

(19) World Intellectual Property Organization
International Bureau

PCT

(43) International Publication Date
29 December 2005 (29.12.2005)(10) International Publication Number
WO 2005/123140 A3

(51) International Patent Classification:

A61K 47/48 (2006.01)

(21) International Application Number:

PCT/US2005/020138

(22) International Filing Date: 8 June 2005 (08.06.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/578,199 8 June 2004 (08.06.2004) US

(71) Applicant (for all designated States except US): **ALZA CORPORATION** [US/US]; 1900 Charleston Road, Mountain View, CA 94043 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **ZALIPSKY, Samuel** [US/US]; 1202 Truman Street, Redwood City, CA 94061 (US).(74) Agents: **GORTHEY, Leeann** et al.; Perkins Coie LLP, P.O. Box 2168, Menlo Park, CA 94026 (US).

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

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

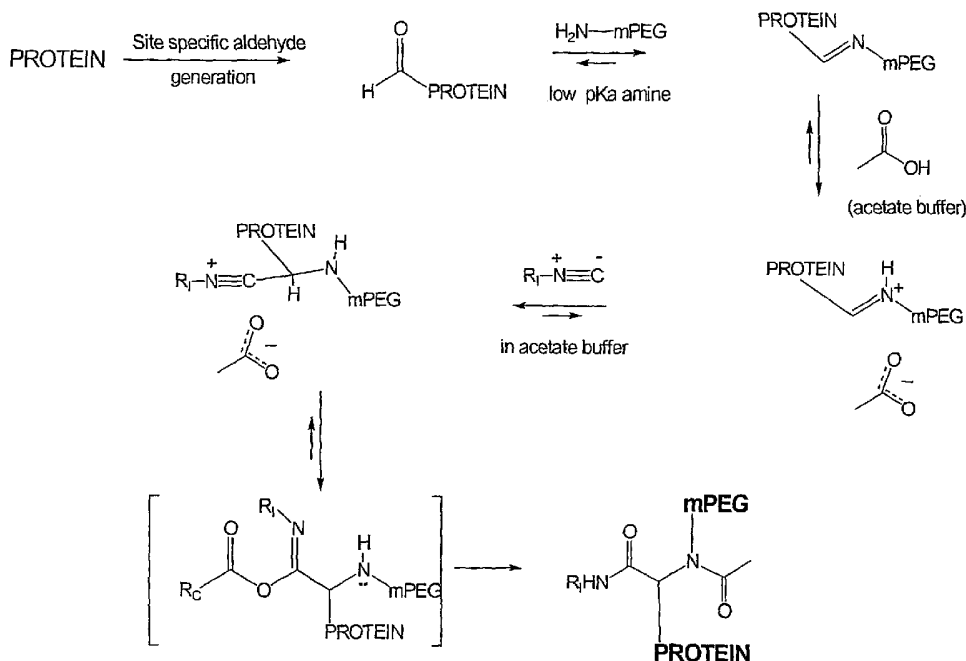
Published:

- 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:
3 August 2006

[Continued on next page]

(54) Title: PREPARATION OF MACROMOLECULAR CONJUGATES BY FOUR-COMPONENT CONDENSATION REACTION



(57) Abstract: Polymer-biomolecule conjugates are prepared, generally in a site-specific or -selective manner, by a four-component condensation reaction. The method may be used to prepare conjugates having two polymer molecules attached at a single site on a biomolecule. The conjugates are typically water soluble and have beneficial pharmacological properties, such as reduced immunogenicity and increased circulation time.



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.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/020138

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K47/48

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)
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 practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/51697 A (MORPHOCHEM GMBH; DOEMLING, ALEXANDER; RICHTER, WOLFGANG) 19 November 1998 (1998-11-19) Abstract; claim 1	1-5, 9-12
P, X	WO 2004/108634 A (CELARES GMBH; KRAEHMER, RALF; LEENDERS, FRANK) 16 December 2004 (2004-12-16)	25, 26, 29, 30
P, Y	Abstract; pag. 5 line 11-pag.6 line 25; pag. 14 lines 4,5; claim 7; pag. 36 line 15-pag. 38 line 30	1-42
Y	DE 101 50 077 A1 (MORPHOCHEM AKTIENGESELLSCHAFT FUER KOMBINATORISCHE CHEMIE) 30 April 2003 (2003-04-30) paragraphs [0005], [0009], [0016]	34-42
	----- -/-	

☒ 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 document 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

7 June 2006

Date of mailing of the international search report

22/06/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bettio, A

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/020138

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 03/051795 A (MORPHOCHEM AG; HENKEL, BERND) 26 June 2003 (2003-06-26) Formula 1 pag. 2; pag 7 line 5	34-42
Y	EP 0 400 472 A (SUMITOMO PHARMA; SEIKAGAKU KOGYO CO LTD; SUMITOMO PHARMACEUTICALS COMP) 5 December 1990 (1990-12-05) page 7, line 46	34-42
Y	PARK W. K. C. ET AL.: "Rapid combinatorial synthesis of aminoglycoside antibiotic mimetics: use of a polyethylene glycol-linked amine and neamine-derived aldehyde in multiple component condensation as a strategy for the discovery of new inhibitors of the HIV RNA rev responsive element" J. AM. CHEM. SOC., vol. 118, 1996, pages 10150-10155, XP002382631 pag. 10151 2nd paragraph Scheme 1	1-42
A	DÖMLING A. AND UGI I.: "Multicomponent reaction with Isocyanides" ANGEW. CHEM. INT. ED., vol. 39, 2000, pages 3168-3210, XP002382632 cited in the application pag. 3181 last par.- pag. 3186	1-42
A	OBRECHT D ET AL: "5. A NOVEL AND EFFICIENT APPROACH FOR THE COMBINATORIAL SYNTHESIS OF STRUCTURALLY DIVERSE PYRIMIDINES ON SOLID SUPPORT" HELVETICA CHIMICA ACTA, VERLAG HELVETICA CHIMICA ACTA. BASEL, CH, vol. 80, 1997, pages 65-72, XP002915327 ISSN: 0018-019X abstarct; pag. 67; pag. 69 last 2 par.	1-42
A	EP 0 832 898 A (BAYER AG) 1 April 1998 (1998-04-01) pag. 2 line 1-pag. 3 line 19	1-42

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/020138

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9851697 A	19-11-1998	AU 750974 B2 AU 8017598 A CA 2290614 A1 DK 983290 T3 EP 0983290 A1 JP 2002500643 T NO 995551 A US 6355726 B1	01-08-2002 08-12-1998 19-11-1998 14-06-2004 08-03-2000 08-01-2002 12-01-2000 12-03-2002
WO 2004108634 A	16-12-2004	CA 2528667 A1 DE 10326303 A1 EP 1631545 A2	16-12-2004 30-12-2004 08-03-2006
DE 10150077 A1	30-04-2003	WO 03033547 A1	24-04-2003
WO 03051795 A	26-06-2003	AU 2002358734 A1 DE 10162134 A1	30-06-2003 10-07-2003
EP 0400472 A	05-12-1990	AT 136315 T CA 2017543 A1 DE 69026306 D1 DE 69026306 T2 DK 400472 T3 ES 2085297 T3 GR 3019991 T3	15-04-1996 27-11-1990 09-05-1996 17-10-1996 13-05-1996 01-06-1996 31-08-1996
EP 0832898 A	01-04-1998	CA 2214728 A1 DE 19636538 A1 JP 10101634 A	09-03-1998 12-03-1998 21-04-1998