We claim:

1. A fusion protein comprising an insulin polypeptide and an Fc fragment, wherein the insulin polypeptide and the Fc fragment are connected by a linker, comprising domains in the following orientation from N- to C- terminus: (N-terminus)—insulin polypeptide—linker—Fc fragment—(C-terminus), wherein the Fc fragment is of human origin and comprises the following sequence:

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYX$_1$STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
(SEQ ID NO: 77) wherein X_1 is S, or R, wherein the insulin polypeptide comprises the following sequence:
FVNQHLCGSHLVEALALVCGERGFHYGGGGGGSGGGGGIVEQCCTSTCSLDQLENY
C (SEQ ID NO: 10); and wherein the linker comprises the following sequence: GGGGGAGGGGAGGGGAGGGGG (SEQ ID NO: 67);

GGGGGQGGGGQGGGGQGGGGGQGGGG (SEQ ID NO: 99); or GGGGGQGGGGQGGGGQGGGGG (SEQ ID NO: 13).

2. The fusion protein of claim 1 comprising the insulin polypeptide and the Fc fragment, wherein the insulin polypeptide and the Fc fragment are connected by a linker, wherein the fusion protein comprises the following sequence:

FVNQHLCGSHLVEALALVCGERGFHYGGGGGGSGGGGGIVEQCCTSTCSLDQLENY
CGGGGGAGGGGAGGGGAGGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS
RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYSSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 87).

3. The fusion protein of claim 1, wherein the fusion protein comprises the following sequence:
FVNQHLCGSHLVEALALVCGERGFHYGGGGGGSGGGGGIVEQCCTSTCSLDQLENY
CGGGGGQGGGGQGGGGQGGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS
RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYSSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 78).

4. The fusion protein of claim 1, wherein the fusion protein comprises the following sequence:

FVNQHLCGSHLVEALALVCGERGFHYGGGGGGSGGGGGIVEQCCTSTCSLDQLENY
CGGGGGQGGGGQGGGGQGGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS
RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYRSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 84).

5. The fusion protein of claim 1, wherein the fusion protein comprises the following sequence:
FVNQHLCGSHLVEALALVCGERGFHYGGGGGGSGGGGGIVEQCCTSTCSLDQLENY
CGGGGGQGGGGQGGGGQGGGGGQGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYSSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 96).

6. The fusion protein of any of the preceding claims, wherein the fusion protein is a homodimer, and wherein the percentage homodimer of the fusion protein is greater than 90%.

7. The fusion protein of claim 6, wherein the fusion protein is made using one of HEK293 cells or CHO cells, and the resulting homodimer titer after purification using Protein A beads or a Protein A column is greater than 150 mg/L.

8. The fusion protein of claim 6, wherein the insulin receptor IC50 for the fusion protein is less than or equal to 5000 nM.

9. The fusion protein of claim 6, wherein the human FcRn receptor EC50 for the fusion protein is less than or equal to 1000 ng/mL.

10. The fusion protein of claim 6, wherein the human Fc(gamma)RI receptor assay OD450 Ratio at a biotinylated-Fc(gamma)RI concentration of 3000 ng/mL of the fusion protein is less than or equal to 0.50.

11. The fusion protein of claim 6, wherein the human C1q assay OD450 Ratio at a biotinylated-C1q concentration of 1000 ng/mL is less than or equal to 0.35.

12. The fusion protein of claim 6, wherein the fusion protein is formulated as a pharmaceutical composition, and wherein the fusion protein is present in the pharmaceutical composition at a concentration of about 3 mg/mL or greater.

13. The pharmaceutical composition of claim 12, wherein the composition is suitable for subcutaneous administration.

14. The fusion protein of claim 6 or a pharmaceutical composition thereof for use as a medicament.

15. Use of the fusion protein of claim 6 or a pharmaceutical composition thereof in the manufacture of a medicament for lowering the blood glucose level of a patient.

16. A cell engineered to express the fusion protein of any of the preceding claims.

17. A cDNA encoding the fusion protein of SEQ ID NO: 87 comprising the following nucleic acid sequence:

atggaatggagctgggtctttctcttcttcctgtcagtaacgactggtgtccactccttcgtgaaccagcacctgtgcggctcccacctgg
tggaagctctggcactcgtgtgcggcgagcggggcttccactacgggggtggcggaggaggttctggtggcggcggaggcatcgt
ggaacagtgctgcacctccacctgctccctggaccagctggaaaactactgcggtggcggaggtggtgcaggaggcggtggagcc
ggtggaggtggggctggaggaggcgggggagacaaaactcacacatgcccaccgtgcccagcacctgaactcctgggggggacc
gtcagtcttcctcttccccccaaaacccaaggacaccctcatgatctcccggaccccctgaggtcacatgcgtggtggtggacgtgagc
cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggtgcataatgccaagacaaagccgcgggaggagcagt
acagcagcacgtaccgtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctcca
acaaagccctcccagcccccatcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgccccc
atcccgggatgagctgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggga
gagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctctacagcaagctcac
cgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaaccactacacgcagaaga
gcctctccctgtctccgggttag (SEQ ID NO: 88).

18. A cDNA encoding the fusion protein of SEQ ID NO: 78 comprising the following nucleic acid sequence:

atggaatggagctgggtctttctcttcttcctgtcagtaacgactggtgtccactccttcgtgaaccagcacctgtgcggctcccacctgg
tggaagctctggcactcgtgtgcggcgagcggggcttccactacgggggtggcggaggaggttctggtggcggcggaggcatcgt
ggaacagtgctgcacctccacctgctccctggaccagctggaaaactactgcggtggcggaggtggtcaaggaggcggtggacag
ggtggaggtgggcagggaggaggcgggggagacaaaactcacacatgcccaccgtgcccagcacctgaactcctgggggggacc
gtcagtcttcctcttccccccaaaacccaaggacaccctcatgatctcccggaccccctgaggtcacatgcgtggtggtggacgtgagc
cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggtgcataatgccaagacaaagccgcgggaggagcagt
acagcagcacgtaccgtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctcca
acaaagccctcccagcccccatcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgccccc
atcccgggatgagctgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggga
gagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctctacagcaagctcac
cgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaaccactacacgcagaaga
gcctctccctgtctccgggttag (SEQ ID NO: 79).

19. A cDNA encoding the fusion protein of SEQ ID NO: 84 comprising the following nucleic acid sequence:

atggaatggagctgggtctttctcttcttcctgtcagtaacgactggtgtccactccttcgtgaaccagcacctgtgcggctcccacctgg
tggaagctctggcactcgtgtgcggcgagcggggcttccactacgggggtggcggaggaggttctggtggcggcggaggcatcgt
ggaacagtgctgcacctccacctgctccctggaccagctggaaaactactgcggtggcggaggtggtcaaggaggcggtggacag
ggtggaggtgggcagggaggaggcgggggagacaaaactcacacatgcccaccgtgcccagcacctgaactcctgggggggacc
gtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggacccctgaggtcacatgcgtggtggtggacgtgagc
cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggtgcataatgccaagacaaagccgcgggaggagcagt
acagaagcacgtaccgtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctcca
acaaagccctcccagcccccatcgagaaaaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccctgccccc
atcccgggatgagctgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtggga
gagcaatgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctctacagcaagctcac
cgtggacaagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaaccactacacgcagaaga
gcctctccctgtctccgggttag (SEQ ID NO: 85).