(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 January 2014 (16.01.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/011819 A3

(51) International Patent Classification:
A61K 38/37 (2006.01) *C12P 21/08* (2006.01)
C12N 15/00 (2006.01)

(21) International Application Number:
PCT/US2013/049989

(22) International Filing Date:
10 July 2013 (10.07.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

61/670,401	11 July 2012 (11.07.2012)	US
61/759,819	1 February 2013 (01.02.2013)	US
61/801,504	15 March 2013 (15.03.2013)	US
61/801,544	15 March 2013 (15.03.2013)	US
61/827,158	24 May 2013 (24.05.2013)	US
61/840,811	28 June 2013 (28.06.2013)	US

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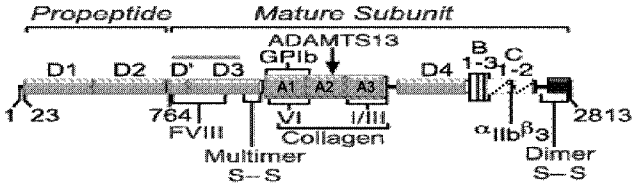
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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(54) Title: FACTOR VIII COMPLEX WITH XTEN AND VON WILLEBRAND FACTOR PROTEIN, AND USES THEREOF

Figure 1D. Von Willebrand Factor



- ~250 kDa protein, forms multimers (> 20 MDa) by disulfide bonding
- Associates with FVIII (95-98%) in non-covalent complex
  - Protects FVIII from protease cleavage/activation
  - Stabilizes heavy & light chain
  - Prevents clearance of FVIII by scavenger receptors

  } **Extends half-life**

  - Clearance of FVIII-vWF complex through vWF-receptors
  - Prevents pinocytosis and recycling of rFVIIIFc?

  } **Limits half-life**

(57) **Abstract**: The present invention includes a chimeric protein comprising a VWF protein with D' domain and D3 domain ofVWF, one or more XTEN sequence, and a FVIII protein, wherein the VWF fragment, the XTEN sequence, or the FVIII protein are linked to or associated with each other. The chimeric protein can further comprise one or more Ig constant region or a portion thereof (e.g., an Fc region). A polypeptide chain of a VWF fragment is associated with a FVIII polypeptide chain linked to an XTEN sequence. The VWF fragment polypeptide chain can prevent or inhibit binding of endogenous VWF toFVIII protein linked to the XTEN sequence. By preventing or inhibiting binding of endogenous VWF to FVIII protein, VWF fragment can extend half-life of chimeric protein comprising FVIII protein. The invention includes nucleotides, vectors, host cells, use of VWF fragment, or chimeric proteins.

WO 2014/011819 A3

WO 2014/011819 A3

Published:

— *with international search report (Art. 21(3))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
6 March 2014