(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 February 2009 (12.02.2009)

PCT

(10) International Publication Number
WO 2009/019708 A3

(51) International Patent Classification:
A61K 31/407 (2006.01) *A61K 31/4706* (2006.01)
A61K 31/415 (2006.01) *A61K 31/496* (2006.01)
A61K 31/433 (2006.01) *A61P 35/00* (2006.01)

(21) International Application Number:
PCT/IL2008/001099

(22) International Filing Date: 10 August 2008 (10.08.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/935,364 9 August 2007 (09.08.2007) US
61/006,455 15 January 2008 (15.01.2008) US

(71) Applicant *(for all designated States except US)*: **URIFER LTD** [IL/IL]; c/o Asher Baharav, 19A Hachorsha Street, Raanana 43613 (IL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **NIR, Uri** [IL/IL]; Hagefen Street 90, Moshav Gamzo, D.N Merkaz 73130 (IL). **SHPUNGIN, Sally** [IL/IL]; Hachula Street 17, Ramat-Gan 52275 (IL). **YAFFE, Etai** [IL/IL]; Haalon Street 48, Oranit 44813 (IL). **COHEN, Moshe** [IL/IL]; c/o Asher Baharav, 19A Hachorsha Street, Raanana 43613 (IL).

(74) Agent: **REINHOLD COHN AND PARTNERS**; P.O. Box 4060, Tel-Aviv 61040 (IL).

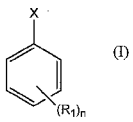
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, 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).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *of inventorship (Rule 4.17(iv))*

[Continued on next page]

(54) Title: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR THE TREATMENT OF CANCER



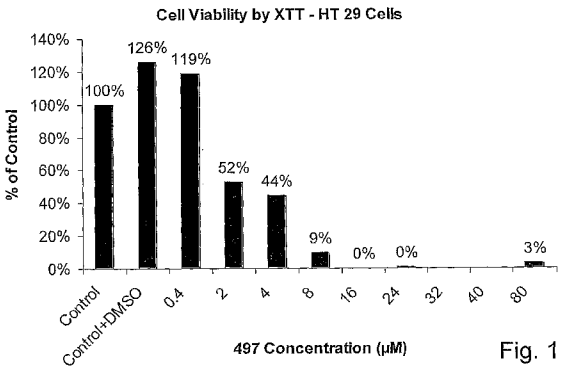


Fig. 1

(57) Abstract: The invention provides a pharmaceutical composition comprising as an active component a compound of formula (I); wherein X and (ROn are as defined, and a physiological acceptable carrier. The invention also provides a method for treating cancer comprising administering to an individual in need of such treatment an effective amount of a pharmaceutical composition of the invention. The invention further provides use of a compound of formula (I) for the preparation of a medicament for the treatment of cancer.

WO 2009/019708 A3

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:
14 May 2009

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2008/001099

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/407 A61K31/415 A61K31/433 A61K31/4706 A61K31/496
A61P35/00

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)
A61K

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)
EPO-Internal, BEILSTEIN Data, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/092086 A (HOFFMANN LA ROCHE [CH]) 21 November 2002 (2002-11-21) abstract; claims 1-18; examples 7,20,22,28,A-C	1,2
X	DATABASE WPI Week 199927 Thomson Scientific, London, GB; AN 1999-323456 XP002519065 -& JP 11 116481 A (SUMITOMO SEIYAKU KK) 27 April 1999 (1999-04-27) abstract; table 1; compounds 17-18 paragraphs [0041] - [0043]	1,2,8,9

-/--

[X] Further documents are listed in the continuation of Box C.

[X] 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 document 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 another 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	Date of mailing of the international search report
13 March 2009	26/03/2009

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, Fax: (+31-70) 340-3016	Madalinska, K

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2008/001099

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KHAZI I M ET AL: "Synthesis and biological activity of some 3-methyl/ethoxycarbonyl-6-arylimidazo[2,1-b]§thiazoles and their 5-bromo/5-formyl derivatives" INDIAN JOURNAL OF CHEMISTRY, vol. 43b, no. 2, February 2004 (2004-02), pages 393-398, XP009113585 ISSN: 0376-4699 abstract; table III; compounds 8A-D page 395, left-hand column, paragraphs ANTI-INFLAMMATORY,ACTIVITY	1,2
X	EP 1 547 996 A (BF RES INST INC [JP]; UNIV TOHOKU [JP]) 29 June 2005 (2005-06-29) paragraphs [0043], [0044]; figure 33; tables 1,4; compounds N-463	1,2
X	ANDREANI A ET AL: "6-Thienyl and 6-phenylimidazo[2,1-b]thiazoles as inhibitors of mitochondrial NADH dehydrogenase" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 34, no. 10, 1 October 1999 (1999-10-01), pages 883-889, XP004202943 ISSN: 0223-5234 abstract; table II; compounds 19-24 page 886, paragraphs BIOLOGICAL,RESULTS	1,2
A	BUU-HOI NG PH ET AL: "2-Arylpyrrocolines and 2-Arylpyrimidazoles" JOURNAL OF ORGANIC CHEMISTRY, 1 January 1954 (1954-01-01), pages 1370-1375, XP002422941 ISSN: 0022-3263 7-methyl-2-(4-fluorophenyl)pyrcoline - Table I abstract	1,2,4,8, 9
A	BARLIN G B ET AL: "Imidazo[1,2-b]pyridazines. XXI. Syntheses of some 3-Acylaminomethyl-6-(chloro and iodo)- 2-(substituted phenyl)-imidazo[1,2-b]pyridazines and -imidazo[1,2-a]pyridines and their Interaction with Central and Mitochondrial Benzodiazepine" AUSTRALIAN JOURNAL OF CHEMISTRY, vol. 50, 1 January 1997 (1997-01-01), pages 61-67, XP001007026 ISSN: 0004-9425 abstract; compounds 41,44	1-9

-/--

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2008/001099

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2007/072093 A (RICHTER GEDEON VEGYESZET [HU]; KESERUE GYOERGY [HU]; WEBER CSABA [HU];) 28 June 2007 (2007-06-28) abstract; claims 1-25; compounds 7,17,126	1,2,7-9
A	WO 2006/101455 A (S BIO PTE LTD [SG]; LEE KEN CHI LIK [SG]; SUN ERIC T [SG]) 28 September 2006 (2006-09-28) abstract; claims 1-47	1-9
A	WO 02/066478 A (ASTRAZENECA AB [SE]; ASTRAZENECA UK LTD [GB]; DOSSETTER ALEXANDER GRAH) 29 August 2002 (2002-08-29) abstract; claims 1-18; examples A1,A2,A3	1-9
A	WO 2004/111061 A (AEGERA THERAPEUTICS INC [CA]; JAQUITH JAMES B [CA]; GILLARD JOHN W [CA) 23 December 2004 (2004-12-23) abstract; claims 1-37; tables 1,2	1-9
A	PRÉVOST G P ET AL: "Anticancer activity of BIM-46174, a new inhibitor of the heterotrimeric Galpha/Gbetagamma protein complex." CANCER RESEARCH 15 SEP 2006, vol. 66, no. 18, 15 September 2006 (2006-09-15), pages 9227-9234, XP009113736 ISSN: 0008-5472 abstract; figure 1	1-10
A	WO 03/017817 A (UNIV BAR ILAN [IL]; NIR URI [IL]; PERI EREZ [IL]; SHPUNGIN SALLY [IL]) 6 March 2003 (2003-03-06) abstract; claims 1-19	1-9

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IL2008/001099

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 02092086 A	21-11-2002	AR 062387 A2	05-11-2008
		AT 284214 T	15-12-2004
		BR 0208387 A	15-06-2004
		CA 2439291 A1	21-11-2002
		CN 1529597 A	15-09-2004
		DE 60202200 D1	13-01-2005
		DE 60202200 T2	15-12-2005
		ES 2232756 T3	01-06-2005
		JP 4088162 B2	21-05-2008
		JP 2004525192 T	19-08-2004
		MX PA03008525 A	08-12-2003
		PT 1381363 T	29-04-2005
		US 2002188128 A1	12-12-2002
		ZA 200306341 A	15-11-2004
JP 11116481 A	27-04-1999	NONE	
EP 1547996 A	29-06-2005	AU 2003261834 A1	04-05-2004
		CA 2496633 A1	29-04-2004
		WO 2004035522 A1	29-04-2004
		US 2005260126 A1	24-11-2005
WO 2007072093 A	28-06-2007	AU 2006327897 A1	28-06-2007
		CA 2629991 A1	28-06-2007
		EP 1962849 A1	03-09-2008
WO 2006101455 A	28-09-2006	AR 056187 A1	26-09-2007
		AU 2006225355 A1	28-09-2006
		CA 2602328 A1	28-09-2006
		EP 1863811 A1	12-12-2007
		JP 2008533198 T	21-08-2008
		KR 20080005207 A	10-01-2008
WO 02066478 A	29-08-2002	NONE	
WO 2004111061 A	23-12-2004	CA 2527906 A1	23-12-2004
		CN 1835956 A	20-09-2006
		EP 1636242 A1	22-03-2006
		JP 2006527209 T	30-11-2006
		KR 20060017645 A	24-02-2006
WO 03017817 A	06-03-2003	AU 2002330724 A1	10-03-2003
		CA 2458640 A1	06-03-2003
		US 2005063973 A1	24-03-2005