

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
24 January 2002 (24.01.2002)

PCT

(10) International Publication Number
WO 02/06236 A1

(51) International Patent Classification⁷: **C07D 213/76**,
213/82, 401/04, A61K 31/44, A61P 25/22, 25/24

(74) Agent: **POPPE, Regina**; Grenzacherstrasse 124,
CH-4070 Basle (CH).

(21) International Application Number: PCT/EP01/07850

(22) International Filing Date: 9 July 2001 (09.07.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
00115287.5 14 July 2000 (14.07.2000) EP

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

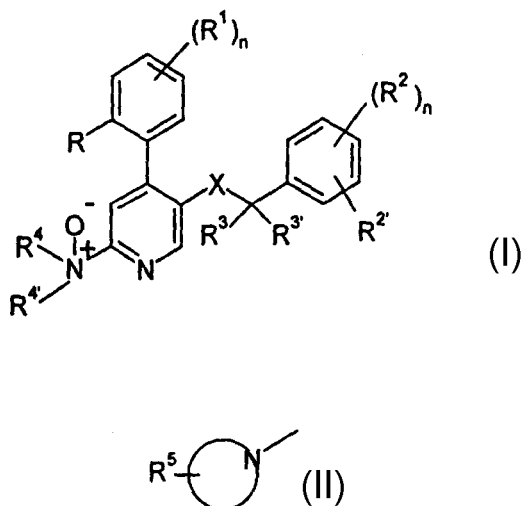
(72) Inventors: **HOFFMANN, Torsten**; Kleinhueninger Strasse 15, 79576 Weil am Rhein (DE). **POLI, Sonia, Maria**; Baerschwilerstrasse 10, CH-4053 Basle (CH). **SCHNIDER, Patrick**; Stallenrain 7, CH-4104 Oberwil (CH). **SLEIGHT, Andrew**; Résidence Le Manoir, 3a, rue de la Lisière, F-68400 Riedisheim (FR).

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.

(54) Title: N-OXIDES AS NK1 RECEPTOR ANTAGONIST PRODRUGS OF 4-PHENYL-PYRIDINE DERIVATIVES



(57) Abstract: The invention relates to compounds of formula (I) wherein R is hydrogen, lower alkyl, lower alkoxy, or trifluoromethyl; R¹ is hydrogen or halogen; or R and R¹ may be together with the ring carbon atoms to which they are attached -CH=CH-CH=CH-; R² and R^{2'} are independently from each other hydrogen, halogen, trifluoromethyl, lower alkoxy or cyano; or R² and R^{2'} may be together -CH=CH-CH=CH-, optionally substituted by one or two substituents selected from lower alkyl or lower alkoxy; R³, R^{3'} are independently from each other hydrogen, lower alkyl or cycloalkyl; R⁴, R^{4'} are independently from each other -(CH₂)_mOR⁶ or lower alkyl; or R⁴ and R^{4'} form together with the N-atom to which they are attached a cyclic tertiary amine of the group (II) R⁵ is hydrogen, hydroxy, lower alkyl, -lower alkoxy, -(CH₂)_mOH, -COOR³, -CON(R³)₂, -N(R³)CO-lower alkyl or -C(O)R³; R⁶ is hydrogen, lower alkyl or phenyl; X is -C(O)N(R⁶)-, -N(R⁶)C(O)-, -(CH₂)_mO- or -O(CH₂)_m-; n is 0, 1, 2, 3 or 4 and; m is 1, 2, or 3; and to pharmaceutically acceptable acid addition salts thereof. It has been found that these compounds may be used as prodrugs for the treatment or prevention of illnesses, related to the NK1 receptor.