CLAIMS

1. An isolated fusion protein comprising at least one human alpha-1 antitrypsin (AAT) polypeptide comprising an amino acid sequence of SEQ ID NO: 32, wherein the AAT polypeptide is operably linked to a modified immunoglobulin G (IgG) Fc polypeptide, wherein the modified IgG Fc polypeptide comprises at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu, and Asn434Ser.

2. An isolated fusion protein comprising at least one human alpha-1 antitrypsin (AAT) polypeptide comprising the amino acid sequence of SEQ ID NO: 32, wherein the AAT polypeptide is operably linked to a modified immunoglobulin G (IgG) Fc polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO: 6.

3. The isolated fusion protein of claim 1 or claim 2, wherein the AAT polypeptide comprises the amino acid sequence of SEQ ID NO: 34.

4. The isolated fusion protein of any one of claims 1-3, wherein the modified IgG Fc polypeptide is derived from a human IgG4 Fc polypeptide.

5. The isolated fusion protein of any one of claims 1-4, wherein the AAT polypeptide is operably linked to the modified IgG Fc polypeptide via hinge region, a linker region, or both a hinge region and linker region.

6. The isolated fusion protein of any one of claims 1-5, wherein the AAT polypeptide is operably linked to the modified IgG Fc polypeptide via a linker region and a hinge region.

7. The isolated fusion protein of any one of claims 1-6, wherein the AAT polypeptide is operably linked to the N-terminus of the modified IgG Fc polypeptide via a linker region and a hinge region.

°°°

8. The isolated fusion protein of any one of claims 5-7, wherein the linker region comprises a peptide sequence.

9. The isolated fusion protein of any one of claims 5-8, wherein the linker region comprises a glycine-serine linker.

10. The isolated fusion protein of any one of claims 5-9, wherein the hinge region comprises a peptide sequence.

11. The isolated fusion protein of any one of claims 1-10, wherein the fusion protein is a dimeric fusion protein.

12. The isolated fusion protein of any one of claims 1-11, wherein the isolated fusion protein exhibits serine protease inhibitory activity and is for use in a method of treating a disease or disorder in a subject selected from the group consisting of AAT deficiency, emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), allergic asthma, cystic fibrosis, cancers of the lung, ischemia-reperfusion injury, ischemia/reperfusion injury following cardiac transplantation, myocardial infarction, rheumatoid arthritis, septic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, psoriasis, type I and/or type II diabetes, pneumonia, sepsis, graft versus host disease (GVHD), wound healing, Systemic lupus erythematosus, and multiple sclerosis.

13. The isolated fusion protein of claim 12, wherein the disease or disorder is AAT deficiency.

14. The isolated fusion protein of claim 12, wherein the disease or disorder is cystic fibrosis, ARDS, smoking-induced emphysema, or COPD.

15. The isolated fusion protein of any one of claims 12-14, wherein the subject is human.

°°°

16. A composition comprising the isolated fusion protein of any one of claims 1-15.

17. The composition of claim 16 further comprising a pharmaceutically acceptable carrier.

°°°