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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: METHOD OF TREATMENT OF HEMORRHAGIC DISEASE USING A FACTOR VIIA/ISSUE FACTOR INHIBITOR

(57) Abstract: The present invention provides methods of treating hemorrhagic fevers where selective inhibitors of fVIIa/TF are used as a treatment for hemorrhagic fevers and have therapeutic effects which include ameliorating and/or preventing coagulopathy and inflammatory responses. These inhibitors include certain proteins which are part of a family termed Nematode-Extracted Anti-coagulant Proteins ("NAPs"). Other inhibitors include Tissue Factor Pathway Inhibitor ("TFPI") and TFPI analogs.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/13942

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) : A61K 38/00

US CL : 530/300

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)

U.S. : 530/300

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See below

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Moons "recombinant nematode anticoagulant protein c2, a novel inhibitor of tissue factor VIIa activity, abrogates endotoxin- induced coagulation in chimpanzees" Thromb Haemost Vol. 88 (2002), pp 627-631.	1-9
	D2: Abraham "Assessment of the safety of recombinant tissue factor pathway inhibitor in patients with severe sepsis: A multicenter, randomized, placebo-controlled, single-blind, dose escalation study" Crit Care Med Vol. 28(2001), pp 2081-2089.	
Y	Abraham "Assessment of the safety of recombinant tissue factor pathway inhibitor in patients with severe sepsis: A multicenter, randomized, placebo-controlled, single-blind, dose escalation study" Crit Care Med Vol. 28(2001), pp 2081-2089.	1-9
Y	US 6, 872,808 (Vlasuk) 29 March 2005 (29.03.2005) Whole document.	1-9



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	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

21 January 2006 (21.01.2006)

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/13942

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:
Please See Continuation 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 additional fees, this Authority did not invite payment of any 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.: 1-9

- 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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/13942

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-9, drawn to a method of treating a mammal having a hemorrhagic fever which comprises administering a selective factor VIIa/TF inhibitor.

Group II, claim(s) 10, in part, 11-18, drawn to a method of treating a mammal having a hemorrhagic fever which comprises administering a compound which specifically inhibits fVIIa/TF complex in the presence of fXa or catalytically inactive fXa derivative.

Group III, claim(s) 10, in part, 11-18, drawn to a method of treating a mammal having a hemorrhagic fever which comprises administering a compound which does not specifically inhibit fVIIa/TF complex in the absence of fXa or catalytically inactive fXa derivative.

Group IV, claim(s) 10, in part, 11-18, drawn to a method of treating a mammal having a hemorrhagic fever which comprises administering a compound which does not specifically inhibit fVIIa in the absence of the TF.

Group V, claim(s) 10, in part, 11-18, drawn to a method of treating a mammal having a hemorrhagic fever which comprises administering a compound which does not specifically inhibit prothrombinase.

Group VI, claim(s) 19-27, drawn to a method of treating coagulopathy and/or an inflammatory response in a mammal which comprises administering fVIIa/TF inhibitor.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid.

If Group I, II, III, IV, V, OR VI above is elected, Applicant is required to elect the claimed inventions wherein the NAP is AcaNAPc2 (SEQ ID No: 3) OR AcaNAPc2/praline (SEQ ID No: 4). Applicant is further required to elect the claimed inhibitor is a TFPI OR a TFPI analog. Applicant should also specify the compound of a TFPI analog.

If Group II above is elected, Applicant is required to elect that the claimed inventions is in the presence of fXa OR catalytically inactive fXa derivative, Applicant should also specify the compound of fXa derivative.

INTERNATIONAL SEARCH REPORT

International application No.
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Continuation of B. FIELDS SEARCHED Item 3:
US patents database/EPO abstract/Medline