CLAIMS:

1. A method of expressing Factor IX in a cell or population of cells, comprising administering:

i) a nucleic acid construct comprising a Factor IX protein coding sequence;

ii) an RNA-guided DNA binding agent; and

iii) a guide RNA (gRNA) comprising the sequence of SEQ ID NO: 8,

thereby expressing Factor IX in a cell or population of cells.

2. The method of claim 1, wherein the RNA-guided DNA binding agent is a Cas9 or a nucleic acid encoding a Cas9.

3. The method of claim 1, wherein the RNA-guided DNA binding agent is a nucleic acid encoding the RNA-guided DNA binding agent, and wherein the nucleic acid encoding the RNA-guided DNA binding agent is an mRNA.

4. The method of claim 1, wherein the nucleic acid construct and/or the gRNA is administered as a nucleic acid vector, and wherein the nucleic acid vector is a viral vector.

5. The method of claim 4, wherein the viral vector is selected from the group consisting of an adeno associate viral (AAV) vector, adenovirus vector, retrovirus vector, and lentivirus vector.

6. The method of claim 1, wherein the nucleic acid construct encodes a Factor IX protein having a mutation R338L.

7. A composition for use in expressing Factor IX in a cell, wherein the composition comprises:

i) a nucleic acid construct comprising a Factor IX protein coding sequence;

ii) an RNA-guided DNA binding agent; and

iii) a guide RNA (gRNA) comprising the sequence of SEQ ID NO: 8.

8. The composition of claim 7, wherein the RNA-guided DNA binding agent is a Cas nuclease or a nucleic acid encoding a Cas nuclease.

9. The composition of claim 8, wherein the Cas nuclease is an *S. pyogenes* Cas9 nuclease or variant thereof.

10. Use of:

i) a nucleic acid construct comprising a Factor IX protein coding sequence;

ii) an RNA-guided DNA binding agent; and

iii) a guide RNA (gRNA) comprising the sequence of SEQ ID NO: 8,

in the manufacture of a medicament for treating a Factor IX deficiency in an individual with the Factor IX deficiency,

wherein the medicament is to be administered to the individual thereby expressing the Factor IX protein in the individual.

11. The method of claim 1, wherein the gRNA comprises the sequence of SEQ ID NO: 40.

12. The method of claim 1, wherein the gRNA comprises the sequence of:

mU*mA*mA*AGCAUAGUGCAAUGGAUGUUUUAGAmGmCmUmAmGmAmA
mAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm
GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGm
CmU*mU*mU*mU (SEQ ID NO: 72),

wherein “mA,” “mC,” “mU,” and “mG” represent nucleotides that have been substituted with 2′-O-Me and * indicates a phosphorothioate (PS) bond.

13. The composition of claim 7, wherein the gRNA comprises the sequence of SEQ ID NO: 40.

14. The composition of claim 7, wherein the gRNA comprises the sequence of:

mU*mA*mA*AGCAUAGUGCAAUGGAUGUUUUAGAmGmCmUmAmGmAmA
mAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm
GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGm
CmU*mU*mU*mU (SEQ ID NO: 72),

wherein “mA,” “mC,” “mU,” and “mG” represent nucleotides that have been substituted with 2′-O-Me and * indicates a phosphorothioate (PS) bond.

15. The use of claim 10, wherein the gRNA comprises the sequence of SEQ ID NO: 40.

16. The use of claim 10, wherein the gRNA comprises the sequence of:
mU*mA*mA*AGCAUAGUGCAAUGGAUGUUUUAGAmGmCmUmAmGmAmA
mAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm
GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGm
CmU*mU*mU*mU (SEQ ID NO: 72),
wherein “mA,” “mC,” “mU,” and “mG” represent nucleotides that have been substituted with 2′-O-Me and * indicates a phosphorothioate (PS) bond.

17. A composition comprising:
i) a nucleic acid construct comprising a Factor IX protein coding sequence;
ii) an RNA-guided DNA binding agent; and
iii) a guide RNA (gRNA) comprising the sequence of SEQ ID NO: 8,
for use in therapy.

18. The composition for use of claim 17, wherein the gRNA comprises the sequence of SEQ ID NO: 40.

19. The composition for use of claim 17, wherein the gRNA comprises the sequence of:
mU*mA*mA*AGCAUAGUGCAAUGGAUGUUUUAGAmGmCmUmAmGmAmA
mAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm
GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGm
CmU*mU*mU*mU (SEQ ID NO: 72),
wherein “mA,” “mC,” “mU,” and “mG” represent nucleotides that have been substituted with 2′-O-Me and * indicates a phosphorothioate (PS) bond.