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(71) Applicant (for all designated States except US): **PENWEST PHARMACEUTICALS CO.** [US/US]; 5 Kendall Drive, Wappingers, NY 12590 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BAICHWAL, Anand, R.** [US/US]; 5 Kendall Drive, Wappingers Falls, NY 12590 (US). **GOLIBER, Philip, A.** [US/US]; 49 Lake George Road, Brookfield, CT 06804 (US). **CARPANZANO, Anthony, E.** [US/US]; 14 Lily Pond Trail, New Milford, CT 06776 (US). **SCIASCIA, Thomas** [US/US]; 108 Oliver Road, Belmont, MA 02478 (US). **DIEHL, Donald, II** [US/US]; 7 Bauer Road, New Fairfield, CT 06812 (US). **VOGLER, Brian** [US/US]; 50 Washington Avenue, N, White Plains, NY 10603 (US).

(74) Agents: **SUPERKO, Colleen et al.; WILMER CUTLER PICKERING HALE AND DORR LLP**, 60 State Street, Boston, MA 02109 (US).

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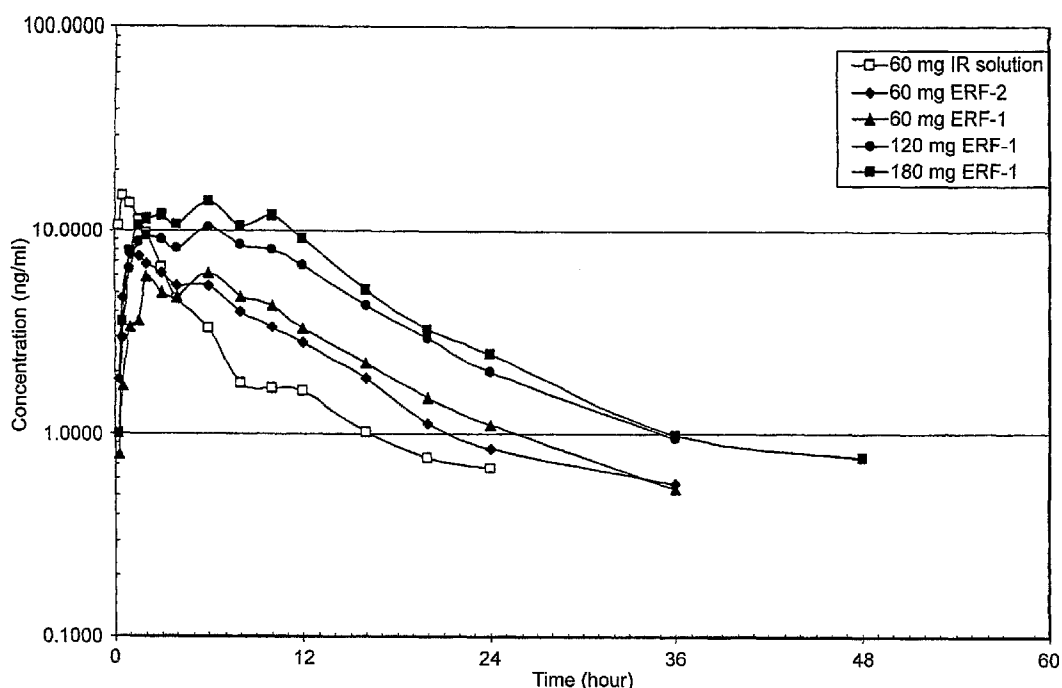
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[Continued on next page]

(54) Title: SUSTAINED RELEASE FORMULATIONS OF NALBUPHINE



(57) Abstract: Sustained release formulations of nalbuphine or pharmaceutically acceptable salts thereof; methods for making the sustained release formulations of nalbuphine or pharmaceutically acceptable salts thereof; and methods for using the sustained release formulations of nalbuphine or pharmaceutically acceptable salts thereof to treat patients suffering from pain are provided.

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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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.

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INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K9/22 A61K9/24

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, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/22940 A (MENDELL CO INC EDWARD [US]; BAICHWAL ANAND R [US]; MCCALL TROY W [US];) 5 April 2001 (2001-04-05) page 21, line 30 - page 23, line 12 table 35 claims 1,2,12,13	1-18, 22-26, 30-52, 56-62, 76-80, 86-88
Y	US 2003/211157 A1 (SIMON DAVID LEW [US]) 13 November 2003 (2003-11-13) examples 9,10,15 ----- -/--	1-18, 22-26, 30-52, 56-62, 76-80, 86-88

☒ 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

9 March 2007

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29/10/2007

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

Sindel, Ulrike

INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	YEN S Y ET AL: "Controlled release of nalbuphine propionate from biodegradable microspheres: in vitro and in vivo studies." INTERNATIONAL JOURNAL OF PHARMACEUTICS 4 JUN 2001, vol. 220, no. 1-2, 4 June 2001 (2001-06-04), pages 91-99, XP002424015 ISSN: 0378-5173 abstract page 91, paragraph 1 paragraph [03.2] - paragraph [03.3] figure 2	19-21, 27-29, 53-55, 81-83
Y	WO 2004/012715 A (PENWEST PHARMACEUTICALS COMPAN [US]) 12 February 2004 (2004-02-12) example 7 claims 1-10	1-18, 22-26, 30-52, 56-62, 76-80
Y	US 5 399 358 A (BAICHWAL ANAND R [US] ET AL) 21 March 1995 (1995-03-21) tables 1,7	1-18, 22-26, 30-52, 56-62, 76-80
Y	US 6 284 274 B1 (MERRILL SONYA [US] ET AL) 4 September 2001 (2001-09-04)	19-21, 27-29, 53-55, 81-83
A	column 1, line 13 - line 23 example 8	1-62, 76-83, 86-88

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/033011

Box 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.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 19-21, 27-29, 53-55 and 81-83 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims 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. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box 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:

see additional sheet

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.:

see annex

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-62, 76-83, 86-88

A sustained release formulation comprising nalbuphine or a pharmaceutically acceptable salt thereof and a sustained delivery system comprising a hydrophilic compound, a cross-linking agent and a pharmaceutical diluent; the process for making this formulation and its use

2. claims: 63-75

A sustained release formulation comprising a first and a second layer; the first layer comprises an immediate release formulation of nalbuphine or a pharmaceutically acceptable salt thereof and the second layer comprises an extended release formulation of nalbuphine or a pharmaceutically acceptable salt thereof

3. claims: 84, 85, 89

A sustained release formulation comprising a first and a second layer; the first layer comprising nalbuphine or a pharmaceutically acceptable salt thereof and the second layer comprising nalbuphine or a pharmaceutically acceptable salt thereof and a sustained delivery system comprising a hydrophilic compound, a cross-linking agent and a pharmaceutical diluent

4. claims: 90-97

An oral unit dosage form comprising nalbuphine or a pharmaceutically acceptable salt thereof showing sustained release of nalbuphine

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/033011

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