

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
1 August 2002 (01.08.2002)

PCT

(10) International Publication Number
WO 02/058736 A3

(51) International Patent Classification⁷: **A61K 47/48**

(21) International Application Number: PCT/US01/48595

(22) International Filing Date:
12 December 2001 (12.12.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/254,910 12 December 2000 (12.12.2000) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
7 August 2003

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.

(54) Title: USE OF 9-SUBSTITUTED PURINE ANALOGUES AND OTHER MOLECULES TO STIMULATE NEUROGENESIS

(57) Abstract: The present invention is directed to a method of inducing neurogenesis by administering to a mammal an effective quantity of a compound that induces neurogenesis, where neurogenesis includes proliferation of neural stem and progenitor cells, differentiation of these cells into neurons, and/or survival of these new neurons. In general, the compound comprises three moieties, A, L, and B, covalently linked. A can be a purine, tetrahydroindole, or pyrimidine; L is a linker, while B is a moiety that promotes absorption of the compound. A particularly preferred compound is N-4-[[3-(6-oxo-1,6-dihydropurin-9-yl)-1-oxopropyl]amino]benzoic acid (also known as AIT-082 or leteprinim potassium). Another aspect of the invention is pharmaceutical compositions for inducing neurogenesis.



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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 01/48595

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K47/48

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)

IPC 7 A61K C07D

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)

CHEM ABS Data, EMBASE, BIOSIS, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RATHBONE M P ET AL: "AIT-082 AS A POTENTIAL NEUROPROTECTIVE AND REGENERATIVE AGENT IN STROKE AND CENTRAL NERVOUS SYSTEM INJURY" EXPERT OPINION ON INVESTIGATIONAL DRUGS, ASHLEY PUBLICATIONS LTD., LONDON, GB, vol. 8, no. 8, 1999, pages 1255-1262, XP000904785 ISSN: 1354-3784 abstract ---	1-6,9, 10, 17-22,62
X	US 5 801 184 A (RATHBONE MICHEL P ET AL) 1 September 1998 (1998-09-01) cited in the application column 5, line 25 - line 40; claims --- -/--	1

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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

Date of the actual completion of the international search

15 April 2003

Date of mailing of the international search report

25/04/2003

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/48595

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 091 432 A (GLASKY ALVIN J) 25 February 1992 (1992-02-25) cited in the application column 35 -column 53; claims ----	1-66
P,X	WILSON R A ET AL: "AIT-082 stimulates the proliferation of neural stem cells in the dentate gyrus of adult mice." SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 27, no. 2, 2001, page 2368 XP001150329 31st Annual Meeting of the Society for Neuroscience; San Diego, California, USA; November 10-15, 2001 ISSN: 0190-5295 abstract ----	1-6,9, 10, 17-22,62
P,X	WO 01 36419 A (NEOTHERAPEUTICS INC ;GLASKY ALVIN (US)) 25 May 2001 (2001-05-25) claims ----	1
P,X	US 6 297 226 B1 (GLASKY ALVIN J) 2 October 2001 (2001-10-02) cited in the application claims ----	1
P,X	WO 01 28545 A (RATHBONE MICHAEL P ;NEOTHERAPEUTICS INC (US); GLASKY ALVIN (US)) 26 April 2001 (2001-04-26) page 5, line 15 - line 19; claims 1,26,74; example 35 ----	1-66
E	WO 02 04451 A (NEOTHERAPEUTICS INC ;FARLOW MARTIN R (US); GLASKY MICHELLE (US); L) 17 January 2002 (2002-01-17) claims 1,36,74 -----	1,17,21, 23,24

INTERNATIONAL SEARCH REPORT

International Application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 1-66 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 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-5,9-10, 17-65 relate to an extremely large number of possible compounds. In fact, the claims contain so many variables and provisos that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely compounds those compounds have been searched which are recited in the examples and closely related homologous compounds in the claims.

The applicant's attention is drawn to the fact that claims, or parts of 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/48595

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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WO 0204451 A		US 2002040032 A1	04-04-2002