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(54) Title: FACTOR VIII-FC CHIMERIC AND HYBRID POLYPEPTIDES, AND METHODS OF USE THEREOF

(57) Abstract: The present invention provides methods of administering Factor VIII; methods of administering chimeric and hybrid polypeptides comprising Factor VIII; chimeric and hybrid polypeptides comprising Factor VIII; polynucleotides encoding such chimeric and hybrid polypeptides; cells comprising such polynucleotides; and methods of producing such chimeric and hybrid polypeptides using such cells.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/59136

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 38/37; C07K 14/755 (2011.01) USPC - 514/14.1 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(8) - A61K 38/37; C07K 14/755 (2011.01) USPC - 514/14.1 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 514/14.1, 13.7; 424/134.1, 809; 530/383 (Text Search) Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PubWEST (PGPB, USPT, USOC, EPAB, JPAB); Google Scholar and PubMed. Search Terms: Factor VIII, FVIII, Fc, chimeric protein, fusion protein, stabil\$, stabl\$, long-acting.		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/0260194 A1 (PETERS et al.) 24 November 2005 (24.11.2005) para [0006], [0013], [0074], [0090], [0118], [0142], [0217], [0218], [0221], [0232].	1-4 and 58-62
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 23 May 2011 (23.05.2011)		Date of mailing of the international search report 02 JUN 2011
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201		Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/59136

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. [X] Claims Nos.: 5-30, 39-57, 63-77, 86, 88-110 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: 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: Claims 1-4 and 58-62, drawn to a method of administering Factor VIII to a subject.

Group II: Claims 31-38 drawn to a method of administering Factor VIII to a subject.

Group III: Claims 78-85, and 87, drawn to a polypeptide.

*****Continued in Supplemental Box*****

- 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 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. [X] 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.: 1-4 and 58-62

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
Information on patent family members

International application No.

PCT/US 10/59136

Continuation of:

Box No. III - Observations where unity of invention is lacking:

The groups listed above do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

The special technical feature of Group I is a method comprising administering chimeric Factor VIII to a subject at a dosing interval at least about one and one-half times longer than the dosing interval required for an equivalent amount of a polypeptide consisting of said Factor VIII portion.

The special technical feature of Group II is a method comprising administering a chimeric Factor VIII to obtain an area under the plasma concentration versus time curve (AUC) at least about one and one-quarter times greater than the AUC obtained by an equivalent amount of a polypeptide consisting of said Factor VIII portion.

The special technical feature of Group III is a polypeptide comprising a Factor VIII at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2.

Groups I-III share the technical feature of a chimeric Factor VIII such as a chimeric polypeptide comprising a Factor VIII and an Fc. Groups I-II further share a method of administering the chimeric Factor VIII to a subject. However, neither of these shared technical features is an improvement over the prior art. Rivera (US 20050147618 A1) discloses a chimeric protein comprising factor VIII and Fc and its administration to treat diseases (claim 57; para [0124], [0125], [0144]).

Accordingly, unity of invention is lacking.

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Continued from Item 4 of first sheet (unsearchable claims)

Claims 5-30, 39-57, 63-77, 86, 88-110 have been held unsearchable because they are multiple dependent claims and not drafted in accordance with PCT Rule 6.4(a).