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

(19) World Intellectual Property Organization
International Bureau

G00002

(43) International Publication Date
20 June 2002 (20.06.2002)

PCT

(10) International Publication Number
WO 02/048106 A3

(51) International Patent Classification[7]: C07D 417/12, 403/12, 401/12, 413/12, A61K 31/4439, 31/427, 31/4709, 31/506

(21) International Application Number: PCT/EP01/14404

(22) International Filing Date: 7 December 2001 (07.12.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/255,273	13 December 2000 (13.12.2000)	US
60/318,715	13 September 2001 (13.09.2001)	US

(71) Applicant: F. HOFFMANN-LA-ROCHE AG [CH/CH]; 124 Grenzacherstrasse, CH-4070 Basel (CH).

(72) Inventor: GUERTIN, Kevin, Richard; 14 Wedgewood Drive, Apt. 20, Verona, NJ 07044 (US).

(74) Agent: WITTE, Hubert; 124 Grenzacherstrasse, CH-4070 Basel (CH).

(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, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, 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).

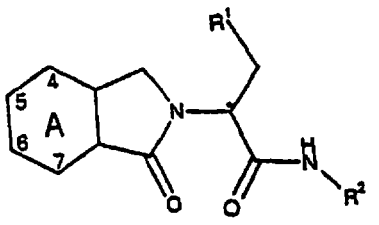
Published:
— *with international search report*

(88) Date of publication of the international search report:
28 November 2002

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.

162162

(54) Title: ISOINDOLIN-1-ONE GLUCOKINASE ACTIVATORS



(I)

(57) Abstract: Isoindolin-1-one-substituted propionamide glucokinase activators which increase insulin secretion in the treatment of type II diabetes of formula (I) wherein A is unsubstituted phenyl or phenyl which is mono- or di-substituted with halo or mono-substituted with lower alkyl sulfonyl, lower alkyl thio or nitro; R^1 is cycloalkyl having from 3 to 9 carbon atoms or lower alkyl having from 2 to 4 carbon atoms; R^2 is an unsubstituted or mono-substituted five- or six-membered heteroaromatic ring connected by a ring carbon atom to the amine group shown, which five- or six- membered heteroaromatic ring contains from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen, with one heteroatom being nitrogen which is adjacent to the connecting ring carbon atom, which ring may be monocyclic or fused with phenyl at two of its ring carbons, said monosubstituted heteroaromatic ring being monosubstituted at a position on a ring carbon atom other than adjacent to said connecting carbon atom with a substituent selected from the group consisting of halo, lower alkyl, nitro, cyano, perfluoro-lower alkyl; hydroxy $-(CH_2)_n-OR^3$, $-(CH_2)_n-C(O)-OR^3$, $-(CH_2)_n-C(O)-NH-R^3$, $-C(O)C(O)-or^3$, or $-(CH_2)_n-NHR^3$; where R^3 is hydrogen or lower alkyl; and n is 0, 1, 2, 3 or 4; or a pharmaceutically acceptable salts or N-oxides thereof.

WO 02/048106 A3