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*A61K 47/48* (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, 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:**
- 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:**  
3 December 2015



(54) **Title:** SPECIFIC SITES FOR MODIFYING ANTIBODIES TO MAKE IMMUNOCONJUGATES

(57) **Abstract:** The present application provides specific sites for modifying antibodies or antibody fragments by replacing at least one native amino acid in the constant region of a parental antibody or antibody fragment with cysteine, which can be used as a site of attachment for a payload or linker-payload combination. In one embodiment, the antibodies are modified with cysteines at positions 152 and 375 of the heavy chain constant region, as defined by EU numbering format. In another embodiment, the antibodies are modified with cysteines at position 360 of the heavy chain constant region, and position 107 of the kappa light chain constant region, as defined by EU numbering format.

INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2015/019984

A. CLASSIFICATION OF SUBJECT MATTER  
INV. C07K16/32 A61K47/48 A61P35/00  
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, BIOSIS, EMBASE, 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 2010/111856 A1 (GILL HERMAN [US] ET AL) 6 May 2010 (2010-05-06) the whole document paragraph [0251] paragraph [0256] page 34 - page 35	1,3, 5-26,28
Y	WO 2008/020827 A2 (BIOGEN IDEC INC [US]; VAN VLIJMEN HERMAN [BE]; LUGOVSKOY ALEXEY ALEXAN) 21 February 2008 (2008-02-21) page 41 - page 43 page 42, line 15	1,3, 5-26,28
Y	WO 2011/061492 A2 (UCB PHARMA SA [BE]; HUMPHREYS DAVID PAUL [GB]; HEYWOOD SAM PHILIP [GB]) 26 May 2011 (2011-05-26) page 36 - page 37 page 58	1,3, 5-26,28
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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  16 July 2015	Date of mailing of the international search report  21/10/2015
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  Wagner, René

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2015/019984

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 2014/124316 A2 (IRM LLC [US]; GEIERSTANGER BERNHARD HUBERT [US]; OU WEIJIA [US]; UNO T) 14 August 2014 (2014-08-14) the whole document	1,3, 5-26,28
A	----- VOYNOV VLADIMIR ET AL: "Design and application of antibody cysteine variants", BIOCONJUGATE CHEMISTRY, ACS, WASHINGTON, DC, US, vol. 21, no. 2, 17 February 2010 (2010-02-17), pages 385-392, XP002598497, ISSN: 1043-1802, DOI: 10.1021/BC900509S [retrieved on 2010-01-21] the whole document -----	1,3, 5-26,28

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2015/019984

## 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, 3, 26, 28(completely); 5-25(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, 3, 26, 28(completely); 5-25(partially)

Modified antibody and immunoconjugate comprising said antibody in which the amino acids in position 360 of the heavy chain and in position 107 of the light chain are substituted by a cysteine

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2. claims: 2, 4, 27, 29(completely); 5-25(partially)

Modified antibody and immunoconjugate comprising said antibody in which the amino acids in positions 152 and 375 of the heavy chain are substituted by a cysteine

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2015/019984
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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