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(54) Title: OPTIMIZED GENE THERAPY FOR TARGETING MUSCLE IN MUSCLE DISEASES

(57) Abstract: The disclosure provides gene therapy vectors, such as adeno-associated virus (AAV), optimized for delivering a transgene to muscles. The optimized vectors contain constitutive or a muscle-specific promoter to deliver whole body or skeletal/heart muscle-specific transgene expression, respectively, in combination with a transgene cDNA to replace the gene mutation found in a muscle disease with a normal copy of the gene, an internal ribosomal entry site (IRES) to allow for production of a second protein from the same transcript, and a muscle growth factor, to build new muscle growth and strength. For example, the invention provides The disclosure provides gene therapy vectors, such as recombinant adeno-associated virus (rAAV), designed for treatment of GNE myopathy in which the rAAV expresses UDP-GlcNAc-epimerase/ManNAc-6 alone or in combination with a muscle growth factor or muscle transdifferentiation factor. The provided AAV replace the mutated GNE gene expression while expressing proteins that stimulate muscle growth.



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