

What is claimed is:

1. A fusion protein comprising a Glucagon-like peptide 1 (GLP1) variant fused to a stabilizing domain, wherein the GLP1 variant comprises the amino acid sequence of SEQ ID NO: 7, and the stabilizing domain is an antibody or antigen-binding fragment thereof that specifically binds GLP1 receptor, and wherein the fusion protein has enhanced resistance to proteolytic cleavage and/or enhanced blood glucose lowering ability as compared to a fusion protein comprising mature GLP1.
2. The fusion protein of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR), and the GLP1 variant is fused to the N-terminus or C-terminus of the HCVR of the antigen-binding protein or antigen-binding fragment thereof.
3. The fusion protein of claim 1 or 2, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR), and the GLP1 variant is fused to the N-terminus or C-terminus of the LCVR of the antigen-binding protein or antigen-binding fragment thereof.
4. The fusion protein of any one of claims 1-3, wherein the stabilizing domain is an antibody.
5. The fusion protein of claim 3, wherein the GLP1 variant is fused to the N-terminus of the LCVR of the antibody or antigen-binding fragment thereof.
6. A pharmaceutical composition comprising a fusion protein of any one of claims 1-5 and a pharmaceutically acceptable carrier or diluent.
7. An isolated polynucleotide molecule comprising a polynucleotide sequence that encodes a fusion protein as set forth in any one of claims 1-5.
8. A vector comprising the polynucleotide molecule of claim 7.
9. A cell expressing the vector of claim 8.
10. Use of the pharmaceutical composition of claim 6 in the manufacture of a medicament for lowering high blood sugar level in a subject in need thereof.

11. The use of claim 10, wherein the subject has a disease or disorder selected from the group consisting of diabetes mellitus, obesity, insulin resistance, hypertension, dyslipidemia, Type 2 diabetes, Type 1 diabetes, pre-diabetes, cardiovascular disease, atherosclerosis, congestive heart failure, coronary heart disease, arteriosclerosis, peripheral artery disease, stroke, respiratory dysfunction, renal disease, fatty liver disease, non-alcoholic steatohepatitis (NASH), and metabolic syndrome.
12. Use of the pharmaceutical composition of claim 6 in the manufacture of a medicament for preventing, treating or ameliorating at least one symptom or indication of Type 2 diabetes in a subject in need thereof.
13. The use of claim 12, wherein the at least one symptom or indication is selected from the group consisting of high blood sugar level, excessive thirst, increased urination, presence of ketones in urine, fatigue, weight fluctuations, blurred vision, slow healing sores, frequent infections, swollen or tender gums, obesity, heart disease, stroke, kidney disease, eye disease, nerve damage and high blood pressure.
14. The use of any one of claims 10-13, wherein the pharmaceutical composition is to be administered in combination with a second therapeutic agent or therapy.
15. The use of claim 14, wherein the second therapeutic agent or therapy is selected from the group consisting of an insulin or insulin analogue, metformin, a thiazolidinedione, a sulfonylurea, a biguanide, chlorpropamide, a glinide, an alpha glucosidase inhibitor, nateglinide, a DPP4 inhibitor, pramlintide, sitagliptin, bromocriptine, a SGLT2 inhibitor, canagliflozin, an anti-hypertensive drug, a statin, aspirin, dietary modification, exercise, and a dietary supplement.
16. The use of any one of claims 10-15, wherein the pharmaceutical composition is to be administered subcutaneously, intravenously, intradermally, intraperitoneally, orally, or intramuscularly.