Title: COMBINATION THERAPY FOR DEPRESSION, PREVENTION OF SUICIDE, AND VARIOUS MEDICAL AND PSYCHIATRIC CONDITIONS

Abstract: The present invention relates to a new method of treatment for persons meeting diagnoses for major depressive disorder, or other unipolar (non-bipolar, nonpsychotic and non-treatment resistant) depression. The method comprises administering a combination of two categories of drugs, antipsychotics or dopamine system stabilizers, in combination with a newer antidepressant such as a selective serotonin reuptake inhibitor, as initial treatment or as soon as possible. The method targets the prevention of suicide, and provides other benefits including preventing disease progression development of tolerance toward the antidepressants. Another aspect of the invention relates to using the method for alleviating cognitive distortion and related functional impairment or health risks, and/or using the method for smoking cessation or nicotine withdrawal.
# INTERNATIONAL SEARCH REPORT

**A. CLASSIFICATION OF SUBJECT MATTER**

<table>
<thead>
<tr>
<th>IPC(7)</th>
<th>US CL</th>
<th>According to International Patent Classification (IPC) or to both national classification and IPC</th>
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<tr>
<td>A61K 31/40, 31/55</td>
<td>514/408, 427, 211.03, 218, 220</td>
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**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/408, 427, 211.03, 218, 220

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 practicable, search terms used)

Please See Continuation Sheet

## 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>X</td>
<td>US 6,228,875 B1 (TSAI et al.) 08 May 2001 (08.05.2001), column 1, line 51 to column 2, line 14; column 2, line 46 to column 4, line 4.</td>
<td>1-13, 16-43, and 49-50</td>
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<td>X</td>
<td>US 6,100,256 A (BAKER et al.) 08 August 2000 (08.08.2000), column 1, line 54 to column 2, line 42 and column 5, line 25 to column 6, line 6.</td>
<td>1-13, 16-43, and 49-50</td>
</tr>
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</table>

* Further documents are listed in the continuation of Box C. | * See patent family annex.

<table>
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<th>Special categories of cited documents:</th>
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<tr>
<td>&quot;A&quot;</td>
<td>document defining the general state of the art which is not considered to be of particular relevance</td>
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<tr>
<td>&quot;E&quot;</td>
<td>earlier application or patent published on or after the international filing date</td>
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<tr>
<td>&quot;L&quot;</td>
<td>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>
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<td>&quot;O&quot;</td>
<td>document referring to an oral disclosure, use, exhibition or other means</td>
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<tr>
<td>&quot;P&quot;</td>
<td>document published prior to the international filing date but later than the priority date claimed</td>
</tr>
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<td>&quot;P&quot;</td>
<td>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>&quot;X&quot;</td>
<td>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>&quot;Y&quot;</td>
<td>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>&quot;A&quot;</td>
<td>document member of the same patent family</td>
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</table>

**Date of the actual completion of the international search**

26 March 2004 (26.03.2004)

**Date of mailing of the international search report**

26 MAY 2004

**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

FAX number: (703) 305-3230

**Authorized officer**

Theodore J. Criaces

Telephone No. (571) 272-1600

Form PCT/ISA/210 (second sheet) (July 1998)
**INTERNATIONAL SEARCH REPORT**

**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

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

2. □ Claim 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. □ Claim Nos.: 14, 15 and 44-48
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 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 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.:

**Remark on Protest**

□ The additional search fees were accompanied by the applicant’s protest.

□ No protest accompanied the payment of additional search fees.

Form PCT/ISA/2.10 (continuation of first sheet(1)) (July 1998)
Continuation of B. FIELDS SEARCHED Item 3:
STN:
terms searched: depression, depressive, depressant, olanzapinesulpiride