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Yonghong [CA/US]; 1144 Nimitz Lane, Foster City, CA
94404 (US). SCARBOROUGH, Robert, M. [US/US];
22 Greenbrier Court, Half Moon Bay, CA 94019 (US).

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(74) Agents: LEE, Christine, S. et al.; Morgan, Lewis & Bock-
ius LLP, 1111 Pennsylvania Avenue, NW, Washington, DC
20004 (US).

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(71) Applicant (*for all designated States except US*): MIL-
LENNIUM PHARMACEUTICALS, INC. [US/US];
256 East Grand Avenue, South San Francisco, CA 94080
(US).

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(72) Inventors; and

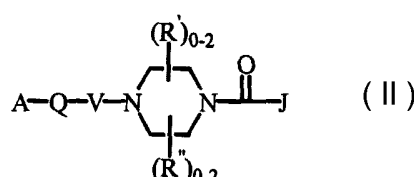
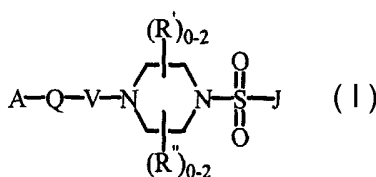
(75) Inventors/Applicants (*for US only*): ZHU, Bing-Yan
[CA/US]; 135 Lois Lane, Palo Alto, CA 94303 (US).
JIA, Zhaozhong, Jon [CN/US]; 1576-E Marina Court,
San Mateo, CA 94404 (US). ZHANG, Penglie [CN/US];
251 Winchester Court, Foster City, CA 94404 (US).
HUANG, Wenrong [CN/US]; 7723 Huntridge Lane,
Cupertino, CA 95014 (US). WU, Yanhong [CN/US];
731 Catamaran Street #2, Foster City, CA 94404 (US).
ZUCKETT, Jingmei, Fan [CN/US]; 5615 West Acoma
Drive #102, Glendale, AZ 85306 (US). GOLDMAN,
Erik, A. [US/US]; 1520 Francisco Street, Berkely, CA
94702 (US). WANG, Lingyan [CN/US]; 25 Hickory
Place, Apt. H-21, Chatham, NJ 07928 (US). SONG,

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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: PIPERAZINE BASED INHIBITORS OF FACTOR Xa



(57) Abstract: Novel compounds of the general formulae (I) or (II), including their pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives having activity against mammalian factor Xa are described. Compositions containing such compounds are also described. The compounds and the compositions are useful *in vitro* or *in vivo* for preventing or treating conditions in mammals characterized by undesired thrombosis.



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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/30315

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C07D209/30 C07D403/12 C07D401/12 C07D333/62 C07D409/12
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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 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)
 EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS 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 09480 A (HAGINOYA NORIYASU ;NAGAHARA TAKAYASU (JP); YOSHINO TOSHIHARU (JP);) 24 February 2000 (2000-02-24) claim 1; examples A-144 -& EP 1 104 754 A 6 June 2001 (2001-06-06) ---	1-6,8-16
X	EP 1 031 563 A (DAIICHI SEIYAKU CO) 30 August 2000 (2000-08-30) page 21, line 49 - line 52; claim 1 ---	1-6,8-16
X	WO 98 54164 A (ITO FUMIO ;MORIYA NORIHIKO (JP); TAWADA HIROYUKI (JP); TAKEDA CHEM) 3 December 1998 (1998-12-03) examples, e.g. working examples 72, 74, 76 claims 1,12,13 -----	1-6,8-16

Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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.</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 17 June 2002	Date of mailing of the international search report 28.06.2002
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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 <p style="text-align: center;">Johnson, C</p>
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/30315

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 14,15 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.: 1 (part)
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:

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.:

1-6 (part), 8 (part), 9-12, 13-16 (part) 'inventions 1 and 2!
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 (part)

Present claim 1 relates to a compound defined by reference to a desirable characteristic or property, namely prodrugs. The claim covers 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 compound 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 compounds of formulae (I) and (II) and their pharmaceutically acceptable isomers, salts, hydrates and solvates.

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. Claims: Claims 1-6 (part), 8 (part), 9-12, 13-16 (part)

Compounds wherein A is an unsaturated non-aromatic heterocyclic ring containing 2 N atoms (i.e. first 2 definitions of A in claim 1)

2. Claims: Claims 1-6 (part), 8 (part), 13-16 (part)

Compounds wherein A contains an amidino group (i.e. 3rd, 4th, 5th and 6th definitions of A in claim 1).

3. Claims: Claims 1-3 (part), 7, 8 (part), 13-16 (part)

Compounds wherein A is an amino or aminomethyl group (i.e. 7th and 8th definitions of A in claim 1).

4. Claims: Claims 1-3 (part), 8 (part), 13-16 (part)

Compounds of claim 1 wherein A contains an aromatic ring (i.e. last 4 definitions of A in claim 1).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/US 01/30315

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