CLAIMS

1. Use of a chimeric protein in the manufacture of a medicament for treating a subject having von Willebrand Disease (VWD), wherein the chimeric protein comprises a first polypeptide chain and a second polypeptide chain,

wherein the first polypeptide chain comprises:

(a) a Factor VIII (FVIII) protein; and

(b) a first immunoglobulin constant region or a portion thereof;

wherein the second polypeptide chain comprises:

(a) a von Willebrand Factor (VWF) fragment comprising a D' domain and a D3 domain of VWF;

(b) a second immunoglobulin constant region; and

(c) a cleavable linker located between the VWF fragment and the second immunoglobulin constant region or a portion thereof,

wherein the first polypeptide and the second polypeptide are linked by one or more covalent bonds between the first and second immunoglobulin constant regions or portions thereof.

2. The use of claim 1, wherein the VWD is Type 2N VWD.

3. The use of claim 1, wherein the VWD is Type 3 VWD.

4. The use of any one of claims 1 to 3, wherein the VWF fragment and the FVIII protein are associated with each other by a non-covalent bond in addition to the covalent bond.

5. The use of any one of claims 1 to 4, wherein the one or more covalent bonds is one or more disulfide bonds.

6. The use of any one of claims 1 to 5, wherein the first polypeptide chain and the second polypeptide chain are linked by two disulfide bonds between the first and second immunoglobulin constant regions or portions thereof.

7. The use of any one of claims 1 to 6, wherein the FVIII protein comprises an amino acid sequence at least 95% identical to amino acid residues 1 to 743 of SEQ ID NO: 16.

8. The use of any one of claims 1 to 7, wherein the FVIII protein comprises a B-domain deletion.

9. The use of any one of claims 1 to 8, wherein the FVIII protein further comprises an a3 acidic region, an A3 region, a C1 region, and a C2 region of FVIII comprising amino acids 1649 to 2332 of SEQ ID NO: 16.

10. The use of any one of claims 1 to 9, wherein the FVIII protein comprises single chain FVIII.

11. The use of any one of claims 1 to 10, wherein the FVIII protein comprises an amino acid sequence at least 95% identical to SEQ ID NO: 18.

12. The use of any one of claims 1 to 11, wherein the FVIII protein further comprises a heterologous moiety.

13. The use of claim 12, wherein the heterologous moiety is inserted between two amino acids of the FVIII protein.

14. The use of any one of claims 1 to 13, wherein the D' domain of the VWF fragment comprises an amino acid sequence at least 95% identical to amino acids 764 to 866 of SEQ ID NO: 2.

15. The use of any one of claims 1 to 14, wherein the D' domain of the VWF fragment comprises an amino acid sequence identical to amino acids 764 to 866 of SEQ ID NO: 2.

16. The use of any one of claims 1 to 15, wherein the D3 domain of the VWF fragment comprises an amino acid sequence at least 95% identical to amino acids 867 to 1240 of SEQ ID NO: 2.

17. The use of any one of claims 1 to 16, wherein the D3 domain of the VWF fragment comprises an amino acid sequence at least 99% identical to amino acids 867 to 1240 of SEQ ID NO: 2.

18. The use of any one of claims 1 to 17, wherein the VWF fragment comprises an alanine substitution for cysteine residues corresponding to residue 1099 and 1142 of SEQ ID NO: 2.

19. The use of any one of claims 1 to 18, wherein both the first and second immunoglobulin constant regions or portions thereof are glycosylated.

20. The use of any one of claims 1 to 19, wherein the first immunoglobulin constant region or portion thereof comprises a first Fc region.

21. The use of any one of claims 1 to 20, wherein the second immunoglobulin constant region or portion thereof comprises a second Fc region.

22. The use of any one of claims 1 to 21, wherein the chimeric protein is administered by a route selected from the group consisting of topical administration, intraocular administration, parenteral administration, intrathecal administration, subdural administration and oral administration.

23. The use of claim 22, wherein the parenteral administration is intravenous administration.

24. The use of claim 22, wherein the parenteral administration is subcutaneous administration.

25. The use of any one of claims 1 to 24, wherein the subject is scheduled to undergo a surgery.

26. The use of any one of claims 1 to 25, wherein the treatment is prophylactic or on-demand.

27. The use of any one of claims 1 to 26, wherein the chimeric protein is freeze dried.

28. The use of any one of claims 1 to 27, wherein the chimeric protein is in powder form for constitution with a suitable vehicle.

29. Use of a chimeric protein in the manufacture of a medicament for treating a subject having von Willebrand Disease (VWD), wherein the chimeric protein comprises a first polypeptide chain and a second polypeptide chain,

wherein the first polypeptide chain comprises:

(a) a Factor Vll ("FVIII") protein comprising an amino acid sequence at least 95% identical to SEQ ID NO: 16; and

(b) a first immunoglobulin constant region;

wherein the second polypeptide chain comprises:

(a) a von Willebrand Factor (VWF) fragment comprising a D' and a D3 domain of VWF, wherein the VWF fragment comprises an alanine substitution for cysteine residues corresponding to residue 1099 and 1142 of SEQ ID NO: 2;

(b) a second immunoglobulin constant region; and

(c) a cleavable linker located between the VWF fragment and the second immunoglobulin constant region,

wherein the D' domain of the VWF fragment comprises an amino acid sequence identical to amino acids 764 to 866 of SEQ ID NO: 2;

wherein the D3 domain of the VWF fragment comprises an amino acid sequence at least 99% identical to amino acids 867 to 1240 of SEQ ID NO: 2; and

wherein the first polypeptide and the second polypeptide are linked by two disulfide bonds between the first and second immunoglobulin constant regions.

30. The use of claim 29, wherein the VWD is Type 2N VWD.

31. The use of claim 29, wherein the VWD is Type 3 VWD.

32. The use of any one of claims 29 to 31, wherein the first immunoglobulin constant region or portion thereof comprises a first Fc region.

33. The use of any one of claims 29 to 32, wherein the second immunoglobulin constant region or portion thereof comprises a second Fc region.