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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 SPHINGOSINE-1-PHOSPHATE (S1P) RECEPTOR AGONISTS FOR THE TREATMENT OF BRAIN DEGENERATIVE DISEASES

(57) Abstract: Disclosed is the use of sphingosine-1-phosphate (S1P) receptor agonists, preferably 2-amino-2-[2-(4-octylphenyl)ethyl] propane-1,3-diol, in the treatment of progressive dementia or brain degenerative diseases.



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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/014436

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/133 A61K31/135 A61K31/00 A61K45/06 A61P25/28

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category ^o	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/094965 A (NEURONOVA AB; LINDQUIST, PER; MERCER, ALEX; RONNHOLM, HARRIET; WIKSTRO) 20 November 2003 (2003-11-20)	1-4,7
Y	page 1, paragraph 2 page 4, paragraph 2 page 5, paragraph 1 page 6, last paragraph - page 7, paragraph 1 page 34, paragraph 2 page 35, paragraph 2 page 35, last paragraph - page 36, paragraph 1 page 43, last paragraph - page 44, paragraph 1 page 44, last paragraph claims 1,11,33 ----- -/--	9,10

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

☒ Patent family members are listed in annex.

^o 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

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"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.

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/014436

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 6 004 565 A (CHIBA ET AL) 21 December 1999 (1999-12-21) column 3, lines 24-43 column 4, line 63 - column 5, line 6 column 8, lines 1-16 column 8, lines 37-41 -----	2,4,7,9, 10
X	WO 02/076995 A (NOVARTIS AG; NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H; ALBER) 3 October 2002 (2002-10-03) cited in the application page 1, paragraph 1 page 5, paragraph 6 - page 6, paragraph 4 example 27 page 22, paragraph 1-3 page 23, paragraph 2 page 25, paragraph 2 claims 3,7,10 -----	1,3,4,7, 9
X	WO 03/062252 A (MERCK & CO., INC; BUGIANESI, ROBERT, L; DOHERTY, GEORGE, A; GENTRY, AM) 31 July 2003 (2003-07-31) cited in the application	1,3,4,7
Y	page 1, lines 7-11 page 14, line 1 - page 15, line 32 -----	9,10
P,X	KANEIDER N C ET AL: "THE IMMUNE MODULATOR FTY720 TARGETS SPHINGOSINE-KINASE-DEPENDENT MIGRATION OF HUMAN MONOCYTES IN RESPONSE TO AMYLOID BETA-PROTEIN AND ITS PRECURSOR" FASEB JOURNAL, vol. 18, no. 11, August 2004 (2004-08), pages 1309-1311, XP008043407 abstract page 1309, column 1, paragraph 1 page 1311, column 2, last paragraph -----	2,7,9,10
P,X	WO 2004/096752 A (NOVARTIS AG; NOVARTIS PHARMA GMBH; HINTERDING, KLAUS; SPANKA, CARSTEN;) 11 November 2004 (2004-11-11) page 1, paragraph 1 - last paragraph examples 11,44 page 17, last paragraph - page 18, paragraph 2 page 19, paragraph 1 page 20, last paragraph page 21, paragraphs 3,4 -----	1-4,7,9
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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP2004/014436

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2004/024673 A (NOVARTIS AG; NOVARTIS PHARMA GMBH; BUEHLMAYER, PETER; HINTERDING, KLAU) 25 March 2004 (2004-03-25) page 1, paragraph 1 - page 2, paragraph 3 examples 57-59 page 29, paragraph 3 - page 30, paragraph 1 page 30, paragraph 4 page 32, paragraph 3 claim 1	1,3,4,7,9
E	----- WO 2005/025553 A (NEURONOVA AB; LINDQUIST, PER) 24 March 2005 (2005-03-24) page 1, lines 6-13 page 5, lines 13-23 page 11, line 22 - page 12, line 12 page 13, lines 1-6 page 15, lines 17-24 page 18, lines 2-5 page 18, line 21 - page 19, line 19 page 29, lines 23-26 page 30, lines 13-29 claims 13-16,25	1-4,9,10
E	----- WO 2005/002559 A (UNIVERSITY OF CONNECTICUT; HLA, TIMOTHY; SANCHEZ, TERESA; PAIK, JI-HYE) 13 January 2005 (2005-01-13) page 2, paragraph 5 page 5, paragraphs 24,26 pages 6-7, paragraphs 27,28 page 8, paragraph 32 page 9, paragraph 37 page 13, paragraph 50 page 14, paragraphs 52,53 page 15, paragraph 56 claims 10-13,17,18 -----	1-4,7,9,10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/014436

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 7, 9 and 10 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:
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:

see additional sheet

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.:

1-4, 7, 9, 10 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4, 7, 9, 10 (all partially)

Use of a sphingosine-1-phosphate (S1P) receptor agonist or a pharmaceutically acceptable salt thereof in the preparation of a medicament for treating progressive dementia, brain degeneration, beta-amyloid-related inflammatory diseases or disorders or for reducing or inhibiting loss of cognitive abilities, without a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia.

A pharmaceutical composition containing such S1P receptor agonists without a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia.

A method for treating progressive dementia, brain degeneration or beta-amyloid-related inflammatory diseases or disorders or for reducing or inhibiting loss of cognitive abilities in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of a sphingosine-1-phosphate (S1P) receptor agonist or a pharmaceutically acceptable salt thereof, without a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia.

2. claims: 1-10 (all partially)

Use of a sphingosine-1-phosphate (S1P) receptor agonist or a pharmaceutically acceptable salt thereof in the preparation of a medicament for treating progressive dementia, brain degeneration, beta-amyloid-related inflammatory diseases or disorders or for reducing or inhibiting loss of cognitive abilities, in combination with a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia, which is an AMPA receptor agonist.

A pharmaceutical composition containing such S1P receptor agonists in combination with a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia, which is an AMPA receptor agonist.

A method for treating progressive dementia, brain degeneration or beta-amyloid-related inflammatory diseases or disorders or for reducing or inhibiting loss of cognitive abilities in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of a sphingosine-1-phosphate (S1P) receptor agonist or a pharmaceutically acceptable salt thereof, in combination with a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia, which is an AMPA receptor agonist.

3. claims: 1-10 (all partially)

INTERNATIONAL SEARCH REPORT

International application No.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

PCT/ EP2004/ 014436

Use of a sphingosine-1-phosphate (S1P) receptor agonist or a pharmaceutically acceptable salt thereof in the preparation of a medicament for treating progressive dementia, brain degeneration, beta-amyloid-related inflammatory diseases or disorders or for reducing or inhibiting loss of cognitive abilities, in combination with a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia, which is a painkiller.

A pharmaceutical composition containing such S1P receptor agonists in combination with a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia, which is a painkiller.

A method for treating progressive dementia, brain degeneration or beta-amyloid-related inflammatory diseases or disorders or for reducing or inhibiting loss of cognitive abilities in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of a sphingosine-1-phosphate (S1P) receptor agonist or a pharmaceutically acceptable salt thereof, in combination with a co-agent useful in the alleviation or treatment of brain degenerative diseases or progressive dementia, which is a painkiller.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/014436

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