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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 March 2002 (21.03.2002)

PCT

G00002

(10) International Publication Number
WO 02/22604 A1

(51) International Patent Classification[7]: C07D 403/12, 401/14, A61K 31/506, 31/4155, A61P 35/00, C07D 403/14, 405/14, 521/00, 409/14, 471/04, 487/04

(21) International Application Number: PCT/US01/28792

(22) International Filing Date:
14 September 2001 (14.09.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/232,795	15 September 2000 (15.09.2000)	US
60/257,887	21 December 2000 (21.12.2000)	US
60/286,949	27 April 2001 (27.04.2001)	US

(71) Applicant *(for all designated States except US)*: **VERTEX PHARMACEUTICALS INCORPORATED** [US/US], 130 Waverly Street, Cambridge, MA 02139-4242 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **DAVIES, Robert** [GB/US]; 65 Orient Avenue, Arlington, MA 02474 (US). **BEBBINGTON, David** [GB/GB], 6 Linden Close, Newbury, Berkshire R6141QA (GB). **BINCH, Haley** [GB/GB]; Vertex Pharmaceuticals Ltd., 2 Orchard Way, Harwell, Oxfordshire OX110LQ (GB). **KNEGTEL, Ronald** [GB/GB]; 3 Bath Court, Bath Street, Abingdom, Oxfordshire OX1X1EE (GB). **GOLEC, Julian M.C.** [GB/GB], 8 Chapel Farm Road, Swindon, Oxfordshire SN6 8LS (GB). **PATEL, Sanjay** [IN/GB]; 2 Alder Close, Abingdom, Oxfordshire OX141YG (GB). **CHARRIER, Jean-Damien** [FR/GB]; Vertex Pharmaceuticals Inc., Cottage Wing, Station Road, Southam, Bishops Itchington, Oxfordshire CV47 2QB (GB). **KAY, David** [US/US]; 123 Orchard Street, Apartment 36, Somerville, MA 02144 (US). **DAVIES, Robert** [GB/US]; 65 Orient Avenue, Arlington, MA 02474 (US).

(74) Agents: **ROBIDOUX, Andrea** et al.; Vertex Pharmaceuticals Inc., 130 Waverly Street, Cambridge, MA 02139-4242 (US).

(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, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, 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*

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

DCS
COPY

WO 02/22604 A1

(54) Title: PYRAZOLE COMPOUNDS USEFUL AS PROTEIN KINASE INHIBITORS

(57) Abstract: This invention describes novel pyrazole compounds of formula III:wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R^x and R^y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-8 membered carbocyclo ring; and R^2 and $R^{2'}$ are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.