CLAIMS

1. A modified Von Willebrand Factor (VWF) which binds Factor VIII wherein the modified VWF comprises a sequence as shown in SEQ ID NO:3 or a fragment thereof; wherein the modified VWF binds to Factor VIII with an off rate lower than a reference VWF comprising an unmodified SEQ ID NO:3 in which the modified VWF comprises a sequence selected from the group consisting of SEQ ID NO:5 (S764P/S766W/V1083A), SEQ ID NO:6 (S764G/S766Y/V1083A), SEQ ID NO:7 (S764E/S766Y/V1083A), SEQ ID NO:8 (N1011S/V1083A/K1181E), SEQ ID NO:17 (S766Y/V1083A), SEQ ID NO:11 (V805A/Q1158L), SEQ ID NO:12 (K912E/T1088S), SEQ ID NO:9 (V1083A), SEQ ID NO:10 (S1042T), and SEQ ID NO:13 (L781P).

2. The modified VWF as claimed in claim 1 in which the modified VWF binds to Factor VIII with an off rate at least 5 fold lower than the reference VWF, preferably with an off rate at least 10 fold lower than the reference polypeptide.

3. The modified polypeptide as claimed in claim 1 in which the modified polypeptide binds to Factor VIII with a KD at least 5 fold lower than the reference polypeptide, preferably with an off rate at least 10 fold lower than the reference polypeptide.

4. The modified VWF as claimed in any one of claims 1 to 3 in which the modified VWF further comprises a half-life extending moiety.

5. The modified VWF as claimed in claim 4 wherein the half-life extending moiety is a heterologous amino acid sequence fused to the truncated VWF, wherein said heterologous amino acid sequence preferably comprises or consists of a polypeptide selected from the group consisting of immunoglobulin constant regions and portions thereof, e.g. the Fc fragment, transferrin and fragments thereof, the C-terminal peptide of human chorionic gonadotropin, solvated random chains with large hydrodynamic volume known as XTEN, homo-amino acid repeats (HAP), proline-alanine-serine repeats (PAS), albumin, afamin, alpha-fetoprotein, Vitamin D binding protein, polypeptides capable of binding under physiological conditions to albumin or immunoglobulin constant regions, and combinations thereof.

6. The modified VWF as claimed in claim 4, wherein the half-life extending moiety is conjugated to the modified VWF, wherein said half-life-extending moiety is preferably selected from the group consisting of hydroxyethyl starch (HES), polyethylene glycol (PEG), polysialic acids (PSAs), elastin-like polypeptides, heparosan polymers, hyaluronic acid and albumin binding ligands, e.g. fatty acid chains, and combinations thereof.

7. The modified VWF as claimed in claim 5 in which the heterologous amino acid sequence comprises albumin.

8. The modified VWF as claimed in claim 7 in which the N-terminus of the albumin is fused to the C-terminus of the modified VWF sequence either directly or via a spacer, optionally, in which 1 to 5 amino acids at the natural C-terminus of the modified polypeptide have been deleted.

9. A complex comprising a Factor VIII molecule and the modified VWF of any one of claims 1 to 8.

10. The modified VWF of any one of claims 1 to 8 or the complex of claim 9 for use in the treatment or prophylaxis of a bleeding disorder.

11. The modified VWF or complex for use according to claim 10, wherein the bleeding disorder is von Willebrand's disease (VWD) or hemophilia A.

12. A pharmaceutical composition comprising the modified VWF of any one of claims 1 to 8 or the complex of claim 9.

13. A polynucleotide encoding the modified VWF of any one of claims 1 to 8.

14. A plasmid or vector comprising the polynucleotide of claim 13; said plasmid or vector being an expression vector.

15. A host cell comprising the polynucleotide of claim 13 or the plasmid of claim 14.

16. A method of producing a polypeptide comprising a modified VWF, comprising:

(i) culturing the host cells of claim 15 under conditions such that the polypeptide comprising a modified VWF is expressed; and

(ii) optionally recovering the polypeptide comprising a modified VWF from the host cells or from the culture medium.