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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 March 2004 (04.03.2004)

PCT

(10) International Publication Number
WO 2004/017964 A1

(51) International Patent Classification[7]: A61K 31/425, A61P 35/00, A61K 31/4745, 31/505, 31/282, 31/337, 31/70

(21) International Application Number: PCT/IB2003/003550

(22) International Filing Date: 7 August 2003 (07.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/404,461 19 August 2002 (19.08.2002) US

(71) Applicant *(for all designated States except US)*: **PFIZER PRODUCTS INC.** [US/US]; Eastern Point Road, Groton, CT 06340 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **BEEBE, Jean, Saccuzzo** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **FERRANTE, Karen, Jean** [US/US]; Pfizer Global Research and Development, 50 Pequot Avenuead, New London, CT 06320 (US). **JANI, Jitesh, Pranlal** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **SCHAEFFER, Tracey, Lee** [US/US]; Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340 (US). **HEALEY, Diane, Ingeborg** [US/US]; Pfizer Global Research and Development, 50 Paquot Avenue, New London, CT 06320 (US). **O'LEARY, James, John** [US/US]; Pfizer Global Research and Development, 50 Paquot Avenue, New London, CT 06320 (US).

(74) Agents: **LUMB, J., Trevor** et al.; Pfizer Inc., 201 Tabor Road, Morris Plains, NJ 07950 (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, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, 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, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, 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.

WO 2004/017964 A1

(54) Title: COMBINATION THERAPY FOR HYPERPROLIFERATIVE DISEASES

(57) Abstract: This invention relates a method of treating hyperproliferative diseases. More particularly, the present invention relates to a method of treating hyperproliferative diseases, such as cancer, comprising the step of adminestering to a mammal in need of such treatment, either simultaneously or sequentially, (i) a therapeutically effective amount of a taxane derivative, a platinium coordination complex selected from the group consisting of carboplatin, tetraplatin, and topotecan, a nucleoside analog selected from the group consisting of gemcitabine, hydrochloride and 5-FU, an anthracycline, a topoisomerase selected from the group consisting of etoposide, teniposide, amsacrine, topotecan and CamptosarÚ, an aromatase inhibitor; and (ii) a therapeutically effective amount of an isothiazole derivative. The combinations of the present invention may optionally include an anti-hypertensive agent. This invention also relates to pharmaceutical compositions useful in the treatment of hyperproliferative diseases in mammals, containing such combinations. The present invention also relates to kits having a first compartment with a compound of formula 1 and a second compartment containing a taxane derivative, a platinum coordination complex, a nucleoside analog, an anthracycline, a topoisomerase inhibitor, or an aromatase inhibitor and a third compartment containing an anti-hypersensitive agent.