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(71) Applicant (for all designated States except US): JINA PHARMACEUTICALS, INC. [US/US]; 28100 North Ashley Circle, Suite 103, Libertyville, IL 60048 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): AHMAD, Ateeq [US/US]; 4795 West Pebble Beach Drive, Wadsworth, IL 60083 (US). ALI, Shoukath, M. [US/US]; 10 Southfield Drive, Vernon Hills, IL 60061 (US). AHMAD, Moghis, U. [US/US]; 3050 North Forrest Hills Court, Wadsworth, IL 60083 (US). SHEIKH, Saifuddin [US/US]; 1059

South West Avenue, Waukegan, IL 60085 (US). AHMAD, Imran [US/US]; 5420 Belmont Court, Libertyville, IL 60048 (US).

(74) Agent: BROW, Mary Ann, D.; Casimir Jones, S.C., 2275 Deming Way, Suite 310, Middleton, WI 53562 (US).

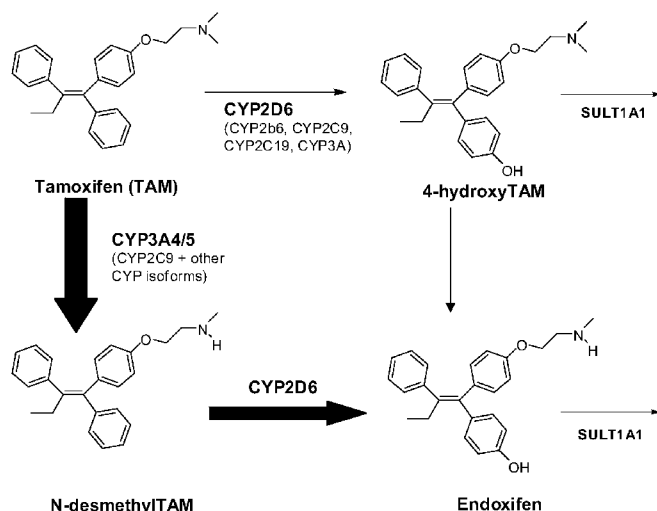
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[Continued on next page]

(54) Title: ENDOXIFEN METHODS AND COMPOSITIONS IN THE TREATMENT OF MAMMALIAN DISEASES

Figure 3



(57) Abstract: The present invention provides compositions containing endoxifen, formulations and liposomes of endoxifen, methods of preparation of such agents and formulations, and use of such agents and formulations for the treatment of a subject having or at risk for psychiatric and neurodegenerative diseases, infectious diseases, fertility disorders, osteoporosis, osteoarthritis, and/or cardiovascular diseases. Specifically, the present invention relates to compositions comprising endoxifen for use in the treatment of such disorders or predisposition to such disorders, for use in manufacture of medicaments for treating such disorders, and methods comprising use of such compositions in such treatments.

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LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK,  
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
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— with international search report (Art. 21(3))

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13 January 2011

INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 10/35852

<p>A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 31/135 (2010.01) USPC - 514/648 According to International Patent Classification (IPC) or to both national classification and IPC</p>																							
<p>B. FIELDS SEARCHED</p> <p>Minimum documentation searched (classification system followed by classification symbols) USPC - 514/648</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 514/648; 424/463, 424/474 (words only)</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST (PGPB, USPT, USOC, EPAB, JPAB); Google</p> <p>*** See Extra Sheet for search terms used ***</p>																							
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1"> <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 --- Y</td> <td>WO 2008/070463 A2 (Ahmad et al.) 12 June 2008 (12.06.2008); especially para [0001], [0004]-[0005], [0008], [0014], [0016], [0020]-[0021], [0023], [0027], [0033] and [0052]</td> <td>14-15, 31-32, 44 ----- 1-13, 16-30, 33, 43, 45</td> </tr> <tr> <td>Y</td> <td>WO 2008/048194 (Yesiloglu) 24 April 2008 (24.04.2008); especially claim 1; and pg 4, ln 2-3</td> <td>1-13, 18-30, 43</td> </tr> <tr> <td>Y</td> <td>Cooke et al., "Tamoxifen Use and Osteoporotic Fracture Risk: A Population-Based Analysis," 10 November 2008 (10.11.2008); Journal of Clinical Oncology, Vol. 26, Num. 32, pg 5227-5232; especially pg 5230, col 2, para 1</td> <td>16, 33, 45</td> </tr> <tr> <td>Y</td> <td>Steiner et al., "Comparison of tamoxifen and clomiphene citrate for ovulation induction: a meta-analysis," 21 April 2005 (21.04.2005); Human Reproduction Vol.20, No.6 pp. 1511?1515; especially pg 1511, col 1, para 2 and col 2, para 1</td> <td>17, 33</td> </tr> <tr> <td>Y</td> <td>Post, "Comparative pharmacology of bipolar disorder and schizophrenia," 29 September 1999 (29.09.1999), pg 1 [online abstract]; document retrieved on 02 July 2010, [retrieved from <a href="http://www.schres-journal.com/article/S0920-9964(99)00115-2/abstract">http://www.schres-journal.com/article/S0920-9964(99)00115-2/abstract</a>]; especially abstract</td> <td>4, 30</td> </tr> <tr> <td>P(X)</td> <td>US 2009/0291134 A1 (Ahmad et al.) 26 November 2009 (26.11.2009); entire document</td> <td>1-33, 43-45</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X --- Y	WO 2008/070463 A2 (Ahmad et al.) 12 June 2008 (12.06.2008); especially para [0001], [0004]-[0005], [0008], [0014], [0016], [0020]-[0021], [0023], [0027], [0033] and [0052]	14-15, 31-32, 44 ----- 1-13, 16-30, 33, 43, 45	Y	WO 2008/048194 (Yesiloglu) 24 April 2008 (24.04.2008); especially claim 1; and pg 4, ln 2-3	1-13, 18-30, 43	Y	Cooke et al., "Tamoxifen Use and Osteoporotic Fracture Risk: A Population-Based Analysis," 10 November 2008 (10.11.2008); Journal of Clinical Oncology, Vol. 26, Num. 32, pg 5227-5232; especially pg 5230, col 2, para 1	16, 33, 45	Y	Steiner et al., "Comparison of tamoxifen and clomiphene citrate for ovulation induction: a meta-analysis," 21 April 2005 (21.04.2005); Human Reproduction Vol.20, No.6 pp. 1511?1515; especially pg 1511, col 1, para 2 and col 2, para 1	17, 33	Y	Post, "Comparative pharmacology of bipolar disorder and schizophrenia," 29 September 1999 (29.09.1999), pg 1 [online abstract]; document retrieved on 02 July 2010, [retrieved from <a href="http://www.schres-journal.com/article/S0920-9964(99)00115-2/abstract">http://www.schres-journal.com/article/S0920-9964(99)00115-2/abstract</a> ]; especially abstract	4, 30	P(X)	US 2009/0291134 A1 (Ahmad et al.) 26 November 2009 (26.11.2009); entire document	1-33, 43-45
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/></p>																							
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent but published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent but published on or after the international filing date	"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	"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)	"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	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed												
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"P" document published prior to the international filing date but later than the priority date claimed																							
<p>Date of the actual completion of the international search 02 July 2010 (02.07.2010)</p>		<p>Date of mailing of the international search report <b>19 NOV 2010</b></p>																					
<p>Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201</p>		<p>Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774</p>																					

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/35852

**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.: 34-42 and 46-49  
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:

- 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 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.:

- 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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/35852

**\*\* Search Terms Used \*\***

endoxifen, tamoxifen, neurodegenerative, psychiatric, multiple sclerosis, schizophrenia, Alzheimer's disease, Parkinson's disease, Huntington's disease, epilepsy, hydroalcoholic, cryoprotectant, isopropyl myristate, aqueous vehicle and gelling agent, fertility, infertility, ovulation and osteoporosis