Or After Challenge With Virulent Venezuelan Equine Encephalomyelitis Virus. NCBI GenBank Accession No. ABH10632.1, Humanized Murine Anti-VEEV Antibody Hy4-26C Heavy Chain, Partial [synthetic construct]. 14 August 2006. Submitted 06 October 2010; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/111606535?report=genbank&amp;log">\$=protalign&amp;blast_rank=2&amp;RID=5688JA97013</a> > on 30 October 2014, page 1.	19
A	PROSNAK, M et al. Development Of A Cocktail Of Recombinant-Expressed Human Rabies Virus-Neutralizing Monoclonal Antibodies For Postexposure Prophylaxis Of Rabies. NCBI GenBank Accession No. AAO17821.1, Anti-Rabies SO57 Immunoglobulin Heavy Chain [Homo sapiens]. 26 June 2003. Submitted 31 October 2002; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/27728677?report=genbank&amp;log">\$=protalign&amp;blast_rank=5&amp;RID=5688JA97013</a> > on 30 October 2014, page 1.	19
A	LUO, J et al. Co-Evolution Of Antibody Stability And Vk Cdr-L3 Ca Structure. NCBI PDB Accession No. 3NCJ_L, Chain L, Crystal Structure Of Fab15 Mut8. 10 October 2012. Submitted 4 June 2010; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/303325094?report=genbank&amp;log">\$=protalign&amp;blast_rank=4&amp;RID=568P9JTD013</a> > on 30 October 2014; pages 1-2.	19
A	TAKEKOSHI, M et al. Human Monoclonal Anti-HBs Antibody. NCBI GenBank Accession No. BAD08204.1, Anti-HBs Antibody Heavy Chain, Partial [Homo sapiens]. 22 January 2004. Submitted 20 January 2004; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/41059927?report=genbank&amp;log">\$=protalign&amp;blast_rank=28&amp;RID=570E23F9015</a> > on 31 October 2014, page 1.	20

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International application No.

PCT/US14/00052

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MOUQUET, H et al. Complex-Type N-Glycan Recognition By Potent Broadly Neutralizing HIV Antibodies. NCBI PDB Accession No. 4FQQ_L, Chain L, Crystal Structure Of Germline Antibody Pgt121-GI Fab. 13 December 2012. Submitted 25 June 2012; downloaded from the internet < <a href="http://www.ncbi.nlm.nih.gov/protein/414145741?report=genbank&amp;log\$=proalign&amp;blast_rank=5&amp;RID=5714KG5B013">http://www.ncbi.nlm.nih.gov/protein/414145741?report=genbank&amp;log\$=proalign&amp;blast_rank=5&amp;RID=5714KG5B013</a> > on 31 October 2014; pages 1-2.	20
E, X	US 2014/0301946 A1 (BATT, DB et al.) October 9, 2014; abstract	1-6, 13, 17/13

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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.: 7-12, 18, 21-42, 47-57  
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:

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 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.:

**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.