CLAIMS:

1. A Factor IX (FIX) fusion protein comprising a R338L FIX (Padua) variant polypeptide and an XTEN that is inserted within the FIX variant polypeptide, wherein the FIX fusion protein comprises the amino acid sequence of SEQ ID NO: 2 with the XTEN inserted at an insertion site selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 2, and any combination thereof, wherein the FIX fusion protein exhibits procoagulant activity, and wherein the FIX fusion protein is capable of exhibiting at least a 1.5 fold greater in vivo half-life when compared to a R338L FIX (Padua) variant polypeptide lacking said XTEN insertion.

2. The FIX fusion protein of claim 1, wherein the insertion site corresponds to an amino acid selected from the group consisting of amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2 and any combination thereof.

3. The FIX fusion protein of claim 1, wherein the XTEN comprises at least 36 amino acids.

4. The FIX fusion protein of claim 1, which further comprises a second XTEN.

5. The FIX fusion protein of claim 1, wherein the XTEN is inserted within the FIX polypeptide at an insertion site corresponding to amino acid 166 of SEQ ID NO: 2.

6. The FIX fusion protein of claim 1, further comprising a first Fc domain.

7. The FIX fusion protein of claim 6, comprising a second Fc domain.

8. The FIX fusion protein of claim 7, which comprises two polypeptide chains, wherein (i) the first polypeptide chain comprises the first Fc domain fused to the N-terminus or C-terminus of the FIX polypeptide comprising the XTEN, and (ii) the second polypeptide chain comprises the second Fc domain, wherein the first Fc domain and the second Fc domain are associated by a covalent bond, wherein the covalent bond is a disulfide bond.

9. The FIX fusion protein of claim 1, wherein the XTEN comprises 76 amino acids.

10. The FIX fusion protein of claim 9, wherein the XTEN is inserted within the FIX polypeptide at an insertion site corresponding to amino acid 166 of SEQ ID NO: 2.

11. The FIX fusion protein of claim 1, comprising an amino acid sequence having at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 227.

12. The FIX fusion protein of claim 1, wherein the FIX fusion protein is capable of exhibiting at least a 2-fold greater in vivo half-life as compared to a R388L FIX polypeptide lacking said XTEN insertion.

13. The FIX fusion protein of claim 1, wherein the FIX fusion protein is capable of exhibiting at least a 3-fold greater in vivo half-life as compared to a R388L FIX polypeptide lacking said XTEN insertion.

14. The FIX fusion protein of claim 1, wherein the in vivo half-life is measured following intravenous (IV) administration of a single bolus injection of 200 IU/kg of the FIX fusion protein to Factor IX deficient mice.

15. A Factor IX (FIX) fusion protein comprising a first polypeptide chain and a second polypeptide chain, wherein: a) the first polypeptide chain comprises: i) a R338L FIX (Padua) variant polypeptide and an XTEN that is inserted within the FIX variant polypeptide, wherein the FIX fusion protein comprises the FIX polypeptide amino acid sequence of SEQ ID NO: 2 with the XTEN inserted at amino acid 166 of SEQ ID NO: 2, and wherein the XTEN comprises an amino acid sequence having 76 amino acids; and ii) a first Fc domain, wherein the first Fc domain is fused to the FIX variant polypeptide comprising the XTEN; and b) the second polypeptide chain comprises a second Fc domain; wherein the first Fc domain and the second Fc domain are associated by a covalent bond, wherein the covalent bond is a disulfide bond; wherein the FIX fusion protein exhibits procoagulant activity, and wherein the FIX fusion protein is capable of exhibiting at least a 1.5 fold greater in vivo half-life when compared to a R338L FIX (Padua) variant polypeptide lacking said XTEN insertion.

16. The FIX fusion protein of claim 15, wherein the first polypeptide chain comprises an amino acid sequence having at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 227.

17. The FIX fusion protein of claim 15, wherein the second polypeptide chain comprises an amino acid sequence having at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 228.

18. The FIX fusion protein of claim 15, wherein the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 227, without the signal peptide and without the pro-peptide (amino acids 1-46), and wherein the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 228.

19. The FIX fusion protein of claim 15, wherein the FIX fusion protein is capable of exhibiting at least a 2-fold greater in vivo half-life as compared to a R388L FIX polypeptide lacking said XTEN insertion.

20. The FIX fusion protein of claim 15, wherein the FIX fusion protein is capable of exhibiting at least a 3-fold greater in vivo half-life as compared to a R388L FIX polypeptide lacking said XTEN insertion.

21. The FIX fusion protein of claim 15, wherein the in vivo half-life is measured following intravenous (IV) administration of a single bolus injection of 200 IU/kg of the FIX fusion protein to Factor IX deficient mice.

22. A Factor IX (FIX) fusion protein comprising a first polypeptide chain and a second polypeptide chain, wherein the first polypeptide chain comprises FIX fusion protein comprising R338L FIX (Padua) variant and an XTEN that is inserted within the FIX variant polypeptide and Fc domain, said first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 227, without the signal peptide and without the pro-peptide (amino acids 1-46), and wherein the second polypeptide chain comprises an Fc domain, said second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 228.

23. A composition comprising the FIX fusion protein of claim 1 and a pharmaceutically acceptable carrier.

24. An isolated polynucleotide comprising a sequence encoding the FIX fusion protein of claim 1.

25. An expression vector comprising the polynucleotide of claim 24.

26. A host cell comprising the polynucleotide of claim 24.

27. The FIX fusion protein of claim 1 for use in preventing, treating, ameliorating, or managing hemophilia B in a patient in need thereof.