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(71) Applicant (*for all designated States except US*): **OMNIO AB** [SE/SE]; Villavagen 1, S-90187 Umea (SE).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **NY, Tor** [SE/SE]; Villavagen 1, s-90336 Umea (SE). **HOLMDAHL, Rikard** [SE/SE]; Siriusgatan 2, S-224 57 (SE). **LI, Jinan** [CN/SE]; Pedagoggrand 1D-206, S-90730 Umea (SE).

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: NOVEL DRUG TARGETS FOR ARTHRITIS

(57) Abstract: Novel drug targets for the treatment or prevention of arthritis are provided. Screening methods for inhibitors of the plasminogen-activation pathway, such as, for example, antagonists or inhibitors of the urokinase-type okasubigeb actuvatir (uPA), plasminogen-activator tzpe 1 (PAI-1), the urokinase activator receptor (uPAR), and plasmin, are used to identify novel drugs for treating or preventing the progression of arthritis. Such screening methods, or methods for evaluating whether a drug is useful for treating or preventing arthritis, can also be conducted in animal models described herein. Methods of treating or preventing such diseases are also provided.



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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/55 A61K39/395 G01N33/68 A61P29/00

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 G01N

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)

EP0-Internal, BIOSIS, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 24474 A (NIELSEN JOHN ROEMER ;BRUENNER NILS (DK); STEPHENS ROSS (DK); DANOE) 11 June 1998 (1998-06-11)	1,2,7,8, 12-17, 29-31, 46,47
Y	claims 1,25,29,61-63	18-22, 24,25, 27, 32-40, 43-45
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☒ 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.

"&" document member of the same patent family

Date of the actual completion of the international search

9 July 2003

Date of mailing of the international search report

- 8. 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

IDA CHRISTENSEN/JA A

INTERNATIONAL SEARCH REPORT

Int. Application No

PCT/IB 02/05797

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>WO 92 07083 A (CANCERFORSKNINGSFONDET AF 1989) 30 April 1992 (1992-04-30)</p> <p>claims 53-55,58,62,63</p>	<p>1,4,5, 10, 12-17, 23,26, 28,31, 41,42, 46,47</p>
Y	<p>EP 0 835 931 A (DAIICHI PURE CHEMICALS CO LTD) 15 April 1998 (1998-04-15) page 4, line 14 - line 17 page 4 -page 5; example 1</p>	<p>18-20, 27,32-34</p>
Y	<p>TEWODROS WEZENET ET AL: "Streptokinase activity among group A streptococci in relation to streptokinase genotype, plasminogen binding, and disease manifestations." MICROBIAL PATHOGENESIS, vol. 18, no. 1, 1995, pages 53-65, XP002246934 ISSN: 0882-4010 page 61, paragraph 2</p>	<p>35-37</p>
Y	<p>JENSEN S ET AL: "The role of beta-strand 5A of plasminogen activator inhibitor-1 in regulation of its latency transition and inhibitory activity by vitronectin" BIOCHIMICA ET BIOPHYSICA ACTA. PROTEIN STRUCTURE AND MOLECULAR ENZYMOLOGY, ELSEVIER, AMSTERDAM,, NL, vol. 1597, no. 2, 3 June 2002 (2002-06-03), pages 301-310, XP004361034 ISSN: 0167-4838 page 302, paragraph 2.3 -page 303, paragraph 2.4</p>	<p>21,22, 24,25, 38-40, 43-45</p>
X	<p>RONDAY H K ET AL: "Bone matrix degradation by the plasminogen activation system. Possible mechanism of bone destruction in arthritis." BRITISH JOURNAL OF RHEUMATOLOGY, vol. 36, no. 1, 1997, pages 9-15, XP002246935 ISSN: 0263-7103 page 13, Discussion</p>	<p>1,4,5,7, 8,10, 12-15, 46,47</p>
X	<p>US 4 595 674 A (SCHMUCK RAINER ET AL) 17 June 1986 (1986-06-17) column 13, line 1 - line 19</p>	<p>1,7,8, 46,47</p>
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INTERNATIONAL SEARCH REPORT

Inter national Application No

PCT/IB 02/05797

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 6 051 576 A (CYNKOWSKA GRAZYNA ET AL) 18 April 2000 (2000-04-18) column 18 -column 20; example 20 ---	1,4,7,9, 46,47
A	US 5 164 482 A (HOERLEIN DIETRICH ET AL) 17 November 1992 (1992-11-17) column 1, line 17 - line 19 column 1, line 44-51 -----	1-15

INTERNATIONAL SEARCH REPORT

national application No.
PCT/IB 02/05797

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.: 1-15
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 1-6, 46-47 (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.1

Claims Nos.: 1-15

Claims 1-15 relate to methods of treatment of the human or animal body by surgery or by therapy or diagnostic methods practiced on the human or animal body (Rule 39.1(iv)). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds or compositions.

Continuation of Box I.2

Claims Nos.: 1-6, 46-47 (PARTIALLY)

Present claims 1-6 and 46-47 relate to the use of an agent defined by reference to a desirable characteristic or property, namely that inhibits at least one member selected from the group consisting of plasmin, plasminogen, urokinase-type plasminogen activator, urokinase-type plasminogen activator receptor and plasminogen-activator inhibitor type 1. The claims cover all agents having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such agents. 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 agent 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 the agent exemplified in the description (i.e. aprotinin). The general aspects of the invention have also been searched to some extent.

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/IB 02/05797

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