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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 May 2011 (05.05.2011)

PCT

(10) International Publication Number
WO 2011/053518 A1

(51) International Patent Classification:
A61K 31/497 (2006.01)

(21) International Application Number:
PCT/US2010/053678

(22) International Filing Date:
22 October 2010 (22.10.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/254,917 26 October 2009 (26.10.2009) US
61/328,480 27 April 2010 (27.04.2010) US

(71) Applicant *(for all designated States except US)*: **SIGNAL PHARMACEUTICALS, LLC** [US/US]; 4550 Towne Centre Court, San Diego, CA 92121 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **HARRIS, Roy, L.** [US/US]; 1075 Chalcedony St., Apt. A, San Diego, CA 92109 (US). **SAPIENZA, John** [US/US]; 1654 Ridge Rock Court, Chula Vista, CA 91913 (US). **SHEVLIN, Graziella** [US/US]; 13508 Bidwell Court, San Diego, CA 92129 (US). **PAPA, Patrick** [US/US]; 5320 Forecastle Ct., Carlsbad, CA 92008 (US). **LEE, Branden, Gingsee** [US/US]; 11363 Stable Glen Pl., San Diego, CA 92130 (US). **PACKARD, Garrick** [US/US]; 4485 Vision Drive, #6, San Diego, CA 92121 (US). **ZHAO, Jingjing** [CN/US]; 8323 Bryn Glen Way, San Diego, CA 92129 (US). **JOKIEL, Patrick, Anthony** [US/US]; 2 Scarlet Oak Drive, Princeton, NJ 08540 (US). **MORTENSEN, Deborah** [US/US]; 4302 Lodi Court, San Diego, CA 92117 (US). **RIGGS, Jennifer** [US/US]; 2136 Wales Drive, Cardiff, CA 92007 (US). **GAMBOA, Juan, Antonio** [US/US]; 400 East 14th Street, #5F, New York, NY 10009 (US). **BEAUCHAMPS, Marie, Georges** [US/US]; 8 Red Maple Lane, Flanders, NJ 07836 (US). **KREILEIN, Matthew, Michael** [US/US]; 14307 Crystal Ridge Dr., Watchung, NJ 07069 (US). **KOTHARE, Mohit, Atul** [IN/US]; 46 Reinhart Way, Bridgewater, NJ 08807 (US). **PERRIN-NINKOVIC, Sophie** [FR/US]; 8902 Nottingham Place, La Jolla, CA 92037 (US). **PYE, Philip** [GB/US]; 2691 Deer Path, Scotch Plains, NJ 07076 (US). **LEONG, William, Wei-Hwa** [US/US]; 342 Edgewood Avenue, Westfield, NJ 07090 (US). **ELSNER, Jan** [US/US]; 7564 Charmant Dr., #1828, San Diego, CA 92122 (US). **CHOUDHURY, Anusuya** [IN/US]; 131 Edwards Dr., Churchville, PA 18966 (US).

(74) Agents: **INSOGNA, Anthony, M.** et al.; Jones Day, 222 East 41st Street, New York, NY 10017-6702 (US).

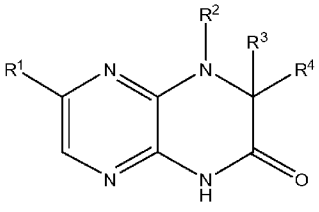
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, 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, RO, RS, RU, 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, 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).

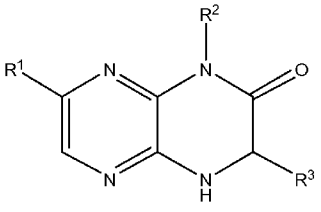
Published:

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

(54) **Title**: METHODS OF SYNTHESIS AND PURIFICATION OF HETEROARYL COMPOUNDS



(I)



(II)

(57) **Abstract**: Provided herein are methods to prepare Heteroaryl Compounds having the following structure: Forumula (I) or Formula (II): wherein R^1-R^4 are as defined herein. The Heteroaryl compounds are useful for treating or preventing cancer, inflammatory conditions, immunological conditions, neurodegenerative diseases, diabetes, obesity, neurological disorders, age-related diseases, or cardiovascular conditions.

WO 2011/053518 A1