



(51) International Patent Classification:

C07D 211/94 (2006.01) *A61K 31/4427* (2006.01)
C07D 217/24 (2006.01) *A61P 35/00* (2006.01)
C07D 239/22 (2006.01) *A61P 1/00* (2006.01)
A61K 31/4412 (2006.01) *A61P 43/00* (2006.01)

(21) International Application Number:

PCT/CN2015/089332

(22) International Filing Date:

10 September 2015 (10.09.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

PCT/CN2014/000834

10 September 2014 (10.09.2014)

CN

(71) Applicant: **GLAXOSMITHKLINE INTELLECTUAL PROPERTY DEVELOPMENT LIMITED** [GB/GB];
 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

(71) Applicant (for PG only): **GLAXOSMITHKLINE (CHINA) R & D COMPANY LIMITED** [CN/CN]; No. 3 Building, 898 Halei Road, Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai 201203 (CN).

(72) Inventors: **CHEUNG, Mui**; 709 Swedeland Road, King of Prussia, PA Pennsylvania 19406 (US). **DEMARTINO, Michael P.**; 709 Swedeland Road, King of Prussia, PA Pennsylvania 19406 (US). **EIDAM, Hilary Schenck**; 709 Swedeland Road, King of Prussia, PA Pennsylvania 19406 (US). **GUAN, Huiping Amy**; No. 3 Building, 898 Halei Rd., Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai 201203 (CN). **QIN, Donghui**; 709 Swedeland Road, King of Prussia, PA Pennsylvania 19406 (US). **WU, Chengde**; No. 3 Building, 898 Halei Rd., Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai 201203 (CN). **GONG, Zhen**; No. 3 Building, 898 Halei Rd., Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai 201203 (CN). **YANG, Haiying**; No. 3 Building, 898 Halei Rd., Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai 201203

(CN). **YU, Haiyu**; No. 3 Building, 898 Halei Rd., Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai 201203 (CN). **ZHANG, Zhiliu**; No. 3 Building, 898 Halei Rd., Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai 201203 (CN).

(74) Agent: **KING & WOOD MALLESONS**; 20th Floor, East Tower, World Financial Centre, No. 1 Dongsanhuan Zhonglu, Chaoyang District, Beijing 100020 (CN).

(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, BN, 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, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, 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, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, 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, KM, 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))
- of inventorship (Rule 4.17(iv))

Published:

- with international search report (Art. 21(3))

(54) Title: NOVEL COMPOUNDS AS REARRANGED DURING TRANSFECTION (RET) INHIBITORS

(57) Abstract: This invention relates to novel compounds which are inhibitors of the Rearranged during Transfection (RET) kinase, to pharmaceutical compositions containing them, to processes for their preparation, and to their use in therapy, alone or in combination, for the normalization of gastrointestinal sensitivity, motility and/or secretion and/or abdominal disorders or diseases and/or treatment related to diseases related to RET dysfunction or where modulation of RET activity may have therapeutic benefit including but not limited to all classifications of irritable bowel syndrome (IBS) including diarrhea-predominant, constipation-predominant or alternating stool pattern, functional bloating, functional constipation, functional diarrhea, unspecified functional bowel disorder, functional abdominal pain syndrome, chronic idiopathic constipation, functional esophageal disorders, functional gastroduodenal disorders, functional anorectal pain, inflammatory bowel disease, proliferative diseases such as non-small cell lung cancer, hepatocellular carcinoma, colorectal cancer, medullary thyroid cancer, follicular thyroid cancer, anaplastic thyroid cancer, papillary thyroid cancer, brain tumors, peritoneal cavity cancer, solid tumors, other lung cancer, head and neck cancer, gliomas, neuroblastomas, Von Hippel-Lindau Syndrome and kidney tumors, breast cancer, fallopian tube cancer, ovarian cancer, transitional cell cancer, prostate cancer, cancer of the esophagus and gastroesophageal junction, biliary cancer, adenocarcinoma, and any malignancy with increased RET kinase activity.

