A61K 31/05 (2006.01) A61K 31/58 (2006.01)
A61K 31/122 (2006.01) A61K 31/6615 (2006.01)
A61K 31/167 (2006.01) A61K 38/09 (2006.01)
A61K 31/277 (2006.01) A61K 45/06 (2006.01)
A61K 31/4166 (2006.01) A61K 49/00 (2006.01)
A61K 31/565 (2006.01) G01N 33/50 (2006.01)
A61K 31/57 (2006.01) A61P 35/00 (2006.01)

(21) International Application Number:
PCT/US2011/046474

(22) International Filing Date:
3 August 2011 (03.08.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/370,534 4 August 2010 (04.08.2010) US

(71) Applicant (for all designated States except US): PELLFLUCURE PHARMACEUTICALS, INC. [US/US]; 2325 Camino del Collado, La Jolla, CA 92037 (US).

Inventor: and

(75) Inventor/Applicant (for US only): BORSTRÖM, Per [US/US]; 2323 Camino del Collado, La Jolla, CA 92037 (US).

Agent: HART, Daniel; Knobbe Martens Olson & Bear LLP, 2040 Main Street, 14th Floor, Irvine, CA 92614 (US).

(51) International Patent Classification:
A61K 31/05 (2006.01) A61K 31/58 (2006.01)
A61K 31/122 (2006.01) A61K 31/6615 (2006.01)
A61K 31/167 (2006.01) A61K 38/09 (2006.01)
A61K 31/277 (2006.01) A61K 45/06 (2006.01)
A61K 31/4166 (2006.01) A61K 49/00 (2006.01)
A61K 31/565 (2006.01) G01N 33/50 (2006.01)
A61K 31/57 (2006.01) A61P 35/00 (2006.01)


Published:
— with international search report (Art. 21(3))

(88) Date of publication of the international search report:
26 October 2012

(51) Title: COMBINATION THERAPY FOR THE TREATMENT OF PROSTATE CARCINOMA

(57) Abstract: Disclosed herein are naphthoquinone analogs, such as plumbagin, pharmaceutical compositions that include naphthoquinone analogs, such as plumbagin, and methods of treating diseases and/or conditions such as cancer with naphthoquinone analogs, such as plumbagin. Also included are combination therapies wherein a naphthoquinone analog, such as plumbagin, and a hormone therapy agent are provided to a subject suffering from a condition such as cancer.

![Graph](https://example.com/graph.png)

**FIG. 1**
## INTERNATIONAL SEARCH REPORT

**International application No**
PCT/US2011/046474

### A. CLASSIFICATION OF SUBJECT MATTER

|------|-----------|-----------|------------|------------|-------------|-----------|----------|------------|------------|------------|------------|-------------|-------------|-------------|------------|

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 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practicable, search terms used)
EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>CN 1 095 275 A (JIANG YUANHUI [CN]) 23 November 1994 (1994-11-23) abstract; claims 1-2 -----</td>
<td>1-6, 10-25, 27,43-45</td>
</tr>
</tbody>
</table>

* 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 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

* "A" document member of the same patent family

<table>
<thead>
<tr>
<th>Date of the actual completion of the international search</th>
<th>Date of mailing of the international search report</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 June 2012</td>
<td>04/07/2012</td>
</tr>
</tbody>
</table>

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Madalinska, K
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>HAFEEZ BILAL B ET AL: &quot;Pitumbagina non-toxic natural agent, induces apoptosis and inhibits the growth of prostate cancer LNCaP and C4-2 cells via blocking of both androgen and non-androgen activation of androgen receptor signaling&quot;, PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 51, April 1, 2010 (2010-04), pages 919-3780, XP001526037. &amp; 101ST ANNUAL MEETING OF THE AMERICAN-ASSOCIATION-FOR-CANCER-RESEARCH; WASHINGTON, DC, USA; APRIL 17-21, 2010 ISSN: 0197-016X abstract</td>
<td>1-6, 10-25, 27,43,44</td>
</tr>
<tr>
<td>Y</td>
<td>M. H. AZIZ ET AL: &quot;Pitumbagina, a Medicinal Plant-Derived Naphthoquinone, is a Novel Inhibitor of the Growth and Invasion of Hormone-Refractory Prostate Cancer&quot;, CANCER RESEARCH, vol. 68, no. 21, 1 November 2008 (2008-11-01), pages 9024-9032, XP055022365. ISSN: 0008-5472, DOI: 10.1158/0008-5472.CAN-08-2494 abstract</td>
<td>1-6, 10-25, 27,43-45</td>
</tr>
<tr>
<td>Y</td>
<td>wo 2007/147128 A2 (SUMMA HEALTH SYSTEM [US]; MILLER THOMAS M [US]; JAMISON JAMES M [US]) 21 December 2007 (2007-12-21) abstract example I; table 5 example IV; table 9</td>
<td>1-6, 10-25, 27,43-45</td>
</tr>
<tr>
<td>Category</td>
<td>Citation of document, with indication, where appropriate, of the relevant passages</td>
<td>Relevant to claim No.</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Category</td>
<td>Citation of document, with indication, where appropriate, of the relevant passages</td>
<td>Relevant to claim No.</td>
</tr>
<tr>
<td>----------</td>
<td>----------------------------------------------------------------------------------</td>
<td>----------------------</td>
</tr>
</tbody>
</table>
INTERNATIONAL SEARCH REPORT

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

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 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:

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 fees, this Authority did not invite payment of additional fees.

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.:
   
   3-6 (completely) ; 1, 2, 10-25, 27, 43-45 (partially)

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

1. claims: 3-6 (completely) ; 1, 2, 10-25, 27, 43-45 (partially)

   Compound of formula (I) in combination with an anti-androgen compound for use in inhibiting or delaying the growth of prostate tumour

2. claims: 7 (completely) ; 1, 2, 10-25, 27, 43-45 (partially)

   Compound of formula (I) in combination with an estrogen for use in inhibiting or delaying the growth of prostate tumour

3. claims: 8 (completely) ; 1, 2, 10-25, 27, 43-45 (partially)

   Compound of formula (I) in combination with a luteinizing hormone-relaxing hormone (LHRH) agonist for use in inhibiting or delaying the growth of prostate tumour

4. claims: 9 (completely) ; 1, 2, 10-25, 27, 43-45 (partially)

   Compound of formula (I) in combination with a luteinizing hormone-relaxing hormone (LHRH) antagonist for use in inhibiting or delaying the growth of prostate tumour

5. claims: 26, 28-42

   A method of identifying a compound that inhibits or delays prostate cancer cell growth
<table>
<thead>
<tr>
<th>Patent document cited in search report</th>
<th>Publication date</th>
<th>Patent family member(s)</th>
<th>Publication date</th>
</tr>
</thead>
<tbody>
<tr>
<td>CN 1095275</td>
<td>A</td>
<td></td>
<td>23-11-1994</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NONE</td>
<td></td>
</tr>
<tr>
<td>WO 2007147128</td>
<td>21-12-2007</td>
<td>CA 2689717</td>
<td>21-12-2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 2034835</td>
<td>18-03-2009</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2010056625</td>
<td>04-03-2010</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WO 2007147128</td>
<td>21-12-2007</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>