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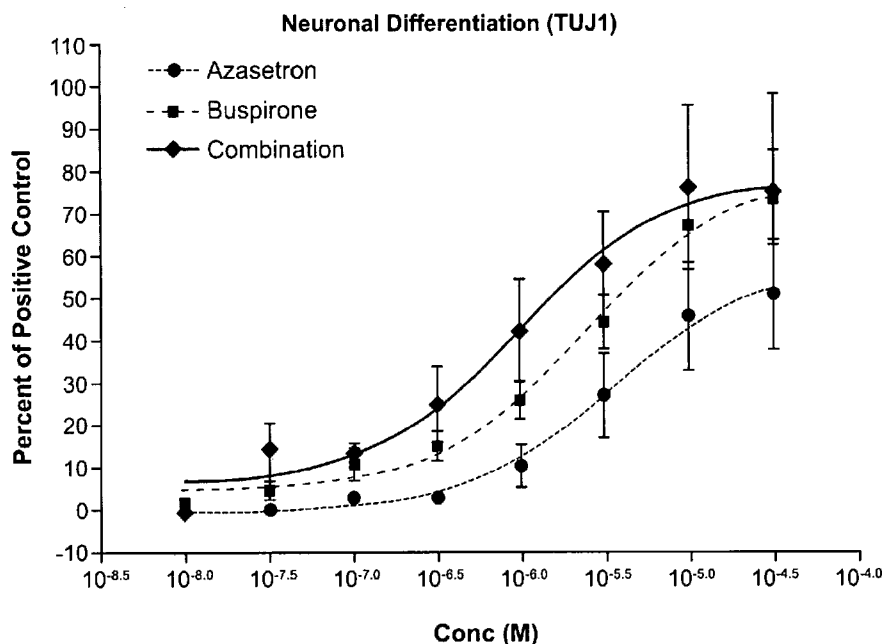
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[Continued on next page]

(54) Title: 5 HT RECEPTOR MEDIATED NEUROGENESIS

Human Neurogenesis Assay: Azasetron + Buspirone



(57) Abstract: The instant disclosure describes methods for treating diseases and conditions of the central and peripheral nervous system by stimulating or increasing neurogenesis. The disclosure includes compositions and methods based on use of a 5HTR agent, optionally in combination with one or more other neurogenic agents, to stimulate or activate the formation of new nerve cells.

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# INTERNATIONAL SEARCH REPORT

International application No PCT/US2007/068503
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**A. CLASSIFICATION OF SUBJECT MATTER**

INV. A61K31/538	A61K31/505	A61K31/135	A61K31/415	A61K31/64
A61K31/435	A61K31/40	A61K31/165	A61K31/485	A61K31/519
A61K31/195	A61K31/401	A61K31/437	A61K31/4458	A61K31/551

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 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, EMBASE, SCISEARCH, BIOSIS, WPI Data, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 2007/047978 A (BRAINCCELLS INC [US]; BARLOW CARROLEE [US]; CARTER TODD A [US]; LORRAIN) 26 April 2007 (2007-04-26) claims; figures; example 8	1-3, 5, 6, 31
P, X	WO 2007/008758 A (BRAINCCELLS INC [US]; BARLOW CARROLEE [US]; PIRES JAMMIESON C [US]; LOR) 18 January 2007 (2007-01-18) claims	1-3, 6, 7, 30, 31, 44-46
X	WO 2004/045592 A (NEURONOVA AB [SE]; BERTILSSON GOERAN [SE]; ERLANDSSON RIKARD [SE]; FRI) 3 June 2004 (2004-06-03) claims	1-3, 6, 31, 44-46
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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.
- \*G\* document member of the same patent family

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## 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.
X	<p>MALBERG JESSICA E ET AL: "CHRONIC ANTIDEPRESSANT TREATMENT INCREASES NEUROGENESIS IN ADULT RAT HIPPOCAMPUS" JOURNAL OF NEUROSCIENCE, NEW YORK, NY, US, vol. 20, no. 24, 15 December 2000 (2000-12-15), pages 9104-9110, XP009077904 ISSN: 0270-6474 the whole document</p>	1-3,6,7, 11-14
X	<p>BANASR, M. ET AL.: "Agomelatine, a new antidepressant, induces regional changes in hippocampal neurogenesis" BIOL PSYCHIATR, vol. 59, 24 February 2006 (2006-02-24), pages 1087-1096, XP002455949 the whole document</p>	1-3,6,7, 11-14,31
X	<p>KODAMA, M. ET AL.: "Chronic olanzapine or fluoxetine administration increases cell proliferation in hippocampus and prefrontal cortex of adult rat" BIOL PSYCHIATR, vol. 56, 2004, pages 570-580, XP002455950 the whole document</p>	1-3,6,7, 11-14
X	<p>BANASR, M. ET AL.: "Antidepressant agomelatine increases proliferation and survival of newly formed granule cells and accelerates their maturation in adult rat hippocampus"[Online] 2004, XP002455951 Retrieved from the Internet: URL:http://sfn.scholarone.com/itin2004/main.html?new_page_id=126&amp;abstract_id=1958&amp;p_num=353.6&amp;is_tech=0&gt; [retrieved on 2007-10-18] abstract</p>	1-3,6,7, 11-14,31
X	<p>MORLEY-FLETCHER,S. ET AL.: "Chronic treatment with agomelatine increases hippocampal cell proliferation in prenatally stressed rats"[Online] 2003, XP002455952 Retrieved from the Internet: URL:http://sfn.scholarone.com/itin2003/main.html?new_page_id=126&amp;abstract_id=18497&amp;p_num=506.20&amp;is_tech=0&gt; [retrieved on 2007-10-22] abstract</p>	1-3,7, 11-14,31

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2007/068503

## 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 1-14, 29-32, 44-47 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:  
see FURTHER INFORMATION sheet PCT/ISA/210
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:

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.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box II.1

Although claims 1-14,29-32,44-47 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.

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Continuation of Box II.2

Claims Nos.: -

The present claims 1-14,29,32,44-46 encompass compounds defined only by their desired function, namely 5HT modulation, contrary to the requirements of clarity of Article 6 PCT. The result-to-be-achieved type of definition does not allow the scope of the claim to be ascertained. The term 5HTR agent is not clear, in that it does not allow the person skilled in the art to determine the scope of the intended subject-matter. The term "5HTR agent" includes both agonists and antagonists of widely varying structures, and is therefore open ended, with no clear delimitation of the compounds intended. Moreover it is to mention that 5HT receptors belongs to multiple subtypes, which renders the subject-matter even more unclear. This reasoning also applies to the term "neurogenic agent"

Moreover claim 1 refers to a use for increasing neurogenesis. this is a definition by a result to be achieved, and hence unclear (Art.6 PCT) as it does not clearly define the group of disease for which protection is presently sought.

The search of claims 1-14,29,32,44-46 was consequently restricted to compounds explicitly described in the examples .

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2007047978	A	26-04-2007	NONE	
WO 2007008758	A	18-01-2007	NONE	
WO 2004045592	A	03-06-2004	AU 2003280117 A1	15-06-2004
			CA 2506850 A1	03-06-2004
			EP 1583541 A2	12-10-2005
			JP 2006514630 T	11-05-2006