

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 February 2009 (05.02.2009)

PCT

(10) International Publication Number
WO 2009/018551 A3

(51) International Patent Classification:
C07D 498/22 (2006.01) *A61P 35/00* (2006.01)
A61K 31/424 (2006.01)

(21) International Application Number:
PCT/US2008/072025

(22) International Filing Date: 1 August 2008 (01.08.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/953,648 2 August 2007 (02.08.2007) US

(71) Applicant (*for all designated States except US*): **RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY** [US/US]; Office of Corporate Liaison & Tech. Transfer, ASB 111. 3 Rutgers Plaza, 3rd Floor, New Brunswick, NJ 08901 (US).

(71) Applicants and

(72) Inventors: **LAVOIE, Edmond, J.** [US/US]; 3 Guilford Court, Princeton Junction, NJ 08550 (US). **RICE, Joseph, E.** [US/US]; 5 Oxford Drive, East Windsor, NJ 08529 (US).

(74) Agents: **HARRIS, Robert, J.** et al.; P.O. Box 111098, St. Paul, MN 55111-1098 (US).

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (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*

(88) Date of publication of the international search report:
19 March 2009

(54) Title: THERAPEUTIC COMPOUNDS

(57) Abstract: The invention provides compounds of formula I, II, and III as defined herein, as well as salts thereof. The compounds may have activity as anti -proliferative agents.



WO 2009/018551 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/072025**A. CLASSIFICATION OF SUBJECT MATTER***C07D 498/22(2006.01)i, A61K 31/424(2006.01)i, A61P 35/00(2006.01)i*

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)

IPC as above

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 practicable, search terms used)
eKIPASS(KIPO internal), STN(CA plus), "Keywords: macrocyclic oxazole and cancer "**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	SATYANARAYANA M et al., "Ring-closing metathesis for the synthesis of a highly G-quadruplex selective macrocyclic hexaoxazole having enhanced cytotoxic potency.", Bioorg Med Chem Lett. 1 Jul 2008(Epub 2008 May 15), Vol.18, No.13, pp.3802-4. See Scheme 3 HXDV	34-36
X A	MINHAS G.S. et al., "Synthesis and G-quadruplex stabilizing properties of a series of oxazole-containing macrocycles", Bioorganic & medicinal chemistry letters, 2006, vol.16 no.15, pp.3891-3895 See Scheme 2	34-36 1-3,38-39
X A	BARBIERI CM et al., "Defining the mode, energetics and specificity with which a macrocyclic hexaoxazole binds to human telomeric G-quadruplex DNA.", Nucleic Acids Res. 2007(Epub 2007 Apr 22.), Vol.35, No.10, pp.3272-86. See Figure 1	34-36 1-3,38-39
A	SOHDA KY et al, "YM-216391, a novel cytotoxic cyclic peptide from Streptomyces nobilis. II. Physico-chemical properties and structure elucidation.", J Antibiot (Tokyo). Jan 2005, Vol.58, No.1, pp.32-6. See Figure 1	1-3,34-36,38-39

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"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

"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 documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

16 JANUARY 2009 (16.01.2009)

Date of mailing of the international search report

19 JANUARY 2009 (19.01.2009)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
Government Complex-Daejeon, 139 Seonsa-ro, Seo-
gu, Daejeon 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

YEO, Kyeong Sook

Telephone No. 82-42-481-5612



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2008/072025

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KR 10-2004-0014437 A (TAIHO PHARMACEUTICAL CO., LTD.) 20 June 2002 See Formula (II)	1-3,34-36,38-39
A	CHATTOPADHYAY S.K et al., "Convergent synthesis of a 24-membered macrocyclic hexaoxazole derivative related to the novel telomerase inhibitor telomestatin", Tetrahedron letters, 2006, v.47 no.45, pp.7897-7900 See Scheme 1-3	1-3,34-36,38-39
A	MARSON, CHARLES M et al., "Synthesis of the penta-oxazole core of telomestatin in a convergent approach to poly-oxazolemacrocyces", Organic & biomolecular chemistry, 2006, vol.4 no.21, pp.3892-3893 See Scheme 3	1-3,34-36,38-39

INTERNATIONAL SEARCH REPORTInternational application No.
PCT/US2008/072025**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 41-42
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 41-42 pertain to methods for treatment (or screening) of the human or animal body by therapy/diagnostic methods, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulation under the PCT, to search.
2. ☒ Claims Nos.: 46-47
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:
Claims 46-47 can not make meaningful search because they refer to multiple dependent claims not to be drafted in accordance with the second and third sentences of Rule 6.4(a).
3. ☒ Claims Nos.: 4-33,37,40-45
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International 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 payment of any additional fee.
3. ☐ 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.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2008/072025

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
KR 10-2004-0014437 A	14.02.2004	AT 298342 T	15.07.2005
		AU 2002-222604 B2	24.06.2002
		AU 2002-22604 A1	24.06.2002
		AU 2260402 A	24.06.2002
		CA 2436942 A1	20.06.2002
		CA 2436942 C	20.06.2002
		CN 1253458 C	26.04.2006
		CN 1479742 A	03.03.2004
		DE 60111651 D1	28.07.2005
		DE 60111651 T2	18.05.2006
		EP 1350794 A1	08.10.2003
		EP 1350794 B1	22.06.2005
		EP 1350794 A4	22.12.2004
		ES 2240336 T3	16.10.2005
		JP 4006589 B2	14.11.2007
		PT 1350794 T	30.09.2005
		US 2004-0049029 A1	11.03.2004
		US 6818764 B2	16.11.2004
		WO 02-48153 A1	20.06.2002