CLAIMS

What is claimed is:

1. A fusion protein for treatment of companion animals, comprising a proinsulin and serum albumin, wherein the proinsulin is a canine proinsulin or a feline proinsulin.

2. The fusion protein of claim 1, wherein proinsulin is canine proinsulin.

3. The fusion protein of claim 2, wherein the canine pro insulin sequence shares at least 80%, at least 85%, at least 90%, at least 95%, at least 99%, or 100% identity SEQ ID NO: 12.

4. The fusion protein of claim 1, wherein proinsulin is feline proinsulin.

5. The fusion protein of claim 4, wherein feline proinsulin sequence shares at least 80%, at least 85%, at least 90%, at least 95%, at least 99%, or 100% identity SEQ ID NO: 15.

6. The fusion protein of claim 1 or claim 2, wherein the fusion protein comprises a polypeptide that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 99%, or 100% identity to SEQ ID NO: 1.

7. The fusion protein of any one of claims 1 to 6, wherein the fusion protein comprises an N-terminal signal peptide.

8. The fusion protein of claim 7, wherein the signal peptide is a canine insulin signal peptide.

9. The fusion protein of claim 7 or claim 8, wherein the signal peptide comprises the sequence that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 99%, or 100% identity to MALWMRLLPLLALLALWAPAPTRA (SEQ ID NO: 7).

10. The fusion protein of any one of claims 1 to 3 or 6 to 9, wherein the canine proinsulin is a canine proinsulin variant having a mutation at one or more cleavage sites compared to a reference polypeptide sequence as set forth in SEQ ID NO: 10.

11. The fusion protein of any one of claims 1 to 3 or 6 to 10, wherein the canine proinsulin comprises K53R, R55K, and L86R mutations compared to a reference polypeptide sequence as set forth in SEQ ID NO: 10.

12. The fusion protein of any one of claims 1 to 3 or 6 to 11, wherein the canine proinsulin-serum albumin fusion protein comprises a linker that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 99%, or 100% identity to SEQ ID NO: 8.

13. A pharmaceutical composition comprising the fusion protein of any one of claims 1 to 12.

14. Use of an effective amount of the fusion protein of any one of claims 1 to 12 or the pharmaceutical composition of claim 13, in the manufacture of a medicament for the treatment of a canine or feline subject having a metabolic disease.

15. The use of claim 14, wherein the metabolic disease is diabetes.

16. The use of claim 15, wherein the diabetes is Type 1 diabetes.

17. The use of claim 15, wherein the diabetes is Type 2 diabetes.

18. The use of any one of claims 14 to 17, wherein the fusion protein or pharmaceutical composition is formulated to be administered intravenously.

19. The use of claim 18, wherein the therapeutically effective amount is between 0.01 mg/kg and 15 mg/kg of the fusion protein, preferably between 1 mg/kg and 15 mg/kg of the fusion protein.

20. The use of any one of claims 14 to 18, wherein the fusion protein is formulated to be administered at a concentration of at least about 0.01 mg/kg, at least about 0.05 mg/kg, at least about 0.1 mg/kg, at least about 1 mg/kg, at least about 2 mg/kg, at least about 5 mg/kg, at least about 10 mg/kg, or at least about 15 mg/kg of the fusion protein.

21. The use of any one of claims 14 to 20, wherein the use decreases fasting blood glucose in the subject by about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, or about 50%.

22. A polynucleotide encoding a fusion protein for use in the treatment of companion animals, the fusion protein according to any one of claims 1 to 12.

23. The polynucleotide according to claim 22, wherein the polynucleotide encoding the fusion protein is operatively linked to a promoter, preferably a cytomegalovirus enhancer/chicken b-actin promoter.

24. The polynucleotide of any one of claims 22 to 23, wherein the canine proinsulin-serum albumin fusion polynucleotide shares at least 80%, at least 85%, at least 90%, at least 95%, at least 99%, or 100% identity to SEQ ID NO: 2.

25. The polynucleotide of any one of claims 22 to 23, wherein the feline proinsulin-serum albumin fusion polynucleotide shares at least 80%, at least 85%, at least 90%, at least 95%, at least 99%, or 100% identity to SEQ ID NO: 19.