CLAIMS

1. An isolated fusion protein comprising at least one human alpha-1 antitrypsin (AAT) polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 32, and SEQ ID NO: 33, wherein the AAT polypeptide is operably linked to a~~n~~ modified immunoglobulin IgG4 Fc polypeptide that is at least 98% identical to the amino acid sequence of SEQ ID NO: 6, wherein the modified IgG4 Fc polypeptide comprises at least one mutation at a position selected from the group consisting of Met252, Ser254, Thr256, Met428, and Asn434, wherein the isolated fusion protein exhibits serine protease inhibitory activity and is for use in a method of treating a ~~treatinga~~ 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.

2. The isolated fusion protein for the use of claim 1, wherein the disease or disorder is AAT deficiency.

3. The isolated fusion protein for the use of claim 1, wherein the disease or disorder is cystic fibrosis, ARDS, smoking-induced emphysema, or COPD.

4. The isolated fusion protein for the use of any one of claims 1 to 3, wherein the subject is human.

5. The isolated fusion protein for the use of claim 1, wherein the AAT polypeptide and the immunoglobulin Fc polypeptide are operably linked via hinge region, a linker region, or both a

hinge region and linker region~~, optionally wherein the hinge region, the linker region or both the hinge region and the linker region comprise a polypeptide sequence~~.

6. The isolated fusion protein for the use of claim 5, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a polypeptide sequence.

7~~6~~. The isolated fusion protein for the use of claim 1, wherein the human AAT polypeptide comprises the amino acid sequence of SEQ ID NO:1.

8~~7~~. The isolated fusion protein for the use of claim 1, wherein the human AAT polypeptide comprises the amino acid sequence of SEQ ID NO:2.

9~~8~~. The isolated fusion protein for the use of claim 1, wherein the human AAT polypeptide comprises the amino acid sequence of SEQ ID NO:32.

10~~9~~. The isolated fusion protein for the use of claim 1, wherein the human AAT polypeptide comprises the amino acid sequence of SEQ ID NO:33.

11~~10~~. The isolated fusion protein for the use of claim 1, wherein the fusion protein further comprises a WAP domain containing polypeptide sequence, ~~optionally~~ wherein:

a. the WAP domain containing polypeptide sequence comprises a SLPI polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 10, 9, and 8; or

b. the WAP domain containing polypeptide sequence comprises an elafin polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 13, 12, and 11.

12~~11~~. The isolated fusion protein for the use of any one of claims 1 to ~~10~~11, wherein~~:~~

~~c. the immunoglobulin Fc polypeptide is modified to enhance FcRn binding;~~

~~d. the immunoglobulin Fc polypeptide comprising at least one mutation at a position selected from the group consisting of Met252, Ser254, Thr256, Met428, and Asn434; or~~

~~e.~~ the immunoglobulin Fc polypeptide comprises at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser.

13. The isolated fusion protein for the use of claim 12, wherein the immunoglobulin Fc polypeptide comprises a Met252Tyr and a Met428Leu mutation.