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Previous Correction:

see Notice of 13 March 2008

(54) Title: MODIFIED COAGULATION FACTOR IX POLYPEPTIDES AND USE THEREOF FOR TREATMENT

(57) Abstract: Provided are modified factor IX (FIX) polypeptides and methods of generating modified FIX polypeptides. Also provided are pharmaceutical compositions, including compositions formulation for oral administration, that contain the modified FIX polypeptides, and methods of treatment using modified FIX polypeptides.



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INTERNATIONAL SEARCH REPORT

CORRECTED VERSION

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. C12N9/64 C12N15/55 A61K38/43

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)

C12N 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, Sequence Search, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/110675 A1 (SHEEHAN JOHN P [US]) 10 June 2004 (2004-06-10) cited in the application paragraphs [0012], [0162]; claim 2 -----	88-110, 112-148
A	CHANG YU-JIA ET AL: "Identification of functionally important residues of the epidermal growth factor-2 domain of factor IX by alanine-scanning mutagenesis. Residues Asn(89)-Gly(93) are critical for binding factor VIIla." THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 28, 12 July 2002 (2002-07-12), pages 25393-25399, XP002464800 ISSN: 0021-9258 the whole document ----- -/--	1-8, 19-148

☒ 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 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.

"8" document member of the same patent family

Date of the actual completion of the international search

7 May 2008

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13. 06. 2008

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/014219

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HSU YA-CHU ET AL: "The distinct roles that Gln-192 and Glu-217 of factor IX play in selectivity for macromolecular substrates and inhibitors". BIOCHEMISTRY, vol. 40, no. 37, 18 September 2001 (2001-09-18), pages 11261-11269, XP002464801 ISSN: 0006-2960 the whole document	1-8, 19-148
X	----- BEGBIE M E ET AL: "An important role for the activation peptide domain in controlling factor IX levels in the blood of haemophilia B mice." THROMBOSIS AND HAEMOSTASIS DEC 2005, vol. 94, no. 6, December 2005 (2005-12), pages 1138-1147, XP008087521 ISSN: 0340-6245 page 1146, paragraph 2	19-148
A	----- CHANG J ET AL: "Changing residue 338 in human factor IX from arginine to alanine causes an increase in catalytic activity." THE JOURNAL OF BIOLOGICAL CHEMISTRY 15 MAY 1998, vol. 273, no. 20, 15 May 1998 (1998-05-15), pages 12089-12094, XP002464802 ISSN: 0021-9258 table II	1-8, 19-148
A	----- HERTZBERG M S ET AL: "An Arg/Ser substitution in the second epidermal growth factor-like module of factor IX introduces an O-linked carbohydrate and markedly impairs activation by factor XIa and factor VIIa/Tissue factor and catalytic efficiency of factor IXa." BLOOD 1 JUL 1999, vol. 94, no. 1, 1 July 1999 (1999-07-01), pages 156-163, XP002464803 ISSN: 0006-4971 the whole document -----	1-8, 19-148

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/014219

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:
Although claims 112-126 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 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 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 allsearchable 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 reportcovers only those claims for which fees were paid, specifically claims Nos.:
1-7,19-110, 112-148
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 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:

Invention 1: Claims 1-7, and 19-148 (partly)

Modified factor IX polypeptide, comprising a modification at a position corresponding to F192 in SEQ ID NO: 2, and containing at least one further amino acid modification.

Inventions 2- 39: Claims 8-11, and 19-148 (partly)

Modified factor IX polypeptide, comprising a modification at a position corresponding to E36, R37, T39, E40, S61, S68, E70, P74, K80, D85, T87, S102, E119, K122, E125, P126, P129, R134, S136, T144, E147, P151, D166, T169, S171, T172, S174, D177, E224, T225, T241, E242, T244, K247, E294, T371, E372, and L414 in SEQ ID NO: 2.

Inventions 40-233: Claims 12-18, and 19-148 (partly)

Modified factor IX polypeptide, comprising a modification at a position corresponding to Y1, S3, G4, K5, L6, E7, E8, F9, E15, R16, E17, E20, E21, K22, S24, F25, E26, E27, R29, E30, F32, T35, T38, F41, K43, Y45, D47, G48, D49, E52, S53, L57, N58, G59, G60, K63, D64, D65, Y69, F75, G76, F77, E78, G79, E83, L84, K91, N92, R94, E96, F98, K100, D104, K106, S110, T112, E113, Y115, R116, L117, E119, S123, A127, P131, G133, S138, T140, S141, K142, R145, A146, T148, D152, D154, Y155, S158, T159, E160, E162, T163, L165, F175, F178, T179, E185, D186, K188, P189, F192, P193, W194, L198, N199, G200, D203, F205, G207, S209, E213, K214, T218, A219, A220, G226, K228, T230, E239, E240, E245, R248, R252, P255, Y259, K265, Y266, L272, E274, L275, D276, E277, P278, S283, Y284, T286, P287, D292, K293, Y295, T296, F299, K301, F302, G303, S304, Y306, S308, G309, G311, R312, F314, K316, R318, L321, Y325, R327, P329, D332, T335, L337, R338, S339, T340, K341, F342, T343, Y345, F349, G352, F353, G363, D364, S365, G399, G367, P368, E374, G375, T376, S377, F378, L379, T380, S384, G386, E387, M391, T399, K400, S402, R403, Y404, K409, E410, K411, T412, K413, and T415 in SEQ ID NO: 2.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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Patent document
cited in search report

Publication
date

Patent family
member(s)

Publication
date

US 2004110675 A1 10-06-2004 NONE
