What is Claimed is:

1. A nucleic acid variant encoding Factor VIII (FVIII) having a B domain deletion, wherein the nucleic acid variant

(i) has no more than 2 cytosine-guanine dinucleotides (CpGs) and has 95% or greater sequence identity to the sequence of SEQ ID NO:7; or

(ii) has 98% or greater identity to the sequence of SEQ ID NO:7.

2. The nucleic acid variant of claim 1, wherein the nucleic acid variant has no more than 2 cytosine-guanine dinucleotides (CpGs) and has 96% or greater sequence identity to the sequence of SEQ ID NO:7.

3. The nucleic acid variant of claim 1, wherein the nucleic acid variant has no more than 2 cytosine-guanine dinucleotides (CpGs) and has 97% or greater sequence identity to the sequence of SEQ ID NO:7.

4. The nucleic acid variant of claim 1, wherein the nucleic acid variant has no more than 2 cytosine-guanine dinucleotides (CpGs) and has 98% or greater sequence identity to the sequence of SEQ ID NO:7.

5. The nucleic acid variant of claim 1, wherein the nucleic acid variant has 99% or greater sequence identity to the sequence of SEQ ID NO:7.

6. The nucleic acid variant of claim 1, wherein the nucleic acid variant has 20 or fewer, 15 or fewer, or 10 or fewer cytosine-guanine dinucleotides (CpGs) than the sequence of SEQ ID NO:19.

7. The nucleic acid variant of claim 1, wherein the nucleic acid variant has no more than 5 cytosine-guanine dinucleotides (CpGs).

8. The nucleic acid variant of claim 1, wherein the nucleic acid variant has 4, 3, 2, 1 or 0 cytosine-guanine dinucleotides (CpGs).

9. The nucleic acid variant of claim 1, wherein the nucleic acid variant has 0 cytosine-guanine dinucleotides (CpGs).

10. The nucleic acid variant of claim 1, wherein the nucleic acid variant encodes SEQ ID NO:25 having a deletion of one or more amino acids of the sequence SFSQNPPVLKRHQR (SEQ ID NO:29), or a deletion of the entire sequence SFSQNPPVLKRHQR.

11. The nucleic acid variant of claim 1, wherein the nucleic acid variant encodes SEQ ID NO:25.

12. The nucleic acid variant of claim 1, wherein said FVIII-BDD is mammalian.

13. A nucleic acid variant encoding human Factor VIII having a B domain deletion (hFVIII-BDD), wherein the nucleic acid variant has no more than 2 cytosine-guanine dinucleotides (CpGs) and has 98% or greater identity to the sequence of SEQ ID NO:7.

14. The nucleic acid variant of claim 1 or 13, wherein the nucleic acid variant has 1 cytosine-guanine dinucleotide (CpG).

15. The nucleic acid variant of claim 13, wherein the nucleic acid variant has no cytosine-guanine dinucleotides (CpGs).

16. The nucleic acid variant of any of claims 1-15, wherein the encoded FVIII-BDD or hFVIII-BDD is identical to hFVIII-BDD encoded by SEQ ID NO:19.

17. The nucleic acid variant of any of claims 1-16, wherein the nucleic acid variant is distinct from FVIII-V3 (SEQ ID NO:20) and CO3 (SEQ ID NO:21).

18. The nucleic acid variant of any of claims 1-17, wherein the nucleic acid variant encodes SEQ ID NO:25 having a deletion of one or more amino acids of the sequence SFSQNPPVLKRHQR (SEQ ID NO:29), or a deletion of the entire sequence SFSQNPPVLKRHQR.

19. The nucleic acid variant of any of claims 1-17, wherein the nucleic acid variant encodes SEQ ID NO:25.

20. A vector comprising the nucleic acid variant of any of claims 1-19.

21. An expression vector comprising the nucleic acid variant of any of claims 1-19.

22. The expression vector of claim 21, selected from the group consisting of an adenovirus-associated virus (AAV) vector, a retroviral vector, an adenoviral vector, a plasmid, or a lentiviral vector.

23. The expression vector of claim 22, wherein said AAV vector comprises an AAVserotype or an AAV pseudotype, wherein said AAV pseudotype comprise an AAV capsid serotype different from an ITR serotype.

24. The expression vector of 22 or 23, further comprising an intron, an expression control element, one or more adeno-associated virus (AAV) inverted terminal repeats (ITRs) and/or a filler polynucleotide sequence.

25. The expression vector of claim 24, wherein the intron is within or flanks the nucleic acid variant.

26. The expression vector of claim 24, wherein the expression control element is operably linked to the nucleic acid variant.

27. The expression vector of claim 24, wherein the AAV ITR(s) flanks the 5' or 3' terminus of the nucleic acid variant.

28. The expression vector of claim 24, wherein the filler polynucleotide sequence flanks the 5' or 3'terminus of the nucleic acid variant.

29. The expression vector of any of claims claim 24-28, wherein the intron, expression control element, one or more adeno-associated virus (AAV) inverted terminal repeats (ITRs) and/or a filler polynucleotide sequence has been modified to have reduced cytosine-guanine dinucleotides (CpGs).

30. The expression vector of any of claims claim 24-28, wherein the intron, expression control element, one or more adeno-associated virus (AAV) inverted terminal repeats (ITRs) and/or a filler polynucleotide sequence has been modified to have 20 or fewer, 15 or fewer, 10 or fewer, 5 or fewer or 0 cytosine-guanine dinucleotides (CpGs).

31. The expression vector of any of claims 24, 26, 29 and 30, wherein the expression control element comprises a constitutive or regulatable control element, or a tissue-specific expression control element or promoter.

32. The expression vector of any of claims 24, 26, 29 and 30, wherein the expression control element comprises an element that confers expression in liver.

33. The expression vector of any of claims 24, 26, 29 and 30, wherein the expression control element comprises a TTR promoter or mutant TTR promoter.

34. The expression vector of claim 33, wherein the mutant TTR promoter comprises SEQ ID NO:22.

35. The expression vector of any of claims claim 24-34, wherein the ITR comprises one or more ITRs of any of: AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, Rh10, Rh74 or AAV-2i8 AAV serotypes, or a combination thereof.

36. The expression vector of any of claims claim 23-29, wherein the vector comprises an ITR, a promoter, a polyA signal and/or intron sequence set forth in SEQ ID NO:23.

37. An AAV vector comprising the nucleic acid variant of any of claims 1-19 or the expression vector of any of claims 24-36.

38. The AAV vector of claim 37, wherein the AAV vector comprises a modified or variant AAV VP1, VP2 and/or VP3 capsid sequence, or wild-type AAV VP1, VP2 and/or VP3 capsid sequence.

39. The AAV vector of claim 37, wherein the AAV vector comprises a modified or variant AAV VP1, VP2 and/or VP3 capsid sequence having 90% or more identity to AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, Rh10, Rh74 or AAV-2i8 VP1, VP2 and/or VP3 sequences.

40. The AAV vector of claim 37, wherein the AAV vector comprises a VP1, VP2 or VP3 capsid sequence selected from any of: AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, Rh10, Rh74 or AAV-2i8 AAV serotypes.

41. The AAV vector of claim 37, wherein the AAV vector comprises a capsid having 90% or more sequence identity to LK03 capsid (SEQ ID NO:27).

42. The AAV vector of claim 37, wherein the AAV vector comprises a capsid having 90% or more sequence identity to SPK capsid (SEQ ID NO:28).

43. The AAV vector of claim 37, wherein the AAV vector comprises LK03 capsid (SEQ ID NO:27).

44. The AAV vector of claim 37, wherein the AAV vector comprises SPK capsid (SEQ ID NO:28).

45. The AAV vector of claim 37, wherein the AAV vector comprises the nucleic acid variant SEQ ID NO:7 and LK03 capsid sequence (SEQ ID NO:27).

46. The AAV vector of claim 37, wherein the AAV vector comprises the nucleic acid variant SEQ ID NO:7 and SPK capsid (SEQ ID NO:28).

47. The AAV vector of claim 37, wherein the AAV vector comprises the nucleic acid variant and one or more of a mutated TTR promoter (TTRmut), synthetic intron, poly A and ITR in SEQ ID NO:23.

48. The AAV vector of claim 37, wherein the AAV vector comprises the nucleic acid variant and one or more of a mutated TTR promoter (TTRmut), synthetic intron, poly A and ITR in SEQ ID NO:23 and LK03 capsid sequence (SEQ ID NO:27) or SPK capsid (SEQ ID NO:28).

49. A host cell comprising the nucleic acid variant of any of claims 1-19, or the vector or expression vector of any of claims 20-36.

50. The host cell of claim 49, said host cells expressing the FVIII encoded by said nucleic acid variant.

51. A host cell comprising the AAV vector of any of claims 37-48.

52. The host cell of claim 51, said host cells producing the AAV vector of any of claims 37-48.

53. A pharmaceutical composition comprising the nucleic acid variant of any of claims 1-19, the vector or expression vector of any of claims 20-36, or the AAV vector of any of claims 37-48 in a biologically compatible carrier or excipient.

54. The nucleic acid variant of any claims 1-19, the vector or expression vector of any of claims 20-36, or the AAV vector of any of claims 37-48 encapsulated in a liposome or mixed with phospholipids or micelles.

55. The pharmaceutical composition of claim 53 or 54, further comprising empty capsid AAV.

56. The pharmaceutical composition of claim 53 or 54, further comprising empty capsid of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11 and/or AAV-Rh74 serotype.

57. The pharmaceutical composition of claim 53 or 54, further comprising empty capsid AAV of the same serotype as the AAV vector administered.

58. The pharmaceutical composition of claim 53 or 54, wherein the empty capsid is LK03 capsid (SEQ ID NO:27) or SPK capsid (SEQ ID NO:28).

59. The pharmaceutical composition of any of claims 55-58, wherein the ratio of said empty capsids to said AAV vector is about 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, or 10:1.

60. An in-vitro method for delivering or transferring a nucleic acid sequence into a mammalian cell, comprising administering or contacting the nucleic acid variant of any of claims 1-19, vector or expression vector of any of claims 20-36, or the AAV vector of any of claims 37-48 to said mammalian cell, thereby delivering or transferring the nucleic acid sequence into the mammalian cell.

61. The nucleic acid variant of any of claims 1-19, vector or expression vector of any of claims 20-36, or the AAV vector of any of claims 37-48 for use in therapy.

62. The nucleic acid variant of any of claims 1-19, vector or expression vector of any of claims 20-36, or AAV vector of any of claims 37-48 for use in the treatment of a mammal in need of Factor VIII.

63. Use of the nucleic acid variant of any of claims 1-19, vector or expression vector of any of claims 20-36, or AAV vector of any of claims 37-48 in the manufacture of a medicament for the treatment of a mammal for hemophilia A.

64. The nucleic acid variant, vector or expression vector, or AAV vector of claim 62, or the use of claim 63, wherein said Factor VIII encoded by the nucleic acid variant is expressed in a cell, tissue or organ of said mammal.

65. The nucleic acid variant, vector or expression vector, or AAV vector, or the use of claim 64, wherein, the cell comprises a secretory cell.

66. The nucleic acid variant, vector or expression vector, or AAV vector, or the use of claim 64, wherein the cell comprises an endocrine cell or an endothelial cell.

67. The nucleic acid variant, vector or expression vector, or AAV vector, or the use of claim 64, wherein the cell comprises a hepatocyte, a sinusoidal endothelial cell, a megakaryocyte, a platelet or hematopoetic stem cell.

68. The nucleic acid variant, vector or expression vector, or AAV vector, or the use of claim 64, wherein the tissue or organ of said mammal comprises liver.

69. The nucleic acid variant, vector or expression vector, or AAV vector, or the use of any of claims 62-68, wherein the mammal produces an insufficient amount of Factor VIII protein for blood clotting, or a defective or aberrant Factor VIII protein.

70. The nucleic acid variant, vector or expression vector, or AAV vector, or the use of any of claims 62-68, wherein the mammal has hemophilia A.

71. The nucleic acid variant, vector or expression vector, or AAV vector, or the use of any of claims 62-68, wherein the Factor VIII encoded by the nucleic acid variant is expressed at levels that provide increased blood clotting in the mammal.

72. The nucleic acid variant of any of claims 1-19, vector or expression vector of any of claims 20-36, or the AAV vector of any of claims 37-48 for use in the treatment of a hemostasis related disorder in a patient in need thereof.

73. Use of the nucleic acid variant of any of claims 1-19, vector or expression vector of any of claims 20-36, or the AAV vector of any of claims 37-48 in the manufacture of a medicament for the treatment of a hemostasis related disorder in a patient in need thereof.

74. The nucleic acid variant or vector or expression vector or AAV vector of claim 62 or 72, or the use of claim 63 or 73, wherein said mammal or said patient has a disorder selected from the group consisting of hemophilia A, von Willebrand diseases and bleeding associated with trauma, injury, thrombosis, thrombocytopenia, stroke, coagulopathy, disseminated intravascular coagulation (DIC) and over-anticoagulation treatment disorders.

75. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein the nucleic acid variant, vector or expression vector, or the AAV vector, or the medicament is to be administered to said mammal or said patient intravenously, intraarterially, intramuscularly, subcutaneously, intra-cavity, or by intubation, or via catheter.

76. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein FVIII is expressed at levels without substantially increasing risk of thrombosis.

77. The nucleic acid variant or vector or expression vector or AAV vector or the use of claim 76, wherein said thrombosis risk is determined by measuring fibrin degradation products.

78. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein FVIII is expressed at levels greater than 1% of the levels of FVIII found in a subject that does not have hemophilia A.

79. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein FVIII is expressed at levels greater than 3% of the levels of FVIII found in a subject that does not have hemophilia A.

80. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein activity of FVIII is detectable for at least 1, 2, 3 or 4 weeks, or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 months, or at least 1 year.

81. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein FVIII is expressed at levels greater than 1% or 3% of the levels of FVIII found in a subject that does not have hemophilia A for at least 1, 2, 3 or 4 weeks, or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11 months, or at least 1 year.

82. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein FVIII is expressed at levels having a therapeutic effect for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 days, weeks or months.

83. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein said FVIII is present in the mammal or patient at levels of about 20% FVIII activity or greater than 20% activity for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 continuous days, weeks or months.

84. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein said FVIII is expressed at levels at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 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%, or 50% of normal FVIII levels.

85. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein the AAV vector is to be administered at a dose of less than $1x10^{12}$ vector genomes per kilogram (vg/kg) of the mammal or patient, and said FVIII is produced in the mammal or patient at levels of about 20% activity or greater than 20% activity for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 continuous days, weeks or months

86. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-74, wherein the AAV vector is to be administered at a dose of about $5x10^{11}$ vector genomes per kilogram (vg/kg) of the mammal or patient, and said FVIII is produced in the mammal or patient at levels of about 20% activity or greater than 20% activity for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 continuous days, weeks or months.

87. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-86, wherein said mammal or said patient is human.

88. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-86, wherein said mammal, said patient or said human is sero-positive or sero-negative for AAV.

89. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-88, wherein the treatment further comprises AAV empty capsid to be administered to said mammal or said patient.

90. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-88, wherein the treatment further comprises empty capsid of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11 and/or AAV-Rh74 serotype.

91. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-88, further wherein the treatment further comprises empty capsid AAV of the same serotype as the AAV vector to be administered.

92. The nucleic acid variant or vector or expression vector or AAV vector or the use of claim 91, wherein the empty capsid is LK03 capsid (SEQ ID NO:27) or SPK capsid (SEQ ID NO:28).

93. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 89-92, wherein the ratio of said empty capsids to said AAV vector is about 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, or 10:1.

94. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-93, wherein the treatment further comprises an immunosuppressive agent.

95. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-93, wherein the treatment further comprises an immunosuppressive agent to be administered after the AAV vector is administered.

96. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-93, wherein the treatment further comprises an immunosuppressive agent to be administered from a time period within 1 hour to up to 45 days after the AAV vector is administered.

97. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 94-96, wherein the immunosuppressive agent comprises a steroid, cyclosporine (e.g., cyclosporine A), mycophenolate, Rituximab or a derivative thereof.

98. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-97, wherein the AAV vector is to be administered in a range from about $1X10^{8}$ to about $1X10^{14}$ vector genomes per kilogram (vg/kg) of the weight of the mammal or patient.

99. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-97, wherein the AAV vector is to be administered in a range from about $1X10^{9}$ to about $1X10^{13}$ vector genomes per kilogram (vg/kg) of the weight of the mammal or patient.

100. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-97, wherein the AAV vector is to be administered in a range from about $1X10^{10}$ to about $1X10^{12}$ vector genomes per kilogram (vg/kg) of the weight of the mammal or patient.

101. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-97, wherein the AAV vector is to be administered in a range from about $1X10^{11}$ to about $1X10^{12}$ vector genomes per kilogram (vg/kg) of the weight of the mammal or patient.

102. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-97, wherein the AAV vector is to be administered in a range from about $1X10^{12}$ to about $1X10^{13}$ vector genomes per kilogram (vg/kg) of the weight of the mammal or patient.

103. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-97, wherein the AAV vector is to be administered in a range from about $1X10^{13}$ to about $1X10^{14}$ vector genomes per kilogram (vg/kg) of the weight of the mammal or patient.

104. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-97, wherein the AAV vector is to be administered in a range from about $5X10^{11}$ to about $1X10^{12}$ vector genomes per kilogram (vg/kg) of the weight of the mammal or patient.

105. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-97, wherein the AAV vector is to be administered at a dose of about $5X10^{11}$ vector genomes per kilogram (vg/kg) of the weight of the mammal or patient.

106. The nucleic acid variant or vector or expression vector or AAV vector or the use of any of claims 62-105, wherein the treatment further comprises analyzing or monitoring the mammal for the presence or amount of AAV antibodies, an immune response against AAV, FVIII antibodies, an immune response against FVIII, FVIII amounts, FVIII activity level, amounts or levels of one or more liver enzymes or frequency, and/or severity or duration of bleeding episodes.

107. A method of producing FVIII protein comprising expressing in a cell the nucleic acid variant as claimed in any of claims 1-19, or the vector or expression vector of any of claims 20-36, and recovering said FVIII protein produced by the cells.

108. The method of claim 107, further comprising purifying or isolating said FVIII protein produced by the cells.