(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 22 March 2001 (22.03.2001)

PCT

(10) International Publication Number WO 01/19794 A3

- (51) International Patent Classification⁷: C07D 209/12, A61K 31/404, A61P 43/00, C07F 9/572, 9/24
- (21) International Application Number: PCT/US00/25408
- (22) International Filing Date:

15 September 2000 (15.09.2000)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/154,639

17 September 1999 (17.09.1999) Us

- (71) Applicant (for all designated States except US): BAY-LOR UNIVERSITY [US/US]; P.O. Box 97034, Waco, TX 76798-7034 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): PINNEY, Kevin, G. [US/US]; 100 Russell Lane, Hewitt, TX 76643 (US). WANG, Feng [CN/CN]; 600 American Avenue, Apartment C304, King of Prussia, PA 19406 (US). DEL PILAR MEJIA, Maria [CO/US]; 9999 Linda Lane, Apartment GE, Des Plaines, IL 60016 (US).

- (74) Agent: HODGINS, Daniel, S.; Head, Johnson & Kachigian, 228 West 17th Place, Tulsa, OK 74119 (US).
- (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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- (88) Date of publication of the international search report: 27 September 2001

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.

)4 A

(54) Title: INDOLE-CONTAINING AND COMBRETASTATIN-RELATED ANTI-MITOTIC AND ANTI-TUBULIN POLYMERIZATION AGENTS

(57) Abstract: Trimethoxyphenyl substituted indole ligands have been discovered which demonstrate impressive cytotoxicity as well as a remarkable ability to inhibit tubulin polymerization. Such compounds as well as related derivatives are excellent clinical candidates for the treatment of cancer in humans. In addition, certain of these ligands, as pro-drugs, may well prove to be tumor selective vascular targeting and destruction chemotherapeutic agents or to have anti-angiogenesis activity resulting in the selective prevention and/or destruction of tumor cell vasculature.

INTERNATIONAL SEARCH REPORT

Inter onal Application No PCT/US 00/25408

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07D209/12 A61k C07F9/24 CO7F9/572 A61K31/404 A61P43/00 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) CO7D CO7F IPC 7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. 1-42 WO 98 39323 A (BAYLOR UNIVERSITY) Α 11 September 1998 (1998-09-11) cited in the application claims WO 99 34788 A (ARIZONA BOARD OF REGENTS) 37-42 Α 15 July 1999 (1999-07-15) claims 1-42 P,X WO 00 48606 A (OXIGENE, INC.) 24 August 2000 (2000-08-24) * table 2 and fig. 1B: compound X; fig. 1C: compound XVIII * Patent family members are listed in annex X Further documents are listed in the continuation of box C. ° Special categories of cited documents: *T* later document published after the international filing date or priority date and not in conflict with the application but "A" document defining the general state of the art which is not cited to understand the principle or theory underlying the considered to be of particular relevance invention *E* earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means in the art. *P* document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 07/05/2001 24 April 2001 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Van Bijlen, H Fax: (+31-70) 340-3016

INTERNATIONAL SEARCH REPORT

.formation on patent family members

Inter onal Application No
PCT/US 00/25408

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9839323	Α	11-09-1998	US 5886025 A AU 6688698 A EP 0984954 A	23-03-1999 22-09-1998 15-03-2000	
WO 9934788	Α	15-07-1999	EP	1045689 A	25-10-2000
WO 0048606	Α	24-08-2000	AU	3597300 A	04-09-2000

Form PCT/ISA/210 (patent family annex) (July 1992)