(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 27 May 2004 (27.05.2004)

PCT

(10) International Publication Number WO 2004/044174 A3

- (51) International Patent Classification⁷: A61K 31/4355, C07D 491/04
- (21) International Application Number:

PCT/US2003/036226

(22) International Filing Date:

12 November 2003 (12.11.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/425,503 12 November 2002 (12.11.2002) US 60/425,535 12 November 2002 (12.11.2002) US

- (71) Applicant (for all designated States except US): RUT-GERS, THE STATE UNIVERSITY [US/US]; Old Queens Building, Somerset and George Streets, New Brunswick, NJ 08903 (US).
- (71) Applicant and
- (72) Inventor: LAVOIE, Edmond, J. [US/US]; 3 Guilford Court, Princeton Junction, NJ 08550 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): RUCHELMAN, Alexander, L. [US/US]; 101 Everett Street, Robbinsville, NJ 08691 (US). LIU, Leroy, F. [US/US]; 5 Fairacres Drive, Bridgewater, NJ 08807 (US).

- (74) Agents: STEFFEY, Charles, E. et al.; Schwegman, Lundberg, Woessner & Kluth, P.A., P.O. Box 2938, Minneapolis, MN 55402 (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, 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 (BW, 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
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- $\textbf{(88)} \ \ \textbf{Date of publication of the international search report:}$

12 August 2004

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: TOPOISOMERASE-TARGETING AGENTS

$$R_4$$
 R_3
 Y
 R_5
 R_1
 R_2

(1)

$$R_4$$
 R_5
 R_1
 R_2
 R_1
 R_2
 R_3

(57) Abstract: The invention provides compounds of formula I or formula (II), wherein: the bond represented by --- is a single bond or a double bond, and R_1 - R_5 , X, and Y have any of the meanings defined in the specification and their pharmaceutically acceptable salts. The invention also provides pharmaceutical compositions comprising a compound of formula (I or II), processes for preparing compounds of formula (I or II), intermediates useful for preparing compounds of formula (I or II), and therapeutic methods for treating cancer and other topoisomerase related conditions using compounds of formula (I or II).

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/36226

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A61K 31/4355; C07D 491/04.				
US CL : 514/280; 546/48.				
According to International Patent Classification (IPC) or to both B. 'FIELDS SEARCHED	national classification and IPC			
				
Minimum documentation searched (classification system follows U.S.: 514/280; 546/48.	ed by classification symbols)			
Documentation searched other than minimum documentation to	the extent that such documents are include	d in the fields searched		
Electronic data base consulted during the international search (n CAS ONLINE STRUCTURE SEARCH	ame of data base and, where practicable, s	earch terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category * Citation of document, with indication, where	appropriate, of the relevant passages	Relevant to claim No.		
X US 6,140,328 A (LA VOIE et al.) 31 October 200		1-4, 18		
1-3 and Figure 1.	· .	1 4, 10		
	1			
Further documents are listed in the continuation of Box C.	See patent family annex.			
* Special categories of cited documents:	"T" later document published after the inter- date and not in conflict with the applica	national filing date or priority		
"A" document defining the general state of the art which is not considered to be of particular relevance	principle or theory underlying the inven			
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the considered novel or cannot be considered when the document is taken alone	laimed invention cannot be ad to involve an inventive step		
"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 closest considered to involve an inventive step	when the document is		
"O" document referring to an oral disclosure, use, exhibition or other means	combined with one or more other such a being obvious to a person skilled in the			
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent fa	mily		
Date of the actual completion of the international search	Date of mailing of the international search report			
18 April 2004 (18.04.2004)	Authorized off	718 COO4		
Name and mailing address of the ISA/US Mail Stop PCT, Atm: ISA/US	Authorized officer			
Commissioner for Patents Emily Bernhardt				
P.O. Box 1450 Alexandria, Virginia 22313-1450 Telephone No. (571) 272-1600				
Facsimile No. (703) 305-3230				
orm PCT/ISA/210 (second sheet) (July 1998)				

INTERNATIONAL SEARCH REPORT

International application No.	
DOM/1 1902/26226	

		ervations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:		
1.		Claim Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2.		Claim Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3.	6.4(a).	Claim Nos.: 6-17,19-157 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule
Box	x II Ol	oservations where unity of invention is lacking (Continuation of Item 2 of first sheet)
Thi	s Interna	tional Searching Authority found multiple inventions in this international application, as follows:
1.		As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.		As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite
3.		payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.		No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Rer	nark on	Protest
		No protest accompanied the payment of additional search fees.
-		

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1998)