(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 September 2007 (13.09.2007)

PCT

(10) International Publication Number
WO 2007/103348 A3

(51) International Patent Classification:
A61K 47/48 (2006.01) *A61P 37/06* (2006.01)

(21) International Application Number:
PCT/US2007/005646

(22) International Filing Date: 5 March 2007 (05.03.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/779,939 7 March 2006 (07.03.2006) US

(71) Applicant *(for all designated States except US)*: **Wyeth** [US/US]; Five Giralda Farms, Madison, NJ 07940 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **GU, Jianxin** [CA/US]; 267 Voorhis Avenue, River Edge, NJ 07661 (US). **RUPPEN, Mark** [US/US]; 6 Lea Court, Garnerville, NY 10923 (US). **ZHU, Tianmin** [US/US]; 5 Whitman Place, Monroe, NY 10950 (US). **FAWZI, Mahdi** [US/US]; 1 Dukes Court, Morristown, NJ 07960 (US).

(74) Agents: **KODROFF, Cathy, A.** et al.; Howson and Howson, 501 Office Center Drive, Suite 210, Fort Washington, PA 19034 (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, 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, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, 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, LV, MC, MT, 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:
8 May 2008

WO 2007/103348 A3

(54) Title: PROCESS FOR PREPARING WATER-SOLUBLE POLYETHYLENE GLYCOL CONJUGATES OF MACROLIDE IMMUNOSUPPRESSANTS

(57) Abstract: Processes are described for preparing 42-pegylated rapamycins including reacting a rapamycin with an acylating agent in the presence of a lipase to form an acylated rapamycin and reacting the acylated rapamycin with a methoxy poly(ethylene glycol) derivative in the presence of a base. Also described are processes for preparing 32-pegylated tacrolimus and/or ascomycin using these steps.