

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
4 July 2002 (04.07.2002)

PCT

(10) International Publication Number
WO 2002/051433 A3

(51) International Patent Classification⁷: **A61K 38/18**,
A61P 25/00 // C07K 19/00

(21) International Application Number:
PCT/US2001/050112

(22) International Filing Date:
19 December 2001 (19.12.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/257,601 22 December 2000 (22.12.2000) US

(71) Applicant (for all designated States except US): **GENEN-TECH, INC.** [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SHELTON, David, L.** [US/US]; 5845 Clover Drive, Oakland, CA 94618 (US).
PHILLIPS, Heidi, S. [US/US]; 15 Pine Avenue, San Carlos, CA 94070 (US).

(74) Agent: **ALTMAN, Daniel, E.**; Knobbe, Martens, Olson & Bear, LLP, 620 Newport Center Drive, Sixteenth Floor, Newport Beach, CA 92660 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI (utility model), 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, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK (utility model), SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, 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:
25 March 2004

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 ARTEMIN, A MEMBER OF THE GDNF LIGAND FAMILY FOR PREPARING A NEUROPROTECTIVE MEDICAMENT

(57) Abstract: The present invention concerns the use of artemin for the prevention or treatment of nerve cell injury and changes associated with nerve cell injury. More particularly the present invention provides for a method of protecting neurons in a mammal from injury-induced pathological changes and a method of treating neuronal damage in a mammal by administering artemin or an artemin agonist.



WO 2002/051433 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/50112

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/18 A61P25/00 //C07K19/00

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 C07K

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, PAJ, BIOSIS, MEDLINE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 04050 A (GEERTS HUGO ALFONSO ;MASURE STEFAN LEO JOZEF (BE); CIK MIROSLAV (B) 27 January 2000 (2000-01-27) page 1-4; claims 1,11,22-24	1-21,23, 24
Y	page 11-12, line 32-10 page 18, line 11-29 page 23, line 5-7 page 28-29, line 25-9 page 50-51, line 25-15 ---	1-25
X	WO 00 01815 A (BLOM NIKOLAJ ;HANSEN CLAUS (DK); JOHANSEN TEIT E (DK); NEUROSEARCH) 13 January 2000 (2000-01-13) page 24, line 5-11 page 25, line 5-20 page 26-27, line 31-17 page 4, line 6-14 page 16, line 1-3 ---	1-21,23, 24
Y	---	1-25
	--- -/-	

☒ 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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

30 July 2003

Date of mailing of the international search report

05/08/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Lechner, O

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/50112

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 18799 A (MILBRANDT JEFFREY D ;BALOH ROBERT H (US); UNIV WASHINGTON (US)) 6 April 2000 (2000-04-06)	1-7, 9-21,23
Y	claims 1-4,17,23,33-38 page 6 page 9, line 3-9 figure 3B figure 1B page 31, line 7-19 page 34, line 1-19 page 38, line 4-8 -----	1-25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/50112

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:
2. ☒ Claims Nos.: 1-25 (only partially)
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

Claims Nos.: 1-25 (only partially)

The term artemin as used in present claims 1-25 relates to two completely different compounds, i.e. 1)

RN 22149-38-8 = Naphtho'1,2-b!furan-2(3H)-one, decahydro-6,9a-dihydroxy-3,5a-dimethyl-9-methylene-, (3S,3aS,5aS,6R,9aR,9bS) = Eudesm-4(14)-en-12-oic acid, 1,5,6-trihydroxy-, .gamma.-lactone (8CI) = Naphtho'1,2-b!furan-2(3H)-one, decahydro-6,9a-dihydroxy-3,5a-dimethyl-9-methylene-, '3S-(3.alpha.,3a.alpha.,5a.beta.,6.beta.,9a.alpha.,9b.beta.)! and 2) the neutrophic factor artemin also known as enovin or neublazin.

Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, only for the neutrophic factor. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds relating to the neutrophic factor as disclosed in SeqID 1, 3 and 5.

Claims 1-24 relate to an extremely large number of ill defined possible pathologic conditions/diseases, i.e. e.g. treating damage to neurons in a mammal...., neuropathy, neurodegenerative disease. In fact, the claims contain so many options 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 the specific diseases/pathologic conditions mentioned on page 16, line 12-15 (starting from "such as") as well as line 25-27 (starting from "for example").

Present claims 1-24 relate to compounds defined by reference to a desirable characteristic or property, namely being artemin agonists. Thus in addition to the already mentioned unclarities concerning the nature of artemin, the claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to SeqID 1, 3 and 5.

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

nation on patent family members

Interr | Application No
PCT/US 01/50112

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0004050	A	27-01-2000	AU 5283299 A	07-02-2000
			BG 105107 A	31-10-2001
			BR 9912819 A	02-05-2001
			CA 2333910 A1	27-01-2000
			CN 1342165 T	27-03-2002
			CZ 20010028 A3	15-08-2001
			WO 0004050 A2	27-01-2000
			EP 1097167 A2	09-05-2001
			HR 20010036 A1	31-12-2001
			HU 0102821 A2	28-11-2001
			JP 2002520042 T	09-07-2002
			NO 20010212 A	14-03-2001
			PL 348431 A1	20-05-2002
			SK 142001 A3	05-02-2002
			TR 200100074 T2	21-11-2001
WO 0001815	A	13-01-2000	AU 755114 B2	05-12-2002
			AU 4769399 A	24-01-2000
			BR 9911908 A	27-03-2001
			CA 2336218 A1	13-01-2000
			CN 1311818 T	05-09-2001
			WO 0001815 A2	13-01-2000
			EE 200100008 A	17-06-2002
			EP 1095140 A2	02-05-2001
			HU 0103758 A2	28-01-2002
			JP 2002519061 T	02-07-2002
			NO 20010088 A	06-03-2001
			PL 345950 A1	14-01-2002
			TR 200100056 T2	21-11-2001
			US 2002055467 A1	09-05-2002
WO 0018799	A	06-04-2000	AU 6405499 A	17-04-2000
			CA 2343927 A1	06-04-2000
			EP 1028975 A1	23-08-2000
			JP 2002534957 T	22-10-2002
			WO 0018799 A1	06-04-2000
			US 6284540 B1	04-09-2001
			US 2002002269 A1	03-01-2002