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(54) Title: THERAPY FOR ALPHA-1 ANTITRYPSIN DEFICIENCY

(57) Abstract: A therapeutic genetic construct for addressing alpha-1 antitrypsin deficiency (AATD) and associated disorders. The genetic construct encodes: (a) a first pre-miRNA; (b) a second pre-miRNA; and (c) a transgene encoding AAT(M). The pre-miRNAs inhibit the expression of alleles encoding mutant variants of AAT, such as AAT(Z), AAT(S), AAT(I), AAT(S_{iiyama}), and AAT(M_{malton}). The construct may further comprise a liver-specific promoter. A vector, such as a gorilla adenoviral vector, comprising the genetic construct. A method of treating a disease or disorder, such as COPD, bronchiectasis, neonatal cholestasis, cirrhosis, fibrosis, and hepatocellular carcinoma, comprising administering a therapeutically effective amount of the aforementioned vector. A use of the genetic construct in the manufacture of a medicament for use in treating a disease or disorder. A composition comprising the genetic construct. A kit comprising the genetic construct.



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