CLAIMS

1. A chimeric protein comprising (i) a first polypeptide comprising (1) a von Willebrand Factor (VWF) fragment comprising a D' domain and a D3 domain of VWF, (2) an extended length polypeptide (XTEN) and (3) a first Fc region and (ii) a second polypeptide comprising (4) a factor VIII (FVIII) protein and (5) a second Fc region, wherein the XTEN comprises an amino acid sequence having at least 80% identity to an amino acid sequence as set forth in SEQ ID NO: 141-169, or 170, wherein the VWF fragment does not comprise amino acids 1274 to 2813 corresponding to SEQ ID NO: 2, and wherein the first Fc region is associated with the second Fc region by a disulfide bond.

2. The chimeric protein of claim 1, wherein the first polypeptide and the second polypeptide are not linked by a peptide bond.

3. The chimeric protein of claim 1, wherein the first Fc region is linked to the XTEN.

4. The chimeric protein of claim 3, wherein the first Fc region is linked to the XTEN by a cleavable linker.

5. The chimeric protein of claim 1, wherein the second Fc region is further linked to the first Fc region by a processable linker.

6. The chimeric protein of claim 1, wherein the first polypeptide comprises an amino acid sequence at least 80% identical to an amino acid sequence as set forth in SEQ ID NO: 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, or 117; and wherein the VWF fragment comprises an amino acid sequence at least 80% identical to an amino acid sequence as set forth in SEQ ID NO: 118, 119, or 120.

7. The chimeric protein of claim 1, wherein the FVIII protein comprises a B domain or a portion thereof.

8. The chimeric protein of claim 7, wherein the FVIII protein is SQ B domain deleted FVIII.

9. The chimeric protein of claim 7, wherein an additional XTEN is inserted within the B domain or a portion thereof.

10. The chimeric protein of claim 1, wherein the VWF fragment comprises an amino acid sequence at least 90% identical to amino acids 764 to 1240 of SEQ ID NO: 119.

11. The chimeric protein of claim 10, wherein the VWF fragment consists essentially of amino acids 764 to 1240 of SEQ ID NO: 119.

12. The chimeric protein of claim 1, wherein the XTEN is an amino acid sequence at least 95% identical to SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, or SEQ ID NO: 44.

13. The chimeric protein of claim 1, wherein the XTEN is an amino acid sequence at least 80% identical to SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, or SEQ ID NO: 44.

14. A pharmaceutical composition comprising the chimeric protein of claim 1 and a pharmaceutically acceptable carrier.

15. The chimeric protein of claim 1, wherein the FVIII protein comprises (i) a heavy chain and a light

chain, wherein the heavy chain of the FVIII protein comprises an amino acid sequence at least 90% identical to amino acids 1-740 of SEQ ID NO: 4, and the light chain of the FVIII protein comprises an amino acid sequence at least 90% identical to amino acids 1649-2332 of SEQ ID NO: 4.

16. The chimeric protein of claim 15, wherein the FVIII protein comprises a B-domain or a portion thereof.

17. The chimeric protein of claim 1, wherein the second polypeptide comprises an amino acid sequence at least 90% identical to the amino acid sequence as set forth in SEQ ID NO: 103.

18. The chimeric protein of claim 1, wherein the second polypeptide comprises an amino acid sequence at least 95% identical to the amino acid sequence as set forth in SEQ ID NO:103.

19. The chimeric protein of claim 1, wherein the second polypeptide comprises the amino acid sequence as set forth in SEQ ID NO:103.

20. The chimeric protein of claim 1, wherein the second polypeptide comprises an amino acid sequence at least 90% identical to the amino acid sequence as set forth in SEQ ID NO:103, and the first polypeptide comprises an amino acid sequence at least 90% identical to the amino acid sequence as set forth in SEQ ID NO:119.

21. The chimeric protein of claim 1, wherein the second polypeptide comprises an amino acid sequence at least 95% identical to the amino acid sequence as set forth in SEQ ID NO:103, and the first polypeptide comprises an amino acid sequence at least 95% identical to the amino acid sequence as set forth in SEQ ID NO:119.

22. The chimeric protein of claim 4, wherein the cleavable linker comprises one or more cleavage sites that can be cleaved by a protease.

23. The chimeric protein of claim 22, wherein the protease is factor XIa, factor XIIa, kallikrein, factor VIIa, factor IXa, factor Xa, factor IIa (thrombin), Elastase-2, MMP-12, MMP-13, MMP-17, or MMP-20.

24. The chimeric protein of claim 4, wherein the cleavable linker comprises one or more thrombin cleavage sites.

25. The chimeric protein of claim 9, wherein the additional XTEN comprises an amino acid sequence of 288 amino acids in length.

26. The chimeric protein of claim 1, wherein the XTEN comprises an amino acid sequence having at least 90% identity to an amino acid sequence as set forth in SEQ ID NO: 145, 146, 147, or 148.

27. The chimeric protein of claim 11, wherein the VWF fragment consists of amino acids 764 to 1240 of SEQ ID NO: 119.

28. The chimeric protein of claim 1, wherein the XTEN comprises an amino acid sequence as set forth in SEQ ID NO: 145, 146, 147, or 148.

29. A chimeric protein comprising (i) a first polypeptide and (ii) a second polypeptide, the first polypeptide comprising (1) a VWF fragment, (2) a first XTEN, (3) a thrombin cleavable linker, and (4) a first Fc region, and the second polypeptide comprising (5) a FVIII protein, (6) a second XTEN, and (7) a second Fc region, wherein the VWF fragment consists of amino acids 764 to 1240 of SEQ ID NO: 119; wherein the first XTEN comprises the amino acid sequence as set forth in SEQ ID NO:145, 146, 147, or 148; wherein the FVIII protein comprises a full or partial deletion of the B domain; wherein the second XTEN comprises the amino acid sequence as set forth in SEQ ID NO: 145, 146, 147, or 148, wherein the second XTEN is inserted within the B domain or a portion thereof, and

wherein the XTEN is about 36 to about 3000 amino acid in length; and wherein the first Fc region and the second Fc region form a disulfide bond.

30. The chimeric protein of claim 1, wherein the XTEN is about 36 to about 3000 amino acid in length.

31. A chimeric protein comprising (i) a first polypeptide, (ii) a second polypeptide, and (iii) a third polypeptide, wherein the first polypeptide comprises (1) a VWF fragment, (2) a first XTEN, (3) a thrombin cleavable linker, and (4) a first Fc region; wherein the second polypeptide comprises (5) a heavy chain of a FVIII protein and (6) a second XTEN; and wherein the third polypeptide comprises (7) a light chain of a FVIII protein and (8) a second Fc region; wherein the heavy chain of the FVIII protein and the light chain of the FVIII protein form a metal bond; wherein the first XTEN comprises an amino acid sequence having at least 80% identity to an amino acid sequence as set forth in SEQ ID NO: 141-169, or 170; wherein the second XTEN comprises an amino acid sequence having at least 80% identity to an amino acid sequence as set forth in SEQ ID NO: 141-169, or 170; wherein the VWF fragment does not comprise amino acids 1274 to 2813 corresponding to SEQ ID NO: 2; and wherein the first Fc region and the second Fc region form a disulfide bond.

32. The chimeric protein of claim 31, wherein the first and second XTENs are about 36 to about 3000 amino acid in length.

33. The chimeric protein of claim 1, wherein the VWF fragment in the first polypeptide comprises an amino acid sequence at least 90% identical to amino acids 764 to 1240 of SEQ ID NO: 119 and the second polypeptide comprises an amino acid sequence at least 90% identical to the amino acid sequence as set forth in SEQ ID NO:103.

34. The chimeric protein of claim 1, wherein the VWF fragment in the first polypeptide comprises an amino acid sequence at least 95% identical to amino acids 764 to 1240 of SEQ ID NO: 119 and the second polypeptide comprises an amino acid sequence at least 95% identical to the amino acid sequence as set forth in SEQ ID NO:103.

35. The chimeric protein of claim 31, wherein the VWF fragment in the first polypeptide comprises an amino acid sequence at least 90% identical to amino acids 764 to 1240 of SEQ ID NO: 119.

36. The chimeric protein of claim 31, wherein the VWF fragment in the first polypeptide comprises an amino acid sequence at least 95% identical to amino acids 764 to 1240 of SEQ ID NO: 119.