What is Claimed is:

1. Use of a recombinant adeno-associated virus (rAAV) vector in the preparation of a medicament for the treatment of hemophilia A in a human, wherein the vector genome comprises a nucleic acid variant encoding Factor VIII (FVIII) having a B domain deletion (hFVIII-BDD), wherein the nucleic acid variant ~~has 95% or greater identity to~~ comprises SEQ ID NO:7, wherein the dose of rAAV vector to be administered to the human is $1x10^{11}$ to $5x10^{12}$ vector genomes per kilogram (vg/kg) inclusive, and wherein the human does not exhibit spontaneous bleeds for at least 1 year after the medicament is to be administered to the human.

2. Use of a recombinant adeno-associated virus (rAAV) vector in the preparation of a medicament for the treatment of hemophilia A in a human, wherein the vector genome comprises a nucleic acid variant encoding Factor VIII (FVIII) having a B domain deletion (hFVIII-BDD), wherein the nucleic acid variant has 98% or greater identity to SEQ ID NO:7 and no more than 2 cytosine-guanine dinucleotides (CpGs), wherein the dose of rAAV vector to be administered to the human is $1x10^{11}$ to $5x10^{12}$ vector genomes per kilogram (vg/kg) inclusive, and wherein the human does not exhibit spontaneous bleeds for at least 1 year after the medicament is to be administered to the human.

3. Use of a recombinant adeno-associated virus (rAAV) vector in the preparation of a medicament for the treatment of hemophilia A in the human, wherein the vector genome comprises a nucleic acid variant encoding ~~Factor VIII (FVIII) or encoding~~ Factor VIII (FVIII) having a B domain deletion (hFVIII-BDD), wherein the nucleic acid variant has 98% or greater identity to SEQ ID NO:7, wherein the dose of rAAV vector to be administered to the human is ~~less than $6x10^{12}$~~ between $1x10^{11}$ to $5x10^{12}$ vector genomes per kilogram (vg/kg) inclusive, and wherein the human does not exhibit spontaneous bleeds for at least 1 year after the medicament is to be administered to the human.

4. The use of any of claims 1-3, ~~or 2, or 3~~ wherein the dose of rAAV vector to be administered to the human is between ~~$1x10^{9}$ to $1x10^{14}$~~ $5x10^{11}$ to $5x10^{12}$ vg/kg, inclusive.

5 The use of any of claims 1-3, ~~or 2, or 3~~ wherein the dose of rAAV vector to be administered to the human is between ~~$3x10^{11}$ to $7x10^{12}$~~ $5x10^{11}$ to $2x10^{12}$ vg/kg, inclusive.

6. The use of any of claims 1-5, wherein the amount of ~~FVIII or~~ hFVIII-BDD expressed in the human, as reflected by clotting activity, is greater than predicted based upon data obtained from non-human primate studies administered the rAAV vector.

7. The use of any of claims 1-6, wherein the amount of ~~FVIII or~~ hFVIII-BDD expressed in the human, as reflected by clotting activity, is 1-4 fold greater than predicted expression based upon a liner regression curve derived from non-human primate studies administered the rAAV vector.

8. The use of any of claims 1-7, wherein the amount of ~~FVIII or~~ hFVIII-BDD expressed in the human, as reflected by clotting activity, is ~~about~~ 3% or greater at 14 or more days after rAAV vector administration, is ~~about~~ 4% or greater at 21 or more days after rAAV vector administration, is ~~about~~ 5% or greater at 21 or more days after rAAV vector administration, is ~~about~~ 6% or greater at 21 or more days after rAAV vector administration, is ~~about~~ 7% or greater at 21 or more days after rAAV vector administration, is ~~about~~ 8% or greater at 28 or more days after rAAV vector administration, is ~~about~~ 9% or greater at 28 or more days after rAAV vector administration, is ~~about~~ 10% or greater at 35 or more days after rAAV vector administration, is ~~about~~ 11% or greater at 35 or more days after rAAV vector administration, is ~~about~~ 12% or greater at 35 or more days after rAAV vector administration.

9. The use of any of claims 1-7, wherein the amount of ~~FVIII or~~ hFVIII-BDD expressed in the human, as reflected by clotting activity, averages ~~about~~ 10% or greater over a continuous 14 day period.

10. The use of any of claims 1, 2 and 4-9, wherein ~~the rAAV vector is to be administered at a dose of between $1x10^{9}$ to $1x10^{14}$ vg/kg inclusive to the human, and~~ said ~~FVIII or~~ hFVIII-BDD is produced in the human at levels averaging 12% to 100% activity for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 continuous days, weeks or months after rAAV vector administration.

11. The use of any of claims 1-10, wherein the ~~FVIII or~~ hFVIII-BDD is produced in the human at a steady state wherein activity does not vary by more than 5-50% over 4, 6, 8 or 12 weeks or months.

12. The use of any of claims 1-10, wherein the ~~FVIII or~~ hFVIII-BDD is produced in the human at a steady state wherein activity does not vary by more than 25-100% over 4, 6, 8 or 12 weeks or months.

13. The use of any of claims 1-12, wherein AAV antibodies in the human are not detected prior to rAAV vector administration or wherein said human is sero-negative for AAV.

14. The use of any of claims 1-12, wherein AAV antibodies in the human are at or less than 1:5 prior to rAAV vector administration.

15. The use of any of claims 1-14, wherein said human does not produce a cell mediated immune response against the rAAV vector for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 continuous weeks or months after rAAV vector administration.

16. The use of any of claims 1-15, wherein the human does not develop a humoral immune response against the rAAV vector sufficient to decrease or block the ~~FVIII or~~ hFVIII-BDD therapeutic effect.

17. The use of any of claims 1-16, wherein the human does not produce detectable antibodies against the rAAV vector for at least ~~about~~ 1, 2, 3, 4, 5 or 6 months after rAAV vector administration.

18. The use of any of claims 1-17, wherein an immunosuppressive agent is to be further administered; or wherein an immunosuppressive agent is to be further administered after the rAAV vector is administered.

19. The use of any of claims ~~1~~2-18, wherein the ~~nucleic acid or~~ nucleic acid variant has ~~96%~~99% -100% sequence identity to SEQ ID NO:7.

20. The use of any of claims 1-19, wherein the ~~nucleic acid or~~ nucleic acid variant has ~~20 or fewer, 15 or fewer, or 10 or fewer~~ 0 cytosine-guanine dinucleotides (CpGs).

21. The use of any of claims ~~1~~3-19, wherein the ~~nucleic acid or~~ nucleic acid variant has no more than 5 cytosine-guanine dinucleotides (CpGs).

22. The use of any of claims ~~1~~3-19, wherein the ~~nucleic acid or~~ nucleic acid variant has 4, 3, 2, or 1 ~~or 0~~ cytosine-guanine dinucleotides (CpGs).

23. The use of any of claims ~~1~~2-19, wherein the~~n~~ ~~nucleic acid or~~ nucleic acid variant has 1 cytosine-guanine dinucleotide (CpG).

24. The use of any of claims 1-23, wherein the ~~nucleic acid or~~ 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~~.

25. The use of any of claims 1-23, wherein the ~~nucleic acid or~~ nucleic acid variant encodes SEQ ID NO:25.

26. The use of any of claims 1-23, wherein the hFVIII-BDD is identical to hFVIII-BDD encoded by SEQ ID NO:19.

27. The use of any of claims 1-26, wherein said rAAV vector comprises an AAV serotype or an AAV pseudotype, wherein said AAV pseudotype comprise an AAV capsid serotype different from an inverted terminal repeat (ITR) serotype.

28. The use of any of claims 1-27, wherein the vector genome further comprises ~~an intron,~~ an expression control element, one or more adeno-associated virus (AAV) inverted terminal repeats (ITRs) and/or a filler polynucleotide sequence.

29. The use of claim 28, wherein the ~~intron is within or flanks the nucleic acid variant; or wherein the~~ expression control element is operably linked to the nucleic acid variant; or wherein the AAV ITR(s) flanks the 5' or 3' terminus of the nucleic acid variant; or wherein the filler polynucleotide sequence flanks the 5' or 3'terminus of the nucleic acid variant.

30. The use of claim 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); ~~or wherein the expression control element comprises a constitutive or regulatable control element, or a tissue-specific expression control element or promoter;~~ or wherein the expression control element comprises an element that confers expression in liver; or wherein the expression control element comprises a TTR promoter or mutant TTR promoter, wherein the mutant TTR promoter comprises SEQ ID NO:22.

31. The use of claim 30, 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 AAV12~~ AAV serotype~~s, or a combination thereof~~.

32. The use of any of claims 1-31, wherein the vector genome comprises an ITR, a promoter, and/or a polyA signal ~~and/or intron~~ sequence set forth in SEQ ID NO:23.

33. The use of any of claims 1-32, wherein the rAAV 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.

34. The use of any of claims 1-33, wherein the rAAV 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, AAV12 or AAV-2i8 VP1, VP2 and/or VP3 sequences.

35. The use of any of claims 1-33, wherein the rAAV 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, AAV12 or AAV-2i8 AAV serotypes.

36. The use of any of claims 1-32, wherein the rAAV vector comprises a capsid having 90% or more sequence identity to LK03 capsid (SEQ ID NO:27); or wherein the rAAV vector comprises a capsid having 90% or more sequence identity to SPK capsid (SEQ ID NO:28); or wherein the rAAV vector comprises LK03 capsid (SEQ ID NO:27); or wherein the rAAV vector comprises SPK capsid (SEQ ID NO:28); or wherein the rAAV vector comprises the nucleic acid variant SEQ ID NO:7 and LK03 capsid sequence (SEQ ID NO:27); or wherein the rAAV vector comprises the nucleic acid variant SEQ ID NO:7 and SPK capsid (SEQ ID NO:28).

37. The use of any of claims 1-36, wherein the rAAV 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; or wherein the rAAV 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).

38. The use of any of claims 1-37, wherein the rAAV vector is comprised in a pharmaceutical composition ~~comprises the rAAV vector~~.

39. The use of claim 38, wherein the pharmaceutical composition comprises a biologically compatible carrier or excipient.

40. The use of any of claims 1-39, wherein empty capsid AAV is to be further administered, wherein the empty capsid AAV is to be administered with the rAAV vector.

41. The use of any of claims 1-39, wherein empty capsid of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12 and/or AAV-Rh74 serotype is to be further administered; or wherein empty capsid AAV of the same serotype as the AAV vector administered is to be further administered; or wherein empty capsid having an LK03 capsid (SEQ ID NO:27) or an SPK capsid (SEQ ID NO:28) is to be further administered.

42. The use of any of claims 40-41, wherein the ratio of said empty capsids to said rAAV vector is between 2:1 to 50:1.

43. The use of any of claims 1-42, wherein the ~~FVIII or~~ hFVIII-BDD encoded by the nucleic acid variant is expressed in a cell, tissue or organ of said ~~mammal~~ human.

44. The use of claim 43, wherein the cell comprises a secretory cell; or wherein the tissue or organ of said ~~mammal~~ human comprises liver.

45. The use of any of claims 1-44, wherein the rAAV vector is to be delivered to said human intravenously, intraarterially, intramuscularly, subcutaneously, intra-cavity, or by intubation, or via catheter.

46. The use of any of claims 1-45, wherein the ~~FVIII or~~ hFVIII-BDD is expressed at levels without increasing risk of thrombosis after the medicament is to be administered to the human.

47. The use of any of claims 1-46, wherein activity of the ~~FVIII or~~ hFVIII-BDD 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 after the medicament is to be administered to the human.

48. The use of any of claims 1-47, wherein the human does not require FVIII protein prophylaxis 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 after the medicament is to be administered to the human.

49. The use of any of claims 1-48, further comprising analyzing or monitoring the human for the presence or amount of AAV antibodies, an immune response ~~repsonse~~ against AAV, FVIII or hFVIII-BDD antibodies, an immune response against FVIII or hFVIII-BDD, FVIII or hFVIII-BDD amounts, FVIII or hFVIII-BDD activity, amounts or levels of one or more liver enzymes or frequency, and/or severity or duration of bleeding episodes.