

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 February 2007 (15.02.2007)

PCT

(10) International Publication Number
WO 2007/017331 A3

(51) International Patent Classification:

A61K 31/4745 (2006.01) A61K 9/20 (2006.01)
A61K 9/48 (2006.01) A61K 47/14 (2006.01)
A61K 9/10 (2006.01) A61K 47/26 (2006.01)
A61K 9/107 (2006.01) A61K 47/44 (2006.01)
A61K 9/16 (2006.01)

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(21) International Application Number:

PCT/EP2006/064111

(22) International Filing Date: 11 July 2006 (11.07.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

RM2005A000418 4 August 2005 (04.08.2005) IT

(71) Applicant (for all designated States except US):
SIGMA-TAU INDUSTRIE FARMACEUTICHE RIUNITE S.P.A. [IT/IT]; Viale Shakespeare, 47, I-00144 Rome (IT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **LONGO, Antonio** [IT/IT]; Via Chianesi, 109, I-00128 Rome (IT). **PACE, Silvia** [IT/IT]; Via Leonardo Umile, 31, I-00144 Rome (IT). **PEDRANI, Massimo** [IT/IT]; Salita Rognoni, 18, I-28 836 Gignese (VB) (IT).

(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, HU, IE, IS, IT, LT, LU, LV, MC, NL, 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))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

Published:

- with international search report

(88) Date of publication of the international search report:

27 September 2007

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

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: IMMEDIATE RELEASE THERAPEUTIC SYSTEMS FOR IMPROVED ORAL ABSORPTION OF 7- [(E) -TERT-BUTYLOXYIMINOMETHYL] CAMPTOTHECIN

(57) Abstract: A pharmaceutical composition comprising a camptothecin as active ingredient is herein described. In particular immediate-release therapeutic systems are described for the improved oral absorption of 7-[(E)-t-butyloximinomethyl] camptothecin, comprising a matrix consisting of liquid amphiphilic substances or having a melting point lower than 60°C, in which the active principle is at least partially dissolved and/or dispersed and/or inglobated.



WO 2007/017331 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2006/064111

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/4745 A61K9/48 A61K9/10 A61K9/107 A61K9/16
A61K9/20 A61K47/14 A61K47/26 A61K47/44

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, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2006/067092 A (SIGMA TAU IND FARMACEUTI [IT]; CARMINATI PAOLO [IT]; TINTI MARIA ORNEL) 29 June 2006 (2006-06-29) page 11, paragraph 3	1,2
P,X	WO 2005/092302 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; SCHRAN HORST F [US]; W00) 6 October 2005 (2005-10-06) page 6, paragraph 3	1,13,14, 18
	----- -/-	

☒ 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 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

2 May 2007

Date of mailing of the international search report

~~16/05/2007~~

09.07.07

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

GIMENEZ MIRALLES, J

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2006/064111

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CESARE DE M ET AL: "Potent Antitumor Activity and Improved Pharmacological Profile of ST1481, a Novel 7-substituted Camptothecin" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 61, 2001, pages 7189-7195, XP002340217 ISSN: 0008-5472 the whole document -----	1
X	PETRANGOLINI G ET AL: "ANTIANGIOGENIC EFFECTS OF THE NOVEL CAMPTOTHECIN ST1481 (GIMATECAN) IN HUMAN TUMOR XENOGRAFTS" MOLECULAR CANCER RESEARCH, XX, XX, vol. 1, no. 12, October 2003 (2003-10), pages 863-870, XP008059627 ISSN: 1541-7786 the whole document -----	1
X	WO 00/53607 A (SIGMA TAU IND FARMACEUTICHE S [IT]; IST NAZ STUD CURA DEI TUMORI [IT];) 14 September 2000 (2000-09-14) -----	1
Y	page 28, paragraphs 2,3 -----	1-18
Y	WO 99/06031 A (SMITHKLINE BEECHAM CORP [US]; HERZYK DANUTA & HM [US]; CHRISTENSEN GRE) 11 February 1999 (1999-02-11) examples -----	1-18
Y	WO 99/06024 A (UPJOHN CO [US]; MOROZOWICH WALTER [US]; GAO PING [US]) 11 February 1999 (1999-02-11) page 9, line 7 - line 20; examples 41-43 -----	1-18
Y	US 2003/065024 A1 (LAMBERT KAREL J [US] ET AL) 3 April 2003 (2003-04-03) paragraph [0074] -----	1-18
Y	US 5 859 023 A (HAUSHEER FREDERICK H [US] ET AL) 12 January 1999 (1999-01-12) examples -----	1-18

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2006/064111

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2006067092	A	29-06-2006	NONE	
WO 2005092302	A	06-10-2005	AU 2005226932 A1	06-10-2005
			CA 2559532 A1	06-10-2005
			CN 1929842 A	14-03-2007
			EP 1732554 A2	20-12-2006
WO 0053607	A	14-09-2000	AT 216998 T	15-05-2002
			AU 774174 B2	17-06-2004
			AU 3160400 A	28-09-2000
			BG 105810 A	28-06-2002
			BR 0008840 A	08-01-2002
			CA 2362760 A1	14-09-2000
			CN 1343209 A	03-04-2002
			CZ 20013077 A3	16-01-2002
			DE 69901379 D1	06-06-2002
			DE 69901379 T2	07-11-2002
			DK 1044977 T3	08-07-2002
			EA 3605 B1	26-06-2003
			EE 200100466 A	16-12-2002
			EP 1044977 A1	18-10-2000
			ES 2175919 T3	16-11-2002
			HK 1031222 A1	09-05-2003
			HR 20010667 A2	31-08-2002
			HU 0200210 A2	29-05-2002
			IS 6031 A	31-07-2001
			JP 2002539128 T	19-11-2002
			MX PA01009081 A	30-08-2002
			NO 20014128 A	24-08-2001
			NZ 513393 A	29-04-2003
			PL 355094 A1	22-03-2004
			PT 1044977 T	30-09-2002
			SI 1044977 T1	31-08-2002
			SK 11642001 A3	07-01-2002
			TR 200102603 T2	21-01-2002
			US 6242457 B1	05-06-2001
			ZA 200107408 A	12-03-2002
WO 9906031	A	11-02-1999	AU 8604598 A	22-02-1999
			ZA 9806877 A	15-06-1999
WO 9906024	A	11-02-1999	AT 265847 T	15-05-2004
			AU 728698 B2	18-01-2001
			AU 8573998 A	22-02-1999
			BR 9811058 A	05-09-2000
			CA 2294031 A1	11-02-1999
			CN 1261790 A	02-08-2000
			CZ 20000157 A3	17-05-2000
			DE 69823663 D1	09-06-2004
			DE 69823663 T2	19-05-2005
			EP 0999826 A1	17-05-2000
			ES 2219895 T3	01-12-2004
			FI 20000170 A	28-01-2000
			HK 1028883 A1	17-02-2006
			JP 2002511099 T	09-04-2002
			NO 20000467 A	29-03-2000
			NZ 502569 A	31-05-2002
			PL 338509 A1	06-11-2000

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2006/064111

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9906024	A	PT 999826 T RU 2211021 C2 SK 172000 A3	30-09-2004 27-08-2003 11-07-2000
US 2003065024	A1	03-04-2003	NONE
US 5859023	A	12-01-1999	AT 238053 T 15-05-2003 AU 694677 B2 23-07-1998 AU 6222396 A 24-12-1996 CA 2223259 A1 12-12-1996 CN 1187126 A 08-07-1998 DE 69627651 D1 28-05-2003 DE 69627651 T2 16-10-2003 DK 831825 T3 04-08-2003 WO 9639143 A1 12-12-1996 EP 0831825 A1 01-04-1998 ES 2191760 T3 16-09-2003 JP 11506463 T 08-06-1999 PT 831825 T 30-09-2003 US 5726181 A 10-03-1998 US 5880133 A 09-03-1999 US 5958937 A 28-09-1999 US 5900419 A 04-05-1999 US 5955467 A 21-09-1999 US 5859022 A 12-01-1999