

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
1 April 2004 (01.04.2004)

PCT

(10) International Publication Number
WO 2004/026843 A1

(51) International Patent Classification⁷: **C07D 243/24**,
409/12, 405/12, 413/12, 403/12, 401/12, A61K 31/5513,
A61P 31/12

(21) International Application Number:
PCT/GB2003/004050

(22) International Filing Date:
22 September 2003 (22.09.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0221923.6 20 September 2002 (20.09.2002) GB
0302078.1 29 January 2003 (29.01.2003) GB

(71) Applicant (for all designated States except US): **ARROW THERAPEUTICS LIMITED** [GB/GB]; Britannia House, 7 Trinity Street, London SE1 1DA (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CARTER, Malcolm** [GB/GB]; Arrow Therapeutics Limited, Britannia House, 7 Trinity Street, London SE1 1DA (GB). **HENDERSON, Elisa** [GB/GB]; Arrow Therapeutics Limited, Britannia House, 7 Trinity Street, London SE1 1DA (GB). **KELSEY,**

Richard [GB/GB]; Arrow Therapeutics Limited, Britannia House, 7 Trinity Street, London SE1 1DA (GB). **WILSON, Lara** [GB/GB]; Arrow Therapeutics Limited, Britannia House, 7 Trinity Street, London SE1 1DA (GB). **CHAMBERS, Phil** [GB/GB]; Arrow Therapeutics Limited, Britannia House, 7 Trinity Street, London SE1 1DA (GB). **TAYLOR, Debra** [GB/GB]; Arrow Therapeutics Limited, Britannia House, 7 Trinity Street, London SE1 1DA (GB). **TYMS, Stan** [GB/GB]; Arrow Therapeutics Limited, Britannia House, 7 Trinity Street, London SE1 1DA (GB).

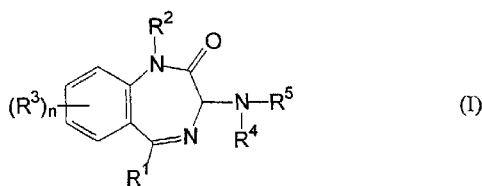
(74) Agents: **SRINIVASAN, Ravi, Chandran et al.**; J.A. Kemp & Co., 14 South Square, Gray's Inn, London WC1R 5JJ (GB).

(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, EG, 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, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, 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),

[Continued on next page]

(54) Title: BENZODIAZEPINE DERIVATIVES AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM



(I)

(57) Abstract: Benzodiazepine derivative of formula (I), and pharmaceutically acceptable salts thereof, are found to be active against RSV. Formula (I) Wherein: - R¹ represents C₁₋₆ alkyl, aryl or heteroaryl; - R² represents hydrogen or C₁₋₆ alkyl; - each R³ is the same or different and represents halogen, hydroxy, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkylthio C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, amino, mono(C₁₋₆ alkyl)amino, di(C₁₋₆ alkyl)amino, nitro, cyano, -CO₂R¹, -CONR¹R², -NH-CO-R¹, -S(O)R¹, -S(O)₂R¹, -NH-S(O)₂R¹, -S(O)NR¹R² or -S(O)₂NR¹R² wherein each R¹ and R² is the same or different and represents hydrogen or C₁₋₆ alkyl; - n is from 0 to 3; R⁴ represents hydrogen or C₁₋₆ alkyl; - R⁵ represents C₁₋₆ alkyl, aryl, heteroaryl, carbocyclyl, heterocyclyl, aryl-(C₁₋₆ alkyl)-, heteroaryl-(C₁₋₆ alkyl)-, carbocyclyl-(C₁₋₆ alkyl)-, heterocyclyl-(C₁₋₆ alkyl)-, aryl-C(O)-C(O)-, heteroaryl-C(O)-C(O)-, carbocyclyl-C(O)-C(O)-, heterocyclyl-C(O)-C(O)- or -XR⁶; - X represents -CO-, -S(O)- or -S(O)₂-; and - R⁶ represents C₁₋₆ alkyl, hydroxy, C₁₋₆ alkoxy, C₁₋₆ alkylthio, aryl, heteroaryl, carbocyclyl, heterocyclyl, aryl-(C₁₋₆ alkyl)-, heteroaryl-(C₁₋₆ alkyl)-, carbocyclyl-(C₁₋₆ alkyl)-, heterocyclyl-(C₁₋₆ alkyl)-, aryl-(C₁₋₆hydroxyalkyl)-, heteroaryl-(C₁₋₆ hydroxyalkyl)-, carbocyclyl-(C₁₋₆ hydroxyalkyl)-, heterocyclyl-(C₁₋₆ hydroxyalkyl)-, aryl-(C₁₋₆alkyl)-O-, heteroaryl-(C₁₋₆alkyl)-O-, carbocyclyl-(C₁₋₆ alkyl)-O-, heterocyclyl-(C₁₋₆ alkyl)-O- or -NR¹R² wherein each R¹ and R² is the same or different and represents hydrogen, C₁₋₆ alkyl, carbocyclyl, heterocyclyl, aryl, heteroaryl, aryl-(C₁₋₆ alkyl)-, heteroaryl-(C₁₋₆ alkyl)-, carbocyclyl-(C₁₋₆ alkyl)- or heterocyclyl-(C₁₋₆ alkyl)-.



WO 2004/026843 A1



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

— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*