

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
9 January 2003 (09.01.2003)

PCT

(10) International Publication Number
WO 03/002561 A1(51) International Patent Classification⁷: **C07D 417/14**,
411/14, 407/14, 413/14, A61K 31/445, A61P 25/00, 3/10,
15/00, C07D 407/06, 491/04, 401/06, 409/14, 471/04

(21) International Application Number: PCT/EP02/07009

(22) International Filing Date: 25 June 2002 (25.06.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0115863.3 28 June 2001 (28.06.2001) GB
0130342.9 19 December 2001 (19.12.2001) GB(71) Applicant (for all designated States except US):
SMITHKLINE BEECHAM P.L.C. [GB/GB]; 980
Great West Road, Brentford, Middlesex TW8 9GS (GB).

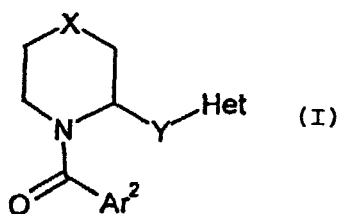
(72) Inventors; and

(75) Inventors/Applicants (for US only): **BRANCH, Clive, Leslie** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **CHAN, Wai, Ngor** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **JOHNS, Amanda** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **JOHNSON, Christopher, Norbert** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **NASH, David, John** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **NOVELLI, Riccardo** [IT/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **PILLEUX, Jean-Pierre** [FR/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB).**PORTER, Roderick, Alan** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **STEAD, Rachel, Elizabeth, Anne** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **STEMP, Geoffrey** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB).(74) Agent: **HOCKLEY, Siân, Catherine**; GlaxoSmithKline, Corporate Intellectual Property CN925.1, 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (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

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: N-AROYL CYCLIC AMINE DERIVATIVES AS OREXIN RECEPTOR ANTAGONISTS

(57) Abstract: This invention relates to N-aroyle cyclic amine derivatives of formula (I), wherein X represents a bond, oxygen, NR³ or a group (CH₂), wherein n represents 1, 2 or 3; Y represents CH₂, CO, CH(OH), or CH₂CH(OH); Het is an optionally substituted bicyclic heteroaryl group containing up to 4 heteroatoms selected from N, O and S; Ar² represents an optionally substituted phenyl or a 5- or 6-membered heterocyclyl group containing up to 3 heteroatoms selected from N, O and S and their use as pharmaceuticals, specifically as orexin receptor antagonists.