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24 January 2013

(54) Title: BLOCKERS OF THE NOGO-A S1PR PATHWAY FOR THE TREATMENT OF DISEASES CHARACTERIZED BY NEURONAL DAMAGE AND LACK OF SUBSEQUENT REPAIR

(57) Abstract: The present invention provides inhibitors capable of binding to a member of the S1PR receptor group comprised of S1PR2 and S1PR5 with a dissociation constant of 5×10^{-7} mol/l or smaller for treating neuronal damage, specifically an antibody, an antibody fragment, an antibody-like molecule, a nucleic acid aptamer or an oligopeptide with 6 to 30 amino acid residues in length. Similarly, an interfering RNA or an antisense modulator of gene expression of G13 or a member of the S1PR receptor group described above are provided for treating of neuronal damage.



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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER INV. A61K31/133 A61K31/138 A61K31/4245 A61K31/661 ADD.		
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		
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) EPO-Internal, BIOSIS		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KIMURA ATSUSHI ET AL: "Antagonism of Sphingosine 1-Phosphate Receptor-2 Enhances Migration of Neural Progenitor Cells Toward an Area of Brain Infarction", STROKE, vol. 39, no. 12, December 2008 (2008-12), pages 3411-3417, XP002682029, ISSN: 0039-2499 figure 6 -----	1,6-9
A	MARSOLAIS D ET AL: "Chemical modulators of sphingosine-1-phosphate receptors as barrier-oriented therapeutic molecules", NATURE REVIEWS. DRUG DISCOVERY, NATURE PUBLISHING GROUP, GB, vol. 8, no. 4, 20 March 2009 (2009-03-20), pages 297-307, XP002617578, ISSN: 1474-1784, DOI: 10.1038/NRD2356 the whole document -----	1,6-9
☐ 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 application or patent 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 "&" document member of the same patent family		
Date of the actual completion of the international search 20 August 2012		Date of mailing of the international search report 26/11/2012
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/060533

Box No. 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:
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 No. 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 fees, this Authority did not invite payment of additional fees.
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(completely); 6-9(partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1(completely); 6-9(partially)

1-(2,6-dicloro-4-pyridyl)-4-[(4-isopropyl-1,3-dimethyl-pyrazolo[3,4-b]pyridin-6-yl)amino]urea and related subject-matter.

2. claims: 2(completely); 6-9(partially)

An inhibitor as described in claim 2 and related subject-matter.

3. claims: 3(completely); 6-9(partially)

A modulator as described in claim 3 and related subject-matter.

4. claims: 4(completely); 6-9(partially)

A soluble polypeptide as described in claim 4 and related subject-matter.

5. claims: 5(completely); 6-9(partially)

A compound as described in claim 5 and related subject-matter.
