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62/181,106 17 June 2015 (17.06.2015) US
- (71) **Applicant** (for all designated States except AL, AT, BE, BG, CH, CN, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IN, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR): **GENENTECH, INC.** [US/US]; 1 DNA Way, South San Francisco, California 94080 (US).
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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, 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.
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Published:

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- with sequence listing part of description (Rule 5.2(a))

- (88) **Date of publication of the international search report:**
9 February 2017



(54) **Title:** ANTI-HER2 ANTIBODIES AND METHODS OF USE

(57) **Abstract:** The invention provides anti-HER2 antibodies, including anti-HER2 antibodies of improved stability or affinity, and methods of using the same.

INTERNATIONAL SEARCH REPORT

International application No PCT/US2016/037891
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A. CLASSIFICATION OF SUBJECT MATTER
 INV. C07K16/28 C07K16/32
 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, EMBASE, 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	WO 03/087131 A2 (GENENTECH INC [US]; LOWMAN HENRY B [US]; GERSTNER RESI B [US]; CARTER) 23 October 2003 (2003-10-23) e.g. tables 5, 7; examples 2,3,4; claim 69; the whole document <div style="text-align: center;">-----</div> <div style="text-align: center;">-/--</div>	1,4-41

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 2 January 2017	Date of mailing of the international search report 12/01/2017
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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 <div style="text-align: center; font-size: 1.2em;">Gruber, Andreas</div>
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2016/037891

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>GERSTNER R B ET AL: "Sequence plasticity in the antigen-binding site of a therapeutic anti-HER 2 antibody", JOURNAL OF MOLECULAR BIOLOGY, ACADEMIC PRESS, UNITED KINGDOM, vol. 321, 1 January 2002 (2002-01-01), pages 851-862, XP002972421, ISSN: 0022-2836, DOI: 10.1016/S0022-2836(02)00677-0 e.g. page 858, right-hand column, last paragraph - page 859, left-hand column, paragraph 2; page 859, left-hand column, paragraphs 3 and 4; page 859, right-hand column, paragraphs 1 and 2; the whole document</p> <p>-----</p>	1,4-41
A	<p>DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; March 2015 (2015-03), YANG YUEMEI ET AL: "Improving Trastuzumab's Stability Profile by Removing the Two Degradation Hotspots.", XP002761546, Database accession no. NLM25820189 abstract & YANG YUEMEI ET AL: "Improving Trastuzumab's Stability Profile by Removing the Two Degradation Hotspots.", JOURNAL OF PHARMACEUTICAL SCIENCES JUN 2015, vol. 104, no. 6, June 2015 (2015-06), pages 1960-1970, ISSN: 1520-6017</p> <p>-----</p>	1,4-41
A	<p>WO 2012/143524 A2 (GENMAB AS [DK]; NEIJSEEN JOOST J [NL]; MEESTERS JOYCE I [NL]; DE GOEIJ) 26 October 2012 (2012-10-26) e.g. example 2, 21; claims 75, 76; the whole document</p> <p>-----</p>	1,4-41
Y	<p>WO 2012/075581 A1 (YM BIOSCIENCES INC [CA]; CA NAT RESEARCH COUNCIL [CA]; TIKHOMIROV ILIA) 14 June 2012 (2012-06-14) e.g. claim 7; SEQ ID NO: 8, 24; examples; the whole document</p> <p>-----</p>	1,4-41
Y	<p>EP 2 482 212 A1 (SHANGHAI NAT ENGINEERING RES CT OF ANTIBODY MEDICINE CO LTD [CN]) 1 August 2012 (2012-08-01) e.g. example 4; SEQ ID NO: 19,20; the whole document</p> <p>-----</p>	1,4-41

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/037891

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, 4-41(all 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.

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, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,57, 62 and 53,48,49

2. claims: 1, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,57, 63 and 54,48,49

3. claims: 1, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,58, 63 and 54,48,49

4. claims: 1, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,51, 62 and 54,48,49

5. claims: 1, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,58, 63 and 55,48,49

6. claims: 1, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,51, 63 and 54,48,49

7. claims: 1, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,51, 65 and 54,48,49

8. claims: 1, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,58, 63 and 53,48,49

9. claims: 1, 4-41(all partially)

antibody of claim 1,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:50,51, 63 and 55,48,49

10. claims: 2(completely); 5-41(partially)

antibody of claim 2,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO:3 and 4

11. claims: 3(completely); 5-41(partially)

antibody of claim 3,23-25, nucleic acid of claim 18, vector of claim 19, host cell of claim 20, method of claim 21,35,36, composition of claim 22, use of claim 30,31, all comprising an antibody with SEQ ID NO: 3 and 5

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2016/037891

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