2002039667

0 2 JUL 2002

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

(19) World Intellectual Property Organization
International Bureau

162162

(43) International Publication Date
2 August 2001 (02.08.2001)

PCT

(10) International Publication Number
WO 01/55114 A1

(51) International Patent Classification[7]: C07D 213/82, 213/89, 401/14, A61K 31/455, A61P 35/00

(21) International Application Number: PCT/EP01/00835

(22) International Filing Date: 25 January 2001 (25.01.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0001930.7 27 January 2000 (27.01.2000) GB

(71) Applicant *(for all designated States except AT, US)*: **NOVARTIS AG** [CH/CH]; Schwarzwaldallee 215, CH-4058 Basel (CH).

(71) Applicant *(for AT only)*: **NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H.** [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MANLEY, Paul, William** [GB/CH]; Bruggweg 12, CH-4144 Arlesheim (CH). **BOLD, Guido** [CH/CH]; Bleumatthöhe 16, CH-5073 Gipf-Oberfrick (CH).

(74) Agent: **BECKER, Konrad**; Novartis AG, Corporate Intellectual Property, Patent & Trademark Department, CH-4002 Basel (CH).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, 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, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

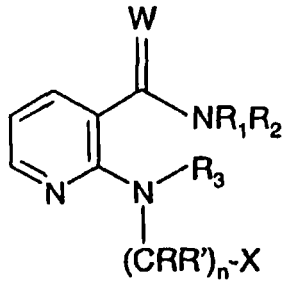
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *with amended claims and statement*

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.

ACTION

(54) Title: 2-AMINO-NICOTINAMIDE DERIVATIVES AND THEIR USE AS VEGF-RECEPTOR TYROSINE KINASE INHIBITORS



(I)

(57) Abstract: The invention relates to the use of 2-amino-nicotinamide derivatives of formula (I) wherein n is from 1 up to and including 6; W is O or S; R_1 and R_3 represent independently of each other hydrogen, lower alkyl or lower acyl; R_2 represents a cycloalkyl group, an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or polysubstituted; R and R' are independently of each other hydrogen or lower alkyl; X represents an aryl group, or a mono- or bicyclic heteroaryl group comprising one or more ring nitrogen atoms and 0, 1 or 2 heteroatoms independently from each other selected from the group consisting of oxygen and sulfur, which groups in each case are unsubstituted or mono- or polysubstituted; or a N-oxide, a possible tautomer thereof or a pharmaceutically acceptale salt of such a compound, alone or in combination with one or more other pharmaceutically active compounds for the preparation of a pharmaceutical composition for use for therapy of a disease which responds to an inhibition of the VEGF-receptor tyrosine kinase activity; and to new 2-amino-nicotinamide derivatives of formula (I) and processes for the preparation thereof.

WO 01/55114 A1