WHAT IS CLAIMED IS:

1. A method of administering Factor VIII to a subject in need thereof, comprising

administering to the subject a therapeutic dose of a chimeric polypeptide comprising a Factor VIII portion and a second portion at a dosing interval at least about one and one-half times longer than the dosing interval required for an equivalent amount of a polypeptide consisting of said Factor VIII portion.

2. The method of claim 1, wherein said chimeric polypeptide comprises a Fc portion.

3. The method of claim 1 or 2, where said dosing interval is at least about one and one-half to six times longer, one and one-half to five times longer, one and one-half to four times longer, one and one-half to three times longer, or one and one-half to two times longer, than the dosing interval required for an equivalent amount of a polypeptide consisting of said Factor VIII portion.

4. The method of claim 3, where said dosing interval is at least about one and one-half, two, two and one-half, three, three and one-half, four, four and one-half, five, five and one-half or six times longer than the dosing interval required for an equivalent amount of a polypeptide consisting of said Factor VIII portion.

5. The method of any of claims 1-4, wherein said dosing interval of said chimeric polypeptide is about every five, six, seven, eight, nine, ten, eleven, twelve, thirteen, or fourteen days or longer.

6. The method of any of claims 1-5, wherein said subject is in need of prophylactic treatment.

7. The method of any of claims 1-4, wherein said subject is in need of on-demand treatment.

8. The method of claim 7, wherein said subject is in need of treatment for a bleeding episode.

9. The method of claim 8, wherein said subject is in need of treatment for hemarthrosis, muscle bleed, oral bleed, hemorrhage, hemorrhage into muscles, oral hemorrhage, trauma, trauma capitis, gastrointestinal bleeding, intracranial hemorrhage, intra-abdominal hemorrhage, intrathoracic hemorrhage, bone fracture, central nervous system bleeding, bleeding in the retropharyngeal space, bleeding in the retroperitoneal space, or bleeding in the illiopsoas sheath.

10. The method of claim 7, wherein said subject is in need of surgical prophylaxis, peri-operative management, or treatment for surgery.

11. The method of claim 10, wherein said 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.

12. The method of any of claims 7-11, wherein said dosing interval of said chimeric polypeptide is about once every 24-36, 24-48, 24-72, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, or 72 hours or longer.

13. The method of any of claims 1-12, wherein said therapeutic dose is 10-100 IU/kg.

14. The method of claim 12, wherein said therapeutic dose is 10-20, 20-30, 30-40, 40-50, 50-60, 60-70, 70-80, 80-90, or 90-100 IU/kg.

15. The method of claim 13, wherein said therapeutic dose is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 IU/kg.

16. The method of any of claims 1-15, wherein said subject is human.

17. The method of any of claims 1-16, wherein said Factor VIII is human Factor VIII.

18. The method of any of claims 1-17, wherein said Factor VIII has a full or partial deletion of the B domain.

19. The method of claim 17, wherein the Factor VIII portion of said chimeric polypeptide is at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2 without a signal sequence (amino acids 1 to 1438 of SEQ ID NO:2; amino acids 1 to 2332 of SEQ ID NO:6; amino acids 1 to 740 of SEQ ID NO:8; amino acids 1 to 745 of SEQ ID NO:10; or amino acids 1 to 684 of SEQ ID NO:12).

20. The method of claim 19, wherein the Factor VIII portion of said chimeric polypeptide is identical to a Factor VIII amino acid sequence shown in Table 2 without a signal sequence (amino acids 1 to 1438 of SEQ ID NO:2; amino acids 1 to 2332 of SEQ ID NO:6; amino acids 1 to 740 of SEQ ID NO:8; amino acids 1 to 745 of SEQ ID NO:10; or amino acids 1 to 684 of SEQ ID NO:12).

21. The method of claim 17, wherein the Factor VIII portion of said chimeric polypeptide is at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2 with a signal sequence (amino acids -19 to 1438 of SEQ ID NO:2; amino acids -19 to 2332 of SEQ ID NO:6; amino acids -19 to 740 of SEQ ID NO:8; amino acids -19 to 745 of SEQ ID NO:10; or amino acids -20 to 684 of SEQ ID NO:12).

22. The method of claim 21, wherein the Factor VIII portion of said chimeric polypeptide is identical to a Factor VIII amino acid sequence shown in Table 2 with a signal sequence (amino acids -19 to 1438 of SEQ ID NO:2; amino acids -19 to 2332 of SEQ ID NO:6; amino acids -19 to 740 of SEQ ID NO:8; amino acids -19 to 745 of SEQ ID NO:10; or amino acids -20 to 684 of SEQ ID NO:12).

23. The method of claim 17 or 18, wherein said second portion of said chimeric polypeptide is at least 90% or 95% identical to the Fc amino acid sequence shown in Table 2 (amino acids 1439 to 1665 of SEQ ID NO:2; amino acids 2333 to 2559 of SEQ ID NO:6; amino acids 741 to 967 of SEQ ID NO:8; amino acids 746 to 972 of SEQ ID NO:10; amino acids 685 to 924 of SEQ ID NO:12).

24. The method of claim 23, wherein said second portion of said chimeric polypeptide is identical to the Fc amino acid sequence shown in Table 2 (amino acids 1439 to 1665 of SEQ ID NO:2; amino acids 2333 to 2559 of SEQ ID NO:6; amino acids 741 to 967 of SEQ ID NO:8; amino acids 746 to 972 of SEQ ID NO:10; amino acids 685 to 924 of SEQ ID NO:12).

25. The method of any of claims 1-24, wherein said chimeric polypeptide is in the form of a hybrid comprising a second polypeptide in association with said chimeric polypeptide, wherein said second polypeptide consists essentially of an Fc.

26. The method of claim 25, wherein said chimeric polypeptide comprises a sequence at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) without a signal sequence (amino acids 1 to 1665 of SEQ ID NO:2) or at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) with a signal sequence (amino acids -19 to 1665 of SEQ ID NO:2).

27. The method of claim 26, wherein said chimeric polypeptide comprises a sequence identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) without a signal sequence (amino acids 1 to 1665 of SEQ ID NO:2) or identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) with a signal sequence (amino acids -19 to 1665 of SEQ ID NO:2).

28. The method of any of claims 25-27, wherein said second polypeptide consists essentially of a sequence at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) without a signal sequence (amino acids 1 to 227 of SEQ ID NO:4) or at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) with a signal sequence (amino acids -20 to 227 of SEQ ID NO:4).

29. The method of claim 28, wherein said second polypeptide consists essentially of a sequence identical to the amino acid sequence shown in Table 2A(ii) without a signal sequence (amino acids 1 to 227 of SEQ ID NO:4) or identical to the amino acid sequence shown in Table 2A(ii) with a signal sequence (amino acids -20 to 227 of SEQ ID NO:4).

30. The method of any of claims 1-29, wherein said chimeric polypeptide is administered as part of a pharmaceutical composition comprising at least one excipient.

31. A method of administering Factor VIII to a subject in need thereof, comprising

administering to the subject a therapeutic dose of a chimeric polypeptide comprising a Factor VIII portion and a second portion to obtain an area under the plasma concentration versus time curve (AUC) at least about one and one-quarter times greater than the AUC obtained by an equivalent amount of a polypeptide consisting of said Factor VIII portion.

32. The method of claim 31, wherein said chimeric polypeptide is administered at a dosing interval of about every five, six, seven, eight, nine, ten, eleven, twelve, thirteen, or fourteen days or longer.

33. The method of any of claims 31-32, wherein said subject is in need of prophylactic treatment.

34. The method of claim 31, wherein said subject is in need of on-demand treatment.

35. The method of claim 32, wherein said subject is in need of treatment for a bleeding episode.

36. The method of claim 33, wherein said subject is in need of treatment for hemarthrosis, muscle bleed, oral bleed, hemorrhage, hemorrhage into muscles, oral hemorrhage, trauma, trauma capitis, gastrointestinal bleeding, intracranial hemorrhage, intra-abdominal hemorrhage, intrathoracic hemorrhage, bone fracture, central nervous system bleeding, bleeding in the retropharyngeal space, bleeding in the retroperitoneal space, or bleeding in the illiopsoas sheath.

37. The method of claim 34, wherein said subject is in need of surgical prophylaxis, peri-operative management, or treatment for surgery.

38. The method of claim 37, wherein said 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.

39. The method of any of claims 34-38, wherein said dosing interval of said chimeric polypeptide is about once every 24-36, 24-48, 24-72, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, or 72 hours or longer.

40. The method of any of claims 31-39, wherein said therapeutic dose is 10-100 IU/kg.

41. The method of claim 40, wherein said therapeutic dose is 10-20, 20-30, 30-40, 40-50, 50-60, 60-70, 70-80, 80-90, or 90-100 IU/kg.

42. The method of claim 41, wherein said therapeutic dose is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 IU/kg.

43. The method of any of claims 31-42, wherein said subject is human.

44. The method of any of claims 31-43, wherein said Factor VIII is human Factor VIII.

45. The method of any of claims 31-44, wherein said Factor VIII has a full or partial deletion of the B domain.

46. The method of claim 44, wherein the Factor VIII portion of said chimeric polypeptide is at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2 without a signal sequence (amino acids 1 to 1438 of SEQ ID NO:2; amino acids 1 to 2332 of SEQ ID NO:6; amino acids 1 to 740 of SEQ ID NO:8; amino acids 1 to 745 of SEQ ID NO:10; or amino acids 1 to 684 of SEQ ID NO:12).

47. The method of claim 46, wherein the Factor VIII portion of said chimeric polypeptide is identical to a Factor VIII amino acid sequence shown in Table 2 without a signal sequence (amino acids 1 to 1438 of SEQ ID NO:2; amino acids 1 to 2332 of SEQ ID NO:6; amino acids 1 to 740 of SEQ ID NO:8; amino acids 1 to 745 of SEQ ID NO:10; or amino acids 1 to 684 of SEQ ID NO:12).

48. The method of claim 44, wherein the Factor VIII portion of said chimeric polypeptide is at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2 with a signal sequence (amino acids -19 to 1438 of SEQ ID NO:2; amino acids -19 to 2332 of SEQ ID NO:6; amino acids -19 to 740 of SEQ ID NO:8; amino acids -19 to 745 of SEQ ID NO:10; or amino acids -20 to 684 of SEQ ID NO:12).

49. The method of claim 48, wherein the Factor VIII portion of said chimeric polypeptide is identical to a Factor VIII amino acid sequence shown in Table 2 with a signal sequence (amino acids -19 to 1438 of SEQ ID NO:2; amino acids -19 to 2332 of SEQ ID NO:6; amino acids -19 to

740 of SEQ ID NO:8; amino acids -19 to 745 of SEQ ID NO:10; or amino acids -20 to 684 of SEQ ID NO:12).

50. The method of claim 43 or 44, wherein said second portion of said chimeric polypeptide is at least 90% or 95% identical to the Fc amino acid sequence shown in Table 2 (amino acids 1439 to 1665 of SEQ ID NO:2; amino acids 2333 to 2559 of SEQ ID NO:6; amino acids 741 to 967 of SEQ ID NO:8; amino acids 746 to 972 of SEQ ID NO:10; amino acids 685 to 924 of SEQ ID NO:12).

51. The method of claim 50, wherein said second portion of said chimeric polypeptide is identical to the Fc amino acid sequence shown in Table 2 (amino acids 1439 to 1665 of SEQ ID NO:2; amino acids 2333 to 2559 of SEQ ID NO:6; amino acids 741 to 967 of SEQ ID NO:8; amino acids 746 to 972 of SEQ ID NO:10; amino acids 685 to 924 of SEQ ID NO:12).

52. The method of any of claims 31-51, wherein said chimeric polypeptide is in the form of a hybrid comprising a second polypeptide in association with said chimeric polypeptide, wherein said second polypeptide consists essentially of an Fc.

53. The method of claim 52, wherein said chimeric polypeptide comprises a sequence at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) without a signal sequence (amino acids 1 to 1665 of SEQ ID NO:2) or at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) with a signal sequence (amino acids -19 to 1665 of SEQ ID NO:2).

54. The method of claim 53, wherein said chimeric polypeptide comprises a sequence identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) without a signal sequence (amino acids 1 to 1665 of SEQ ID NO:2) or at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) with a signal sequence (amino acids -19 to 1665 of SEQ ID NO:2).

55. The method of any of claims 52-54, wherein said second polypeptide consists essentially of a sequence at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) without a signal sequence (amino acids 1 to 227 of SEQ ID NO:4) or at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) with a signal sequence (amino acids -20 to 227 of SEQ ID NO:4).

56. The method of claim 55, wherein said second polypeptide consists essentially of a sequence identical to the amino acid sequence shown in Table 2A(ii) without a signal sequence (amino acids 1 to 227 of SEQ ID NO:4) or at least 90% or 95% identical to the amino acid

sequence shown in Table 2A(ii) with a signal sequence (amino acids -20 to 227 of SEQ ID NO:4).

57. The method of any of claims 31-56, wherein said chimeric polypeptide is administered as part of a pharmaceutical composition comprising at least one excipient.

58. A method of administering Factor VIII to a subject in need thereof, comprising

administering to the subject a therapeutic dose of a polypeptide comprising a Factor VIII and an Fc at a dosing interval of about every five, six, seven, eight, nine, ten, eleven, twelve, thirteen, or fourteen days or longer.

59. The method of any of claim 58, wherein said subject is in need of prophylactic treatment.

60. The method of any of claims 58-59, wherein said therapeutic dose is 10-100 IU/kg.

61. The method of claim 60, wherein said therapeutic dose is 10-20, 20-30, 30-40, 40-50, 50-60, 60-70, 70-80, 80-90, or 90-100 IU/kg.

62. The method of claim 61, wherein said therapeutic dose is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 IU/kg.

63. The method of any of claims 58-62, wherein said subject is human.

64. The method of any of claims 58-63, wherein said Factor VIII is human Factor VIII.

65. The method of any of claims 58-64, wherein said Factor VIII has a full or partial deletion of the B domain.

66. The method of claim 64, wherein said Factor VIII is at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2 without a signal sequence (amino acids 1 to 1438 of SEQ ID NO:2; amino acids 1 to 2332 of SEQ ID NO:6; amino acids 1 to 740 of SEQ ID NO:8; amino acids 1 to 745 of SEQ ID NO:10; or amino acids 1 to 684 of SEQ ID NO:12).

67. The method of claim 66, wherein said Factor VIII is identical to a Factor VIII amino acid sequence shown in Table 2 without a signal sequence (amino acids 1 to 1438 of SEQ ID NO:2; amino acids 1 to 2332 of SEQ ID NO:6; amino acids 1 to 740 of SEQ ID NO:8; amino acids 1 to 745 of SEQ ID NO:10; or amino acids 1 to 684 of SEQ ID NO:12).

68. The method of claim 64, wherein said Factor VIII is at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2 with a signal sequence (amino acids -19 to 1438 of SEQ ID NO:2; amino acids -19 to 2332 of SEQ ID NO:6; amino acids -19 to 740 of SEQ ID NO:8; amino acids -19 to 745 of SEQ ID NO:10; or amino acids -20 to 684 of SEQ ID NO:12).

69. The method of claim 68, wherein said Factor VIII is identical to a Factor VIII amino acid sequence shown in Table 2 with a signal sequence (amino acids -19 to 1438 of SEQ ID NO:2; amino acids -19 to 2332 of SEQ ID NO:6; amino acids -19 to 740 of SEQ ID NO:8; amino acids -19 to 745 of SEQ ID NO:10; or amino acids -20 to 684 of SEQ ID NO:12).

70. The method of claim 64 or 65, wherein said second portion is at least 90% or 95% identical to the Fc amino acid sequence shown in Table 2 (amino acids 1439 to 1665 of SEQ ID NO:2; amino acids 2333 to 2559 of SEQ ID NO:6; amino acids 741 to 967 of SEQ ID NO:8; amino acids 746 to 972 of SEQ ID NO:10; amino acids 685 to 924 of SEQ ID NO:12).

71. The method of claim 70, wherein said second portion is identical to the Fc amino acid sequence shown in Table 2 (amino acids 1439 to 1665 of SEQ ID NO:2; amino acids 2333 to 2559 of SEQ ID NO:6; amino acids 741 to 967 of SEQ ID NO:8; amino acids 746 to 972 of SEQ ID NO:10; amino acids 685 to 924 of SEQ ID NO:12).

72. The method of any of claims 58-71, wherein said chimeric polypeptide is a Factor VIII-Fc chimeric polypeptide in the form of a hybrid comprising a second polypeptide in association with said chimeric polypeptide, wherein said second polypeptide consists essentially of an Fc. .

73. The method of claim 72, wherein said chimeric polypeptide comprises a sequence at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) without a signal sequence (amino acids 1 to 1665 of SEQ ID NO:2) or at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) with a signal sequence (amino acids -19 to 1665 of SEQ ID NO:2).

74. The method of claim 73, wherein said chimeric polypeptide comprises a sequence identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) without a signal sequence (amino acids 1 to 1665 of SEQ ID NO:2) or at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) with a signal sequence (amino acids -19 to 1665 of SEQ ID NO:2).

75. The method of any of claims 72-74, wherein said second polypeptide consists essentially of a sequence at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) without a signal sequence (amino acids 1 to 227 of SEQ ID NO:4) or at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) with a signal sequence (amino acids -20 to 227 of SEQ ID NO:4).

76. The method of claim 75, wherein said second polypeptide consists essentially of a sequence identical to the amino acid sequence shown in Table 2A(ii) without a signal sequence (amino acids 1 to 227 of SEQ ID NO:4) or at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) with a signal sequence (amino acids -20 to 227 of SEQ ID NO:4).

77. The method of any of claims 58-76, wherein said polypeptide is administered as part of a pharmaceutical composition comprising at least one excipient.

78. A polypeptide comprising a Factor VIII at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2 without a signal sequence (amino acids 1 to 1438 of SEQ ID NO:2; amino acids 1 to 2332 of SEQ ID NO:6; amino acids 1 to 740 of SEQ ID NO:8; amino acids 1 to 745 of SEQ ID NO:10; or amino acids 1 to 684 of SEQ ID NO:12), and an Fc.

79. The polypeptide of claim 78, wherein said Factor VIII is identical to a Factor VIII amino acid sequence shown in Table 2 without a signal sequence (amino acids 1 to 1438 of SEQ ID NO:2; amino acids 1 to 2332 of SEQ ID NO:6; amino acids 1 to 740 of SEQ ID NO:8; amino acids 1 to 745 of SEQ ID NO:10; or amino acids 1 to 684 of SEQ ID NO:12).

80. A polypeptide comprising a Factor VIII at least 90% or 95% identical to a Factor VIII amino acid sequence shown in Table 2 with a signal sequence (amino acids -19 to 1438 of SEQ ID NO:2; amino acids -19 to 2332 of SEQ ID NO:6; amino acids -19 to 740 of SEQ ID NO:8; amino acids -19 to 745 of SEQ ID NO:10; or amino acids -20 to 684 of SEQ ID NO:12), and an Fc.

81. The polypeptide of claim 80, wherein said Factor VIII is identical to a Factor VIII amino acid sequence shown in Table 2 with a signal sequence (amino acids -19 to 1438 of SEQ ID NO:2; amino acids -19 to 2332 of SEQ ID NO:6; amino acids -19 to 740 of SEQ ID NO:8; amino acids -19 to 745 of SEQ ID NO:10; or amino acids -20 to 684 of SEQ ID NO:12).

82. The polypeptide of any of claims 78 to 81, wherein said Fc is at least 90% or 95% identical to the Fc amino acid sequence shown in Table 2 (amino acids 1439 to 1665 of SEQ ID NO:2; amino acids 2333 to 2559 of SEQ ID NO:6; amino acids 741 to 967 of SEQ ID NO:8; amino acids 746 to 972 of SEQ ID NO:10; amino acids 685 to 924 of SEQ ID NO:12)

83. The polypeptide of claim 82, wherein said Fc is identical to the Fc amino acid sequence shown in Table 2 (amino acids 1439 to 1665 of SEQ ID NO:2; amino acids 2333 to 2559 of SEQ ID NO:6; amino acids 741 to 967 of SEQ ID NO:8; amino acids 746 to 972 of SEQ ID NO:10; amino acids 685 to 924 of SEQ ID NO:12).

84. The polypeptide of claim 78, which comprises a sequence at least 90% or 95% identical to the Factor VIII and Fc amino acid sequences shown in Table 2A(i) without a signal sequence (amino acids 1 to 1665 of SEQ ID NO:2) or at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) with a signal sequence (amino acids -19 to 1665 of SEQ ID NO:2).

85. The polypeptide of claim 84, which comprises a sequence identical to the Factor VIII and Fc amino acid sequences shown in Table 2A(i) without a signal sequence (amino acids 1 to 1665 of SEQ ID NO:2) or at least 90% or 95% identical to the Factor VIII and Fc amino acid sequence shown in Table 2A(i) with a signal sequence (amino acids -19 to 1665 of SEQ ID NO:2).

86. The polypeptide of any of claims 78-85, which is in the form of a hybrid comprising a second polypeptide, wherein said second polypeptide consists essentially of an Fc.

87. The polypeptide of claim 85, wherein said second polypeptide consists essentially of a sequence at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) without a signal sequence (amino acids 1 to 227 of SEQ ID NO:4) or at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) with a signal sequence (amino acids -20 to 227 of SEQ ID NO:4).

88. The polypeptide of claim 86, wherein said second polypeptide consists essentially of a sequence identical to the amino acid sequence shown in Table 2A(ii) without a signal sequence (amino acids 1 to 227 of SEQ ID NO:4) or at least 90% or 95% identical to the amino acid sequence shown in Table 2A(ii) with a signal sequence (amino acids -20 to 227 of SEQ ID NO:4).

89. The polypeptide of any of claims 78-88, which has a half-life at least one and one-half to six times longer, one and one-half to five times longer, one and one-half to four times longer, one and one-half to three times longer, or one and one-half to two times longer to a polypeptide consisting of said Factor VIII.

90. A polynucleotide encoding the polypeptide of any of claims 78 -85.

91. The polynucleotide of claim 90, which comprises the Factor VIII-Fc nucleotide sequences of Table 1 (SEQ ID NOs:1, 5, 7, 9, or 11).

92. A polynucleotide encoding the Factor VIII-Fc polypeptide and the second peptide of any one of claims 86-89.

93. The polynucleotide of any of claims 90-92, which is a vector, plasmid, phage, or virus.

94. The polynucleotide of any of claims 90-93, which is DNA or RNA.

95. A cultured human embryonic cell comprising the polynucleotide of any one of claims 89-94.

96. The cell of claim 95, which is a HEK293 cell.

97. A method of producing a FactorVIII-Fc hybrid protein comprising

culturing the cell of claim 95 or 96 under conditions that allow expression of the encoded Factor VIII-Fc chimeric polypeptide and the encoded polypeptide consisting essentially of Fc; and

recovering the encoded FactorVIII-Fc hybrid protein.

98. A protein produced by the method of claim 97.

99. The method of any one of claims 1-57, wherein said chimeric polypeptide has one or more characteristics selected from the group consisting of:

an ability to interact with phospholipid vesicles comparable to the ability of a polypeptide consisting of said Factor VIII portion;

an ability to form a Xase complex that activates Factor X comparable to the ability of a polypeptide consisting of said Factor VIII portion;

an ability to be activated by alpha-thrombin within five minutes comparable to the ability of a polypeptide consisting of said Factor VIII portion; and

an ability to interact with Factor IXa comparable to the ability of a polypeptide consisting of said Factor VIII portion.

100. The method of claim 99, wherein said chimeric polypeptide has one or more characteristics selected from the group consisting of:

forms a Xase complex that activates Factor X at a Km within about one, about one and one half, or about two standard deviations of the Km of a polypeptide consisting of said Factor VIII portion, wherein Km is measured as a function of Factor X concentration;

forms a Xase complex that activates Factor X at a Vmax within about one, about one and one half, or about two standard deviations of the Vmax of a polypeptide consisting of said Factor VIII portion, wherein Vmax is measured as a function of Factor X concentration;

forms a Xase complex that activates Factor X at a Kd within about one, about one and one half, or about two standard deviations of the Kd of a polypeptide consisting of said Factor VIII portion, wherein Kd is measured as a function of Factor IXa concentration; and

forms a Xase complex that activates Factor X at a Vmax within about one, about one and one half, or about two standard deviations of the Vmax of a polypeptide consisting of said Factor VIII portion, wherein Vmax is measured as a function of Factor IXa concentration.

101. The method of any one of claims 58-77, wherein said polypeptide has one or more characteristics selected from the group consisting of:

an ability to interact with phospholipid vesicles comparable to the ability of a polypeptide consisting of said Factor VIII portion;

an ability to form a Xase complex that activates Factor X comparable to the ability of a polypeptide consisting of said Factor VIII portion;

an ability to be activated by alpha-thrombin within five minutes comparable to the ability of a polypeptide consisting of said Factor VIII portion; and

an ability to interact with Factor IXa comparable to the ability of a polypeptide consisting of said Factor VIII portion.

102. The method of claim 101, wherein said polypeptide has one or more characteristics selected from the group consisting of:

forms a Xase complex that activates Factor X at a Km within about one, about one and one half, or about two standard deviations of the Km of a polypeptide consisting of said Factor VIII portion, wherein Km is measured as a function of Factor X concentration;

forms a Xase complex that activates Factor X at a Vmax within about one, about one and one half, or about two standard deviations of the Vmax of a polypeptide consisting of said Factor VIII portion, wherein Vmax is measured as a function of Factor X concentration;

forms a Xase complex that activates Factor X at a Kd within about one, about one and one half, or about two standard deviations of the Kd of a polypeptide consisting of said Factor VIII portion, wherein Kd is measured as a function of Factor IXa concentration; and

forms a Xase complex that activates Factor X at a Vmax within about one, about one and one half, or about two standard deviations of the Vmax of a polypeptide consisting of said Factor VIII portion, wherein Vmax is measured as a function of Factor IXa concentration.

103. The polypeptide of any one of claims 78-89 and 98, which has one, about one and one half, or about two or more characteristics selected from the group consisting of:

an ability to interact with phospholipid vesicles comparable to the ability of a polypeptide consisting of said Factor VIII portion;

an ability to form a Xase complex that activates Factor X comparable to the ability of a polypeptide consisting of said Factor VIII portion;

an ability to be activated by alpha-thrombin within five minutes comparable to the ability of a polypeptide consisting of said Factor VIII portion; and

an ability to interact with Factor IXa comparable to the ability of a polypeptide consisting of said Factor VIII portion.

104. The method of claim 101, wherein said polypeptide has one or more characteristics selected from the group consisting of:

forms a Xase complex that activates Factor X at a Km within about one, about one and one half, or about two standard deviations of the Km of a polypeptide consisting of said Factor VIII portion, wherein Km is measured as a function of Factor X concentration;

forms a Xase complex that activates Factor X at a Vmax within about one, about one and one half, or about two standard deviations of the Vmax of a polypeptide consisting of said Factor VIII portion, wherein Vmax is measured as a function of Factor X concentration;

forms a Xase complex that activates Factor X at a Kd within about one, about one and one half, or about two standard deviations of the Kd of a polypeptide consisting of said Factor VIII portion, wherein Kd is measured as a function of Factor IXa concentration; and

forms a Xase complex that activates Factor X at a Vmax within about one, about one and one half, or about two standard deviations of the Vmax of a polypeptide consisting of said Factor VIII portion, wherein Vmax is measured as a function of Factor IXa concentration.

105. The method of any of claims 1-77, wherein said dose has a mean incremental recovery (K-Value) (activity; observed) greater that 1.38 IU/dL per IU/kg.

106. The method of any of claims 1-77 and 104, wherein said dose has a mean incremental recovery (K-Value) (activity; observed) of at least about 1.5, at least about 1.85, or at least about 2.46 IU/dL per IU/kg.

107. The method of any of claims 1-75 and 104-106, wherein said chimeric polypeptide exhibits one or more pharmacokinetic parameters, in said patient population or in said subject, selected from the group consisting of:

a mean clearance (CL) (activity) in said patient population of about 2.33 ± 1.08 mL/hour/kg or less;

a mean clearance (CL) (activity) in said patient population of about 1.8-2.69 mL/hour/kg;

a mean clearance (CL) (activity) in said patient population that is about 65% of the clearance of a polypeptide consisting of said Factor VIII portion;

a clearance (CL) (activity) in said subject of about 1.22 - 5.19 mL/hour/kg

a mean mean residence time (MRT) (activity) in said patient population of at least about 26.3 ± 8.33 hours;

a mean MRT (activity) in said patient population of about 25.9 - 26.5 hours;

a mean MRT (activity) in said patent population that is about 1.5 fold longer than the mean MRT of a polypeptide consisting of said Factor VIII portion;

a mean residence time (MRT) (activity) in said subject of about 14 – 41.3 hours;

a mean t1/2beta (activity) in said patient population of about 18.3 ± 5.79 hours;

a mean t1/2beta (activity)in said patient population that is about 18 - 18.4 hours;

a mean t1/2beta (activity) in said patient population that is about 1.5 fold longer than the mean t1/2beta of a polypeptide consisting of said Factor VIII portion;

a t1/2beta (activity) in said subject of about 11 - 26.4 hours;

a mean incremental recovery (K value) (activity; observed) in said patient population of about 2.01 ± 0.44 IU/dL per IU/kg;

a mean incremental recovery (K value) (activity; observed) in said patient population of about 1.85 - 2.46 IU/dL per IU/kg;

a mean incremental recovery (K value) (activity; observed) in said patient population that is about 90 % of the mean incremental recovery of a polypeptide consisting of said Factor VIII portion;

an incremental recovery (K value) (activity; observed) in said subject of about 1.38 - 2.88 IU/dL per IU/kg;

a mean Vss (activity) in said patient population of about 55.1 ± 12.3 mL/kg;

a mean Vss (activity) in said patient population of about 45.3 - 56.1 mL/kg;

a Vss (activity) in said subject of about 37.7 - 79.4 mL/kg;

a mean AUC/dose (activity) in said patient population of about 49.9 ± 18.2 IU*h/dL per IU/kg;

a mean AUC/dose (activity) in said patient population of about 44.8 - 57.6 IU*h/dL per IU/kg; and

an AUC/dose in said subject of about 19.2 - 81.7 IU*h/dL per IU/kg.

108. The method of any of claims 1-77 and 104-106, wherein said second portion is XTEN or albumin.

109. The method of any of claims 1-77 and 104-106, wherein the therapeutic dose is about 10 to about 150, 100-110, 110-120, 120-130, 130-140, 140-150, 110, 115, 120, 125, 130, 135, 140, 145, or 150 IU/kg.

110. The method of any of claims 1-77 and 104-106, wherein the dosing interval is one and one-half to 5, one and one-half, 2, 3, 4, or 5 days or longer.

WHAT IS CLAIMED IS:

1. An invention not claimed in any divisional application.