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Francisco, CA 94109 (US). **BARBIER, Remi** [US/US]; 1345 Douglas Street, San Francisco, CA 94131 (US). **MCGINITY, James, W.** [US/US]; 4209 Dunning Lane, Austin, TX 78746 (US).

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(74) **Agent:** MCNICHOLAS, Janet, M.; McAndrews Held & Malloy, Ltd., Suite 3400, 500 W. Madison, Chicago, IL 60661 (US).

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(71) **Applicants** (*for all designated States except US*): PAIN THERAPEUTICS, INC. [US/US]; 416 Browning Way, South San Francisco, CA 94080 (US). ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY [US/US]; 1300 Morris Park Avenue, Bronx, NY 10461 (US).

(72) **Inventors; and**
(75) **Inventors/Applicants (for US only): SHERMAN, Barry**
[US/US]; 2830 Churchill, Hillsborough, CA 94010 (US).
REMIEN, Mary [US/US]; 1483 Sutter Street #1104, San

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(54) Title: OPIOID ANTAGONIST COMPOSITIONS AND DOSAGE FORMS

(57) Abstract: The present invention is directed to novel dosage forms, pharmaceutical compositions, kits, and methods of administration of an opioid antagonist in an amount of at least about 0.0001 mg to about or less than about 1.0 mg, including from about 0.0001 mg to less than about 0.5 mg. Solid oral dosage forms are disclosed consisting essentially of an opioid antagonist or alternatively comprising an opioid antagonist and another active ingredient, such as an opioid agonist. Immediate release oral dosage forms are disclosed that release all or a substantial percentage of opioid antagonist, and another active ingredient when present, in a desired time. Concurrent release dosage forms are disclosed that provide concurrent release of an opioid antagonist and another active ingredient.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/485 A61K31/135 A61K31/445 A61K31/4468 A61P25/04
//(A61K31/485,31:135,31:445)

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 7 A61K A61P

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, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 01377 A (SIMON DAVID LEW) 13 January 2000 (2000-01-13) claims 1-20; examples 1,4 ---	1-43, 46-97, 105-171
X	WO 99 32120 A (EURO CELTIQUE SA ;PALERMO PHILIP (US)) 1 July 1999 (1999-07-01) page 10, line 26 -page 13, line 31; claims 1-10; examples 1,2 ---	1-43, 46-97, 105-171
X	WO 99 32119 A (EURO CELTIQUE SA ;KAIKO ROBERT F (US); COLUCCI ROBERT D (US)) 1 July 1999 (1999-07-01) claims 1-10; example 2 ---	1-43, 46-97, 105-171

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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- *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
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- *&* document member of the same patent family

Date of the actual completion of the international search 15 March 2002	Date of mailing of the international search report 28/03/2002
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 Kling, I

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International Application No

PCT/US 01/14377

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 02251 A (EINSTEIN COLL MED) 1 February 1996 (1996-02-01) claims 1-25; examples 1-3 ---	1-43, 46-97, 105-171
X	US 5 580 876 A (SHEN KE-FEI ET AL) 3 December 1996 (1996-12-03) claims 1-29; examples 3-8 ---	1-43, 46-97, 105-171
X	US 5 767 125 A (SHEN KE-FEI ET AL) 16 June 1998 (1998-06-16) claims 1-18; examples 3-8 ---	1-43, 46-97, 105-171
X	US 4 889 860 A (RZESZOTARSKI WACLAW J ET AL) 26 December 1989 (1989-12-26) claims 1-21; figure 19; example XVIII; tables 1-4 -----	1-43, 46-97, 105-171

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-16,18,19,22-37,39,40,43,46-62,68-81,97,105-171

In view of the large number and also the wording of the claims presently on file, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful search is impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and concise), namely the opioid antagonists naltrexone, nalmefene and naloxone have been searched e.g those compounds recited in the examples and closely related homologous compounds etc...

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/14377

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0001377	A	13-01-2000	US AU EP WO	6103258 A 5090099 A 1105134 A2 0001377 A2	15-08-2000 24-01-2000 13-06-2001 13-01-2000
WO 9932120	A	01-07-1999	AU BR CN EP HU JP NO PL TR WO US US	2089999 A 9813826 A 1284879 T 1041988 A1 0100310 A2 2001526229 T 20003278 A 341309 A1 200001828 T2 9932120 A1 6228863 B1 2002004509 A1	12-07-1999 10-10-2000 21-02-2001 11-10-2000 28-06-2001 18-12-2001 22-08-2000 09-04-2001 21-11-2000 01-07-1999 08-05-2001 10-01-2002
WO 9932119	A	01-07-1999	AU BR CN EP JP NO PL TR WO US US	2008499 A 9813827 A 1303287 T 1041987 A1 2001526228 T 20003277 A 342429 A1 200001942 T2 9932119 A1 6277384 B1 2002013301 A1	12-07-1999 10-10-2000 11-07-2001 11-10-2000 18-12-2001 21-08-2000 04-06-2001 21-11-2000 01-07-1999 21-08-2001 31-01-2002
WO 9602251	A	01-02-1996	US AU AU CA EP JP US WO US US US US	5512578 A 3276995 A 4113599 A 2195122 A1 0808165 A1 10507740 T 6096756 A 9602251 A1 2001006967 A1 5580876 A 5767125 A RE36547 E	30-04-1996 16-02-1996 23-09-1999 01-02-1996 26-11-1997 28-07-1998 01-08-2000 01-02-1996 05-07-2001 03-12-1996 16-06-1998 01-02-2000
US 5580876	A	03-12-1996	US US US AU AU CA EP JP US WO US US AU AU CA	5512578 A 5472943 A 5767125 A 3276995 A 4113599 A 2195122 A1 0808165 A1 10507740 T 6096756 A 9602251 A1 2001006967 A1 RE36547 E 691515 B2 7474194 A 2168262 A1	30-04-1996 05-12-1995 16-06-1998 16-02-1996 23-09-1999 01-02-1996 26-11-1997 28-07-1998 01-08-2000 01-02-1996 05-07-2001 01-02-2000 21-05-1998 28-02-1995 09-02-1995

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/14377

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
US 5580876	A	EP	0711167	A1	15-05-1996
		JP	9504267	T	28-04-1997
		WO	9503804	A1	09-02-1995
		US	5585348	A	17-12-1996
		CA	2145207	A1	22-03-1994
		EP	0668764	A1	30-08-1995
		JP	8504189	T	07-05-1996
		WO	9406426	A1	31-03-1994
		US	5633259	A	27-05-1997
		US	5624932	A	29-04-1997

US 5767125	A	16-06-1998	US	5580876 A	03-12-1996
			US	5512578 A	30-04-1996
			US	5472943 A	05-12-1995
			US	6096756 A	01-08-2000
			US	2001006967 A1	05-07-2001
			AU	3276995 A	16-02-1996
			AU	4113599 A	23-09-1999
			CA	2195122 A1	01-02-1996
			EP	0808165 A1	26-11-1997
			JP	10507740 T	28-07-1998
			WO	9602251 A1	01-02-1996
			US	RE36547 E	01-02-2000
			AU	691515 B2	21-05-1998
			AU	7474194 A	28-02-1995
			CA	2168262 A1	09-02-1995
			EP	0711167 A1	15-05-1996
			JP	9504267 T	28-04-1997
			WO	9503804 A1	09-02-1995
			US	5585348 A	17-12-1996
			CA	2145207 A1	22-03-1994
			EP	0668764 A1	30-08-1995
			JP	8504189 T	07-05-1996
			WO	9406426 A1	31-03-1994
			US	5633259 A	27-05-1997
			US	5624932 A	29-04-1997

US 4889860	A	26-12-1989	US	4760069 A	26-07-1988
			AU	6223986 A	07-04-1987
			EP	0238507 A1	30-09-1987
			JP	63501500 T	09-06-1988
			WO	8701703 A1	26-03-1987