

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
26 February 2004 (26.02.2004)

PCT

(10) International Publication Number
WO 2004/016801 A3

- (51) International Patent Classification⁷: **A61K 39/395**, C07K 16/46
- (21) International Application Number: PCT/US2003/022494
- (22) International Filing Date: 5 August 2003 (05.08.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/403,652 16 August 2002 (16.08.2002) US
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- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 1 July 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: CROSS-LINKERS WITH HIGH REACTIVITY AND SOLUBILITY AND THEIR USE IN THE PREPARATION OF CONJUGATES FOR TARGETED DELIVERY OF SMALL MOLECULE DRUGS

(57) Abstract: Disclosed is a method of making conjugates of cell binding agents and small molecule drugs comprising reacting a cell binding agent with a bifunctional cross-linking moiety to thereby provide the cell binding agent with a reactive disulfide group and then reacting the modified cell binding agent with a small molecule drug comprising a free thiol group. Bifunctional cross-linking moieties are also disclosed.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/22494

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/395; C07K 16/46
 US CL : 424/178.1; 530/391.1

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)
 U.S. : 424/178.1; 530/391.1, 536/6.4; 540/474; 546/278.4

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)
 WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	US 6,441,163 B1 (CHARI et al) 27 August 2002 (27.08.2002), see examples 2a and 2b,	1-34
Y	US 4,563,304 A (CARLSSON et al) 07 January 1986 (07.01.1986), see example 10.	1-34
Y	YOKOYAMA et al Molecular design for missile drug: Synthesis of adriamycin conjugated with immunoglobulin G using poly(ethylene glycol-block-(aspartic acid) as intermediate carrier. Makromol. Chem. 1989, Vol. 190 pages 2041-2054, see page 2047, and page 2050	1-34

Further documents are listed in the continuation of Box C.

See patent family annex.

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"P" document published prior to the international filing date but later than the priority date claimed

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"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

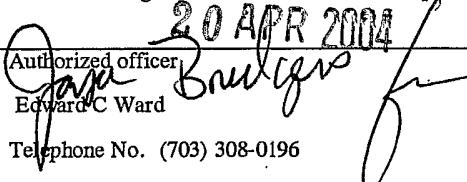
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Date of the actual completion of the international search

30 March 2004 (30.03.2004)

Date of mailing of the international search report

20 APR 2004
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