WHAT IS CLAIMED IS:

1. A nucleic acid composition, comprising a Factor IX polynucleotide encoding a Factor IX protein, said Factor IX polynucleotide comprising a nucleic acid sequence that is at least 99% identical to the nucleic acid sequence of CS06-MP-NA (SEQ ID NO:17).

2. The nucleic acid composition of claim 1, wherein the Factor IX polynucleotide has no more than 10 CpG dinucleotides.

3. The nucleic acid composition of claim 1, wherein the Factor IX polynucleotide has no more than 3 CpG dinucleotides.

4. The nucleic acid composition of claim 1, wherein the Factor IX polynucleotide comprises the nucleic acid sequence of CS06-MP-NA (SEQ ID NO:17).

5. The nucleic acid composition according to any one of claims 1-4, wherein the Factor IX polynucleotide encodes for leucine at the amino acid position corresponding to residue 384 of the full-length wild type Factor IX polypeptide (SEQ ID NO:2), which is an arginine in the wild type Factor IX polypeptide.

6. The nucleic acid composition according to any one of claims 1-5, wherein the Factor IX protein encoded by the Factor IX polynucleotide has from 1 to 10 amino acid substitutions as compared to FIXp-MP-AA (SEQ ID NO:12).

7. The nucleic acid composition according to any one of claims 1-5, wherein the Factor IX protein encoded by the Factor IX polynucleotide has the amino acid sequence of FIXp-MP-AA (SEQ ID NO:12).

8. The nucleic acid composition according to any one of claims 1-7, wherein the Factor IX polynucleotide further comprises a pre-pro-leader polynucleotide encoding a pre-pro-

leader peptide, said pre-pro-leader peptide comprising the amino acid sequence of FIX-PPP-AA (SEQ ID NO:36).

9. The nucleic acid composition of claim 8, wherein the pre-pro-leader polynucleotide has the nucleic acid sequence of CS06-PPP-NA (SEQ ID NO:23).

10. The nucleic acid composition according to any one of claims 1-9, wherein the Factor IX polynucleotide has a nucleic acid sequence that is at least 99% identical to the nucleic acid sequence of CS06-FL-NA (SEQ ID NO:9).

11. The nucleic acid composition according to any one of claims 1-9, wherein the Factor IX polynucleotide has the nucleic acid sequence of CS06-FL-NA (SEQ ID NO:9).

12. The nucleic acid composition according to any one of claims 1-11, further comprising a liver-specific promoter element operably linked to the Factor IX polynucleotide.

13. The nucleic acid composition of claim 12, wherein the liver-specific promoter element comprises one copy of a promoter polynucleotide, said promoter polynucleotide comprising a nucleic acid sequence that is at least 95% identical to CRM8 (SEQ ID NO:39).

14. The nucleic acid composition of claim 12, wherein the liver-specific promoter element comprises three copies of a promoter polynucleotide, said promoter polynucleotide comprising a nucleic acid sequence that is at least 95% identical to CRM8 (SEQ ID NO:39).

15. The nucleic acid composition of claim 13 or 14, wherein said promoter polynucleotide comprises the nucleic acid sequence of CRM8 (SEQ ID NO:39).

16. The nucleic acid composition according to any one of claims 1-11, further comprising an intron operatively linked to the Factor IX polynucleotide.

17. The nucleic acid composition of claim 16, wherein the intron comprises an MVM intron polynucleotide comprising a nucleic acid sequence that is at least 95% identical to MVMI (SEQ ID NO:53).

18. The nucleic acid composition of claim 17, wherein said MVM intron polynucleotide comprises the nucleic acid sequence of MVMI (SEQ ID NO:53).

19. The nucleic acid composition according to any one of claims 16-18, wherein said intron is positioned between a promoter element and the translation initiation site of the nucleotide sequence encoding a Factor IX polypeptide.

20. The nucleic acid composition of claim 1, comprising the nucleic acid sequence of CS06-CRM8.3-ssV (SEQ ID NO:40).

21. The nucleic acid composition according to any one of claims 1-20, wherein said composition is integrated into a mammalian gene therapy vector.

22. The nucleic acid composition of claim 21, wherein the mammalian gene therapy vector is an adeno-associated virus (AAV) vector.

23. The nucleic acid composition of claim 22, wherein said adeno-associated virus vector is a serotype 8 adeno-associated virus (AAV-8) vector.

24. The nucleic acid composition according to any one of claims 21-23, wherein the mammalian gene therapy vector comprises a single-stranded polynucleotide encoding the Factor IX protein.

25. A nucleic acid composition according to any one of claims 1-24 for use as a medicament for treating hemophilia B.

26. Use of a nucleic acid composition according to any one of claims 1-24 for the manufacture of a medicament for the treatment of hemophilia B.

27. An *in vitro* method for producing an adeno-associated virus (AAV) particle comprising introducing a nucleic acid composition according to any one of claims 1-24 into a mammalian host cell, wherein the nucleic acid composition is competent for replication in the mammalian host cell.