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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 September 2012 (13.09.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/121758 A1

(51) International Patent Classification:
A61K 9/14 (2006.01) *A61K 47/22* (2006.01)
A61K 9/20 (2006.01) *A61K 47/26* (2006.01)
A61K 31/437 (2006.01) *A61K 47/32* (2006.01)
A61K 47/02 (2006.01)

(21) International Application Number:
PCT/US2011/054959

(22) International Filing Date:
5 October 2011 (05.10.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/408,527 29 October 2010 (29.10.2010) US

(71) Applicants *(for all designated States except US)*: **ABBVIE INC.** [US/US]; 1 North Waukegan Road, North Chicago, IL 60064 (US). **ABBOTT GMBH & CO.KG** [DE/DE]; Max-Planck-Ring 2, 65205 Wiesbaden-Delkenhim (DE).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **BIRTALAN, Esther** [DE/DE]; Hardstrabe 15, Eingang Lameystrabe, 76185 Karlsruhe (DE). **HOELIG, Peter** [DE/DE]; Hopfengarten 11, 63607 Waechtersbach (DE). **LINDLEY, David J.** [US/US]; 676 Needlegrass Parkway, Antioch, Illinois 60002 (US). **SANZGIRI, Yeshwant D.** [US/US]; 1323 Deer Run Road, Gurnee, Illinois 60031 (US). **TONG, Ping** [US/US]; 1520 Eric Lane, Libertyville, Illinois 60048 (US).

(74) Agents: **MANZARI, Oona A.** et al.; 100 Abbott Park Road, AP6A-1/D0377, Abbott Park, Illinois 60064 (US).

(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, 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, 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.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

WO 2012/121758 A1

(54) Title: MELT-EXTRUDED SOLID DISPERSIONS CONTAINING AN APOPTOSIS-INDUCING AGENT

(57) Abstract: A pro-apoptotic solid dispersion comprises, in essentially non-crystalline form, a Bcl-2 family protein inhibitory compound of Formula I as defined herein, dispersed in a solid matrix that comprises (a) a pharmaceutically acceptable water-soluble polymeric carrier and (b) a pharmaceutically acceptable surfactant. A process for preparing such a solid dispersion comprises subjecting to elevated temperature the compound of Formula I, the water-soluble polymeric carrier and the surfactant, to provide an extrudable semi-solid mixture; extruding the semi-solid mixture; and cooling the resulting extrudate to to provide a solid matrix comprising the polymeric carrier and the surfactant and having the compound dispersed in essentially non-crystalline form therein. The solid dispersion is suitable for oral administration to a subject in need thereof for treatment of a disease characterized by overexpression of one or more anti-apoptotic Bcl-2 family proteins, for example cancer or an immune or autoimmune disease.