PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07D 231/56, A61K 31/415 — A1

(11) International Publication Number: **WO 99/23076**

(43) International Publication Date: 14 May 1999 (14.05.99)

(21) International Application Number: PCT/IB98/01579

(22) International Filing Date: 9 October 1998 (09.10.98)

(30) Priority Data:
60/064,160 4 November 1997 (04.11.97) US

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

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: MARFAT, Anthony [US/US]; 333 Lantern Hill Road, Mystic, CT 06355 (US).

(74) Agents: SPIEGEL, Allen, J. et al.; c/o Simpson, Alison, Urquhart-Dykes & Lord, 91 Wimpole Street, London W1M 8AH (GB).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: THERAPEUTICALLY ACTIVE COMPOUNDS BASED ON INDAZOLE BIOISOSTERE REPLACEMENT OF CATECHOL IN PDE4 INHIBITORS

(57) Abstract

Therapeutically active compositions of matter are described which are useful for treating or preventing diseases and conditions comprising inflammatory diseases including joint inflammation, Crohn's disease, and inflammatory bowel disease; respiratory diseases such as chronic obstructive pulmonary disease (COPD) including asthma, chronic bronchitis, and pulmonary emphysema; infectious diseases including endotoxic shock and toxic shock syndrome; immune diseases including systemic lupus erythematosis and psoriasis; and other diseases including bone resorption diseases and reperfusion injury; wherein said composition of matter comprises a compound which is an inhibitor of phosphodiesterase isozyme 4 (PDE4) and wherein an indazole is one essential component of said compound's overall chemical structure, and wherein said indazole constitutes a bioisosteric replacement of a catechol component or functional derivative thereof in a known compound having the same said therapeutic activity and the same remaining said components of its overall chemical structure. Included are compounds of Formula (IA) or (IB), wherein R^2_a and R^2_b are independently selected from the group consisting essentially of hydrogen and hereinafter recited substituents, provided that one, but not both of R^2_a and R^2_b must be independently selected as hydrogen, wherein said substituents comprise moieties including the following: (IC), (ID), (IE), (IF), (IIA), (IIB), (IIC), (IID), (IIE), (IIF), (IIG), (IIH), (III), (IIIA), (IIIB), (IIIC), (IIID), (IIIE), (IIIF), (IIIG), (IIIH), (IIII), (IIIJ), (IIIK), (IIIL), (IIIM), (IIIN), (IIIO), (IIIP), (IIIQ), (IIIR), (IIIS), (IIIT), (IV), (VA), (VB), (VC), (VD), (VE_a), (VE), (VF), (VG), (VH), (VI), (VJ), (VK), (VL), (VM).



