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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

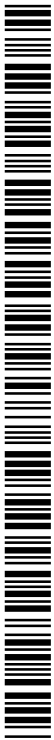
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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:

- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

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29 January 2015



(54) Title: DOSAGE AND ADMINISTRATION OF BISPECIFIC SCFV CONJUGATES IN COMBINATION WITH ANTI-CANCER THERAPEUTICS

(57) Abstract: Provided are methods and compositions for clinical treatment of advanced HER2 positive solid tumors cancer using combination therapies comprising bispecific anti-ErbB2/anti-ErbB3 antibodies. An exemplary bispecific anti-ErbB2/anti-ErbB3 antibody is MM-111 (SEQ ID NO: 1). MM-111 and number of bispecific anti-ErbB2/anti-ErbB3 antibodies suitable for use with the methods and compositions provided herein are described in, e.g., co-pending US patent publication No. 2011-0059076. Suitable bispecific antibodies disclosed therein include A5-HSA-ML3.9, ML3.9-HSA-A5, A5-HSA-BID2, BID2-HSA-A5, B12-HSA-B1D2, B1D2-HSA-25 B12, A5-HSA-F5B6H2, F5B6H2-HSA-A5, H3-HSA-F5B6H2, F5B6H2-HSA-H3, F4-HSAF5B6H2, F5B6H2-HSA-F4, B1D2-HSA-H3, and H3-HSA-B1D2.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2013/040785

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - C07K 16/30 (2013.01) USPC - 424/143.1 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) IPC(8) - A61K 39/395, 47/48; A61P 35/00; C07K 16/28, 16/30 (2013.01) USPC - 424/133.1, 138.1, 139.1, 141.1, 143.1, 178.1; 435/7.23; 530/387.3, 387.9, 388.1, 388.22; 536/023.4 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched CPC - A61K 39/0011, 39/395, 39/39558; C07K 16/32; C12Q 1/6809 (2013.01) Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Orbit, Google Scholar, PubMed		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2011/0059076 A1 (MCDONAGH et al) 10 March 2011 (10.03.2011) entire document	23-26 ----- 3-6
X --- Y	MCDONAGH et al. 'Antitumor activity of a novel bispecific antibody that targets the ErbB2/ErbB3 oncogenic unit and inhibits heregulin-induced activation of ErbB3.' Mol Cancer Ther. (published online 16 January 2012) vol 11, no 3, pp 582-593; entire document	1, 2 ----- 3-6
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 26 September 2013		Date of mailing of the international search report 25 OCT 2013
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: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

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Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

a. (means)

on paper

in electronic form

b. (time)

in the international application as filed

together with the international application in electronic form

subsequently to this Authority for the purposes of search

2. In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

Specifically, SEQ ID NO:1 was searched.

INTERNATIONAL SEARCH REPORT

International application No.

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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.: 7-22, 27-30
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.