CLAIMS

1. Use of a composition comprising a therapeutic dose of a chimeric polypeptide in the manufacture of a medicament for decreasing the incidence of a bleeding episode in a human subject, wherein the chimeric polypeptide comprises a functional Factor VIII (FVIII) portion having coagulant activity and a Fc portion, wherein the composition is to be administered in multiple doses, each of the multiple doses being 25 IU/kg to 100 IU/kg of the chimeric polypeptide at a dosing interval of 72 hours to five days between two doses.

2. Use of a composition comprising a therapeutic dose of a chimeric polypeptide in the manufacture of a medicament for the treatment of a bleeding episode in a human subject suffering from hemophilia A, by decreasing the incidence of the bleeding episode, wherein the chimeric polypeptide comprises a functional Factor VIII (FVIII) portion having coagulant activity and a Fc portion, and wherein the medicament is to be administered in multiple doses, each of the multiple doses being 25 IU/kg to 100 IU/kg of the chimeric polypeptide at a dosing interval of 72 hours to five days between two doses.

3. The use of claim 1 or claim 2, wherein the decreasing the incidence of a bleeding episode prevents or treats the bleeding episodes.

4. The use of any one of claims 1 to 3, wherein the administration is for routine prophylaxis.

5. The use of any one of claims 1 to 3, wherein the administration is for on-demand treatment.

6. The use of any one of claims 1 to 3, wherein the administration is for tailored prophylaxis.

7. The use of any one of claims 1 to 6, wherein a trough level between 1-3% of FVIII activity is maintained.

8. The use of any one of claims 1 to 7, wherein each of the multiple doses is in a therapeutic dose of 25-30 IU/kg, 30-40 IU/kg, 40-50 IU/kg, 50-60 IU/kg, 60-70 IU/kg, 70-80 IU/kg, 80-90 IU/kg, or 90 to 100 IU/kg of the chimeric polypeptide.

9. The use of any one of claims 1 to 8, wherein each of the multiple doses is in a therapeutic dose of 25 IU/kg, 30 IU/kg, 35 IU/kg, 40 IU/kg, 45 IU/kg, 50 IU/kg, 55 IU/kg, 60 IU/kg, 65 IU/kg, 70 IU/kg, 75 IU/kg, 80 IU/kg, 85 IU/kg, 90 IU/kg, or 100 IU/kg of the chimeric polypeptide.

10. The use of any one of claims 1 to 9, wherein the dosing interval is 72 hours to five days.

11. The use of any one of claims 1 to 9, wherein the dosing interval is 72 hours, four days, or five days.

12. The use of any one of claims 1 to 10, wherein the dosing interval is twice a week.

13. The use of any one of claims 1 to 12, wherein each of the multiple doses is in a therapeutic dose of 65 IU/kg to 100 IU/kg of the chimeric polypeptide.

14. The use of any one of claims 1 to 7, wherein the composition is to be administered to the subject twice weekly, in a first therapeutic dose of 25 IU/kg to 65 IU/kg of the chimeric polypeptide and a second therapeutic dose of 25 IU/kg to 65 IU/kg of the chimeric polypeptide.

15. The use of claim 14, wherein the dosing interval between the first dose and the second dose is 72 hours, four days, or five days.

16. The use of any one of claims 1 to 15, wherein the administration resolves 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, or 90% of bleeding episodes.

17. The use of any one of claims 1 to [[17]]15, wherein the administration resolves 80-100%, 80-90%, 85-90%, 90-100%, 90-95%, or 95-100% of bleeding episodes.

18. The use of any one of claims 1 to 17, wherein each of the multiple doses is 25 IU/kg to 65 IU/kg.

19. The use of any one of claims 1 to 17, wherein each of the multiple dose is 25 IU/kg, 30 IU/kg, 35 IU/kg, 40 IU/kg, 45 IU/kg, 50 IU/kg, 55 IU/kg, 60 IU/kg, or 65 IU/kg.

20. The use of claim 18, wherein the dosing interval is three days to five days.

21. The use of any one of claims 1 to 17, wherein each of the multiple doses is 65 IU/kg and the dosing interval is five days.

22. The use of any one of claims 1 to 21, wherein each of the multiple doses is 50 IU/kg or 65 IU/kg.

23. The use of claim 22, wherein the dosing interval is five days.

24. The use of any claims 1 to 21, wherein each of the multiple doses is 50 IU/kg and the dosing interval is five days.

25. The use of any claims 1 to 24, wherein the chimeric polypeptide is a FVIIIFc monomer dimer hybrid.

26. Use of a composition comprising a therapeutic dose of a chimeric polypeptide in the manufacture of a medicament for maintaining homeostasis of a level of Factor VIII ("FVIII") in a human subject in need of a surgery, wherein the chimeric polypeptide comprises a long-acting FVIII polypeptide comprising functional FVIII having coagulant activity and a Fc, wherein the composition is to be administered in multiple doses, each of the multiple doses being 10 IU/kg to 60 IU/kg of the long-acting FVIII polypeptide at a dosing interval of 12 hours to 5 days between two doses.

27. The use of claim 26, wherein a trough level between 3-5% of FVIII activity is maintained.

28. The use of claim 26 or claim 27, wherein the administration prevents a bleeding episode in the subject.

29. The use of any one of claims 26 to 28, wherein the subject is in need of surgical prophylaxis.

30. The use of any one of claims 26 to 28, wherein the subject is in need of treatment for surgery.

31. The use of any one of claims 26 to 28, wherein the subject is in need of peri-operative management.

32. The use of any one of claims 26 to 30, wherein the surgery is minor surgery, major surgery, tooth extraction, tonsillectomy, inguinal herniotomy, synovectomy, total knee replacement, craniotomy, osteosynthesis, trauma surgery, intracranial surgery, intra-abdominal surgery, intrathoracic surgery, or joint replacement surgery.

33. The use of any one of claims 26 to 30, wherein the surgery is an emergency surgery.

34. The use of any one of claims 26 to 33, wherein the therapeutic dose is about 10 IU/kg, about 20 IU/kg, about 30 IU/kg, about 40 IU/kg, or about 50 IU/kg.

35. The use of any one of claims 26 to 34, wherein the dosing interval is 12 hours to 24 hours, 24 hours to 48 hours, or 48 hours to 72 hours.

36. The use of any one of claims 26 to 28, wherein the dosing interval is 12 hours to 24 hours.

37. A composition for use in maintaining homeostasis of a level of Factor VIII ("FVIII") in a human subject in need of surgical prophylaxis, peri-operative management, or treatment of surgery wherein the composition comprises a FVIII polypeptide which is to be administered in multiple doses of about 35 IU/kg to about 50 IU/kg of a long-acting chimeric FVIII polypeptide at a dosing interval of 12 hours to 24 hours, wherein the long-acting FVIII polypeptide is a FVIIIFc monomer dimer hybrid comprising a functional FVIII having coagulant activity and two Fcs, wherein one of the Fcs is fused to the C-terminus of the light chain of the functional FVIII, and wherein a trough level between 3-5% of FVIII activity is maintained between the administration of the doses.

38. Use of a composition for use in maintaining homeostasis of a level of Factor VIII ("FVIII") in a human subject in need of surgical prophylaxis, peri-operative management, or

treatment of surgery wherein the composition comprises a FVIII polypeptide which is to be administered in multiple doses of about 35 IU/kg to about 50 IU/kg of a long-acting chimeric FVIII polypeptide at a dosing interval of 12 hours to 24 hours, wherein the long-acting FVIII polypeptide is a FVIIIFc monomer dimer hybrid comprising a functional FVIII having coagulant activity and two Fcs, wherein one of the Fcs is fused to the C-terminus of the light chain of the functional FVIII, and wherein a trough level between 3-5% of FVIII activity is maintained between the administration of the doses.

39. Use of a composition comprising a therapeutic dose of a chimeric polypeptide in the manufacture of a medicament for prophylactically treating hemophilia A in a human subject in need thereof, wherein the chimeric polypeptide comprises a chimeric Factor VIII (FVIII) polypeptide, wherein the FVIII polypeptide comprises a functional FVIII having coagulant activity and a Fc, wherein the composition is to be administered in multiple doses, each of the multiple doses being 25 IU/kg to 80 IU/kg of the chimeric FVIII polypeptide at a dosing interval of 72 hours to five days between two doses.

40. Use of a composition comprising a therapeutic dose of a chimeric Factor VIII (FVIII) polypeptide, in the manufacture of a medicament for prophylactically treating hemophilia A in a human subject in need thereof, wherein the chimeric FVIII polypeptide comprises a functional FVIII having coagulant activity and a Fc, wherein the composition is to be administered in multiple doses, each of the multiple doses being 25 IU/kg to 80 IU/kg of the chimeric FVIII polypeptide at a dosing interval of 72 hours to five days between two doses.

41. The use of claim 40, wherein a trough level between 1-3% of FVIII activity is maintained.

42. The use of claim 40 or claim 41, wherein each of the multiple doses is about 25 IU/kg, about 30 IU/kg, about 40 IU/kg, about 50 IU/kg, about 55 IU/kg, about 60 IU/kg, about 65 IU/kg, about 70 IU/kg, about 75 IU/kg, or about 80 IU/kg.

43. The use of any one of claims 42 to 44, wherein the dosing interval is 72 hours, four days, or five days.

44. The use of any one of claims 1 to 36, 38, or 40 to 43, wherein the chimeric polypeptide is pegylated.

45. The use of any one of claims 1 to 36, 38, or 40 to 44, wherein the chimeric polypeptide is a FVIIIFc monomer dimer hybrid.

46. The use of any one of claims 1 to 36, 38, or 40 to 45, wherein the functional Factor VIII portion comprises full-length factor VIII, mature factor VIII, or factor VIII with a full or partial deletion of the B domain.

47. The use of any one of claims 1 to 36, 38, or 40 to 46, wherein the functional FVIII portion comprises an amino acid sequence at least 90% or 95% identical to amino acids 1 to 1438 of SEQ ID NO: 2 or amino acids 1 to 2332 of SEQ ID NO: 6.

48. The use of claim 47, wherein the functional FVIII portion comprises amino acids 1 to 1438 of SEQ ID NO: 2 or amino acids 1 to 2332 of SEQ ID NO: 6.

49. The use of any of claims 1 to 36, 38, or 40 to 47, wherein the Fc portion is at least 90% or 95% identical to amino acids 1439 to 1665 of SEQ ID NO: 2 or amino acids 2333 to 2559 of SEQ ID NO: 6.

50. The use of any of claims 1 to 36, 38, or 40 to 49, wherein the Fc portion comprises amino acids 1439 to 1665 of SEQ ID NO: 2 or amino acids 2333 to 2559 of SEQ ID NO: 6.

51. The use of any one of claims 1 to 36, 38, or 40 to 50, further comprising at least one excipient.