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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 November 2009 (19.11.2009)

PCT

(10) International Publication Number
WO 2009/140127 A3

(51) **International Patent Classification**:
C07D 239/70 (2006.01) *C07D 495/04* (2006.01)

(21) **International Application Number**:
PCT/US2009/043068

(22) **International Filing Date**:
7 May 2009 (07.05.2009)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
61/052,816 13 May 2008 (13.05.2008) US

(71) **Applicant** *(for all designated States except DE, US)*: **BOEHRINGER INGELHEIM INTERNATIONAL GMBH** [DE/DE]; Boehringer Ingelheim International Gmbh, Bingerstrasse 173, D-55216 Ingelheim (DE).

(71) **Applicant** *(for DE only)*: **BOEHRINGER INGELHEIM PHARMA GMBH & CO. KG** [DE/DE]; Boehringer Ingelheim Pharma Gmbh & Co. KG, Bingerstrasse 173, D-55216 Ingelheim (DE).

(72) **Inventors; and**

(75) **Inventors/Applicants** *(for US only)*: **FRUTOS, Rogelio, Perez** [US/US]; Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Road, P.O. Box 368, Ridgefield, CT 06877-0368 (US). **TAMPONE, Thomas, G.** [US/US]; Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Road, P.O. Box 368, Ridgefield, CT 06877-0368 (US). **MULDER, Jason, Alan** [US/US]; Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Road, P.O. Box 368, Ridgefield, CT 06877-0368 (US). **KRISHNAMURTHY, Dhileepkumar** [US/US]; Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Road, P.O. Box 368, Ridgefield, CT 06877-0368 (US). **SENANAYAKE, Chris, Hugh** [US/US]; Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Road, P.O. Box 368, Ridgefield, CT 06877-0368 (US).

(74) **Agents**: **MORRIS, Michael P.** et al.; Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Road, P.O. Box 368, Ridgefield, CT 06877-0368 (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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, 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 (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) **Date of publication of the international search report**:
28 January 2010

WO 2009/140127 A3

(54) **Title**: SYNTHESIS OF DIHYDROTHIENO[3,2-*d*]PYRIMIDINE DIOLS AND SIMILAR PYRIMIDINE DIOLS

(57) **Abstract**: The present invention relates to an improved process for the preparation of dihydrothieno[3,2-*d*]pyrimidine diols, and similar pyrimidine diols, that is efficient, high-yielding, and does not require expensive and potentially unstable intermediates. The diols are used as intermediates in the synthesis of pyrimidine compounds which inhibit PDE4, and are thus useful in the treatment of respiratory or gastrointestinal diseases and complaints, peripheral or central nervous system diseases and disorders, inflammatory conditions, and cancers.