

COMPOSITIONS AND METHODS FOR TREATING GLYCOGEN STORAGE DISORDERS

Field of the Invention

The present disclosure relates to the field of gene therapy and provides compositions and methods for ameliorating genetic disorders.

Sequence Listing

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on October 23, 2020 is named 51037-054WO3_Sequence_Listing_10.23.20_ST25 and is 13,144 bytes in size.

Background of the Invention

Pompe disease is a lysosomal storage disorder caused by mutations in the acid alpha-glucosidase (GAA) gene, which encodes an enzyme responsible for processing lysosomal glycogen. Patients with Pompe disease exhibit clinical phenotypes across a variety of tissues, including glycogen buildup in cells, deficits in cardiac, respiratory, and skeletal muscle function, and central nervous system pathology. Some of these deficits are significantly ameliorated by enzyme replacement therapy (ERT) using recombinant human GAA (rhGAA). Clinical efficacy has been limited by the immunogenicity of hGAA ERT and the lack of uptake of rhGAA into some affected tissues. Gene therapy has also been investigated as a potential therapeutic paradigm for this disease. The development of gene therapies for the treatment of Pompe have been hindered by the difficulty associated with achieving expression of therapeutically effective amounts of GAA in affected tissues while suppressing toxic side effects. There remains a need for compositions and methods that achieve this balance.

Summary of the Invention

The present disclosure provides compositions and methods that can be used for treating glycogen storage disorders, such as type II glycogen storage disorder, which is also referred to herein as Pompe disease. Using the compositions and methods of the disclosure, a patient (e.g., a mammalian patient, such as a human patient) having Pompe disease may be administered a viral vector, such as an adeno-associated viral (AAV) vector, that contains a transgene encoding acid alpha-glucosidase (GAA). The AAV vector may be, for example, a pseudotyped AAV vector, such as an AAV vector containing AAV2 inverted terminal repeats packaged within capsid proteins from AAV8 (AAV2/8) or AAV9 (AAV2/9). The transgene may, for example, be operably linked to a transcription regulatory element, such as a promoter that induces gene expression in a muscle cell and/or a neuronal cell. Exemplary promoters that may be used in conjunction with the compositions and methods of the disclosure are a muscle creatine kinase promoter, desmin promoter, and CMV promoter, among others. The AAV vector may be administered to the patient in a therapeutically effective amount, such as in an amount of from about 1×10^{13} vector genomes (vg) per kg of body weight of the subject (vg/kg) to about 3×10^{14} vg/kg (e.g., in an

amount of from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg, such as in an amount of from about 4×10^{13} vg/kg to about 1×10^{14} vg/kg, such as in an amount of about 4×10^{13} vg/kg, 5×10^{13} vg/kg, 6×10^{13} vg/kg, 7×10^{13} vg/kg, 8×10^{13} vg/kg, 9×10^{13} vg/kg, or 1×10^{14} vg/kg).

The present disclosure is based, in part, on the discovery of doses of AAV vectors containing a GAA transgene that effectuate a therapeutic increase in GAA expression and activity in patients suffering from Pompe disease while suppressing toxic side effects. It has presently been discovered, for example, that doses of AAV vectors containing a transgene encoding GAA ranging from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg (e.g., from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg, such as a dose of about 4×10^{13} vg/kg, 5×10^{13} vg/kg, 6×10^{13} vg/kg, 7×10^{13} vg/kg, 8×10^{13} vg/kg, 9×10^{13} vg/kg, or 1×10^{14} vg/kg) can engender a beneficial increase in GAA expression and activity in a patient having Pompe disease while simultaneously avoiding toxic side effects that can be associated with overexpression of GAA or administration of excessive quantities of viral vector. Using the compositions and methods of the disclosure, an AAV vector may be administered to the patient in an amount that is sufficient to enhance the patient's expression of GAA and reduce cellular accumulation of glycogen in the patient's neuronal and muscle tissue, without inducing toxic side effects.

In one aspect, the disclosure provides use of an adeno-associated viral (AAV) vector comprising a transgene encoding acid alpha-glucosidase (GAA) in the manufacture of a medicament for treating Pompe disease in a human patient in need thereof, wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. In a first aspect/example, the disclosure features a method of treating Pompe disease in a human patient in need thereof by administering to the patient an AAV vector containing a transgene encoding acid GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg, such as in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. For example, the AAV vector may be administered to the patient in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14}

vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

5 In another aspect, the disclosure provides use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for improving muscle function in a human patient diagnosed as having Pompe disease, wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. In another aspectexample, the disclosure features a method of improving muscle function in a human patient diagnosed as having Pompe disease by administering to the patient an AAV vector containing a transgene encoding GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg, such as in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. For example, the AAV vector may be administered to the patient in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

35 In yet another aspect, the disclosure provides use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. In a further aspectexample, the disclosure features a method of reducing glycogen accumulation in a human patient diagnosed as having Pompe disease by administering to the patient an AAV vector containing a transgene encoding GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg, such as in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. For example, the AAV vector may be administered to the patient in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13}

vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg. In some

embodiment examples of this aspect, administration of the AAV vector to the patient reduces glycogen accumulation in muscle tissue (e.g., in cardiac and/or skeletal muscle tissue) and/or in neuronal tissue.

In one aspect, the disclosure provides use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for improving pulmonary function in a human patient diagnosed as having Pompe disease, wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. In another aspect example, the disclosure features a method of improving pulmonary function in a human patient diagnosed as having Pompe disease by administering to the patient an AAV vector containing a transgene encoding GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg, such as in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. For example, the AAV vector may be administered to the patient in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, or 1×10^{14} vg/kg.

vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

In another aspect, the present disclosure provides use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for increasing GAA expression in a human patient diagnosed as having Pompe disease, wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. In another ~~aspect~~example, the disclosure features a method of increasing GAA expression in a human patient diagnosed as having Pompe disease by administering to the patient an AAV vector containing a transgene encoding GAA, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg, such as in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. For example, the AAV vector may be administered to the patient in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

In some ~~embodiment~~examples of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of from about 2×10^{13} vg/kg to about 2×10^{14} vg/kg, such as an in amount of about 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, $3.1 \times$

10¹³ vg/kg, 3.2 x 10¹³ vg/kg, 3.3 x 10¹³ vg/kg, 3.4 x 10¹³ vg/kg, 3.5 x 10¹³ vg/kg, 3.6 x 10¹³ vg/kg, 3.7 x 10¹³ vg/kg, 3.8 x 10¹³ vg/kg, 3.9 x 10¹³ vg/kg, 4 x 10¹³ vg/kg, 4.1 x 10¹³ vg/kg, 4.2 x 10¹³ vg/kg, 4.3 x 10¹³ vg/kg, 4.4 x 10¹³ vg/kg, 4.5 x 10¹³ vg/kg, 4.6 x 10¹³ vg/kg, 4.7 x 10¹³ vg/kg, 4.8 x 10¹³ vg/kg, 4.9 x 10¹³ vg/kg, 5 x 10¹³ vg/kg, 5.1 x 10¹³ vg/kg, 5.2 x 10¹³ vg/kg, 5.3 x 10¹³ vg/kg, 5.4 x 10¹³ vg/kg, 5.5 x 10¹³ vg/kg, 5.6 x 10¹³ vg/kg, 5.7 x 10¹³ vg/kg, 5.8 x 10¹³ vg/kg, 5.9 x 10¹³ vg/kg, 6 x 10¹³ vg/kg, 6.1 x 10¹³ vg/kg, 6.2 x 10¹³ vg/kg, 6.3 x 10¹³ vg/kg, 6.4 x 10¹³ vg/kg, 6.5 x 10¹³ vg/kg, 6.6 x 10¹³ vg/kg, 6.7 x 10¹³ vg/kg, 6.8 x 10¹³ vg/kg, 6.9 x 10¹³ vg/kg, 7 x 10¹³ vg/kg, 7.1 x 10¹³ vg/kg, 7.2 x 10¹³ vg/kg, 7.3 x 10¹³ vg/kg, 7.4 x 10¹³ vg/kg, 7.5 x 10¹³ vg/kg, 7.6 x 10¹³ vg/kg, 7.7 x 10¹³ vg/kg, 7.8 x 10¹³ vg/kg, 7.9 x 10¹³ vg/kg, 8 x 10¹³ vg/kg, 8.1 x 10¹³ vg/kg, 8.2 x 10¹³ vg/kg, 8.3 x 10¹³ vg/kg, 8.4 x 10¹³ vg/kg, 8.5 x 10¹³ vg/kg, 8.6 x 10¹³ vg/kg, 8.7 x 10¹³ vg/kg, 8.8 x 10¹³ vg/kg, 8.9 x 10¹³ vg/kg, 9 x 10¹³ vg/kg, 9.1 x 10¹³ vg/kg, 9.2 x 10¹³ vg/kg, 9.3 x 10¹³ vg/kg, 9.4 x 10¹³ vg/kg, 9.5 x 10¹³ vg/kg, 9.6 x 10¹³ vg/kg, 9.7 x 10¹³ vg/kg, 9.8 x 10¹³ vg/kg, 9.9 x 10¹³ vg/kg, 1 x 10¹⁴ vg/kg, 1.1 x 10¹⁴ vg/kg, 1.2 x 10¹⁴ vg/kg, 1.3 x 10¹⁴ vg/kg, 1.4 x 10¹⁴ vg/kg, 1.5 x 10¹⁴ vg/kg, 1.6 x 10¹⁴ vg/kg, 1.7 x 10¹⁴ vg/kg, 1.8 x 10¹⁴ vg/kg, 1.9 x 10¹⁴ vg/kg, or 2 x 10¹⁴ vg/kg. In some [embodiment examples](#), the AAV vector is administered to the patient in an amount of from about 2 x 10¹³ vg/kg to about 7 x 10¹³ vg/kg, such as in an amount of from about 2 x 10¹³ vg/kg to about 4 x 10¹³ vg/kg (e.g., about 3 x 10¹³ vg/kg) or in an amount of from about 5 x 10¹³ vg/kg to about 7 x 10¹³ vg/kg (e.g., about 6 x 10¹³ vg/kg).

In some [embodiment examples](#) of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of from about 3 x 10¹³ vg/kg to about 2 x 10¹⁴ vg/kg, such as an in amount of about 3 x 10¹³ vg/kg, 3.1 x 10¹³ vg/kg, 3.2 x 10¹³ vg/kg, 3.3 x 10¹³ vg/kg, 3.4 x 10¹³ vg/kg, 3.5 x 10¹³ vg/kg, 3.6 x 10¹³ vg/kg, 3.7 x 10¹³ vg/kg, 3.8 x 10¹³ vg/kg, 3.9 x 10¹³ vg/kg, 4 x 10¹³ vg/kg, 4.1 x 10¹³ vg/kg, 4.2 x 10¹³ vg/kg, 4.3 x 10¹³ vg/kg, 4.4 x 10¹³ vg/kg, 4.5 x 10¹³ vg/kg, 4.6 x 10¹³ vg/kg, 4.7 x 10¹³ vg/kg, 4.8 x 10¹³ vg/kg, 4.9 x 10¹³ vg/kg, 5 x 10¹³ vg/kg, 5.1 x 10¹³ vg/kg, 5.2 x 10¹³ vg/kg, 5.3 x 10¹³ vg/kg, 5.4 x 10¹³ vg/kg, 5.5 x 10¹³ vg/kg, 5.6 x 10¹³ vg/kg, 5.7 x 10¹³ vg/kg, 5.8 x 10¹³ vg/kg, 5.9 x 10¹³ vg/kg, 6 x 10¹³ vg/kg, 6.1 x 10¹³ vg/kg, 6.2 x 10¹³ vg/kg, 6.3 x 10¹³ vg/kg, 6.4 x 10¹³ vg/kg, 6.5 x 10¹³ vg/kg, 6.6 x 10¹³ vg/kg, 6.7 x 10¹³ vg/kg, 6.8 x 10¹³ vg/kg, 6.9 x 10¹³ vg/kg, 7 x 10¹³ vg/kg, 7.1 x 10¹³ vg/kg, 7.2 x 10¹³ vg/kg, 7.3 x 10¹³ vg/kg, 7.4 x 10¹³ vg/kg, 7.5 x 10¹³ vg/kg, 7.6 x 10¹³ vg/kg, 7.7 x 10¹³ vg/kg, 7.8 x 10¹³ vg/kg, 7.9 x 10¹³ vg/kg, 8 x 10¹³ vg/kg, 8.1 x 10¹³ vg/kg, 8.2 x 10¹³ vg/kg, 8.3 x 10¹³ vg/kg, 8.4 x 10¹³ vg/kg, 8.5 x 10¹³ vg/kg, 8.6 x 10¹³ vg/kg, 8.7 x 10¹³ vg/kg, 8.8 x 10¹³ vg/kg, 8.9 x 10¹³ vg/kg, 9 x 10¹³ vg/kg, 9.1 x 10¹³ vg/kg, 9.2 x 10¹³ vg/kg, 9.3 x 10¹³ vg/kg, 9.4 x 10¹³ vg/kg, 9.5 x 10¹³ vg/kg, 9.6 x 10¹³ vg/kg, 9.7 x 10¹³ vg/kg, 9.8 x 10¹³ vg/kg, 9.9 x 10¹³ vg/kg, 1 x 10¹⁴ vg/kg, 1.1 x 10¹⁴ vg/kg, 1.2 x 10¹⁴ vg/kg, 1.3 x 10¹⁴ vg/kg, 1.4 x 10¹⁴ vg/kg, 1.5 x 10¹⁴ vg/kg, 1.6 x 10¹⁴ vg/kg, 1.7 x 10¹⁴ vg/kg, 1.8 x 10¹⁴ vg/kg, 1.9 x 10¹⁴ vg/kg, or 2 x 10¹⁴ vg/kg.

In some [embodiment examples](#) of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of from about 4 x 10¹³ vg/kg to about 2 x 10¹⁴ vg/kg, such as an in amount of about 4 x 10¹³ vg/kg, 4.1 x 10¹³ vg/kg, 4.2 x 10¹³ vg/kg, 4.3 x 10¹³ vg/kg, 4.4 x 10¹³ vg/kg, 4.5 x 10¹³ vg/kg, 4.6 x 10¹³ vg/kg, 4.7 x 10¹³ vg/kg, 4.8 x 10¹³ vg/kg, 4.9 x 10¹³ vg/kg, 5 x 10¹³ vg/kg, 5.1 x 10¹³ vg/kg, 5.2 x 10¹³ vg/kg, 5.3 x 10¹³ vg/kg, 5.4 x 10¹³ vg/kg, 5.5 x 10¹³ vg/kg, 5.6 x 10¹³ vg/kg, 5.7 x 10¹³ vg/kg, 5.8 x 10¹³ vg/kg, 5.9 x 10¹³ vg/kg, 6 x 10¹³ vg/kg, 6.1 x 10¹³ vg/kg, 6.2 x 10¹³ vg/kg, 6.3 x 10¹³ vg/kg,

In some embodimentexamples of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of 1.5×10^{14} vg/kg.

In some embodimentexamples of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of 1.6×10^{14} vg/kg.

In some embodimentexamples of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of 1.7×10^{14} vg/kg.

In some embodimentexamples of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of 1.8×10^{14} vg/kg.

In some embodimentexamples of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of 1.9×10^{14} vg/kg.

In some embodimentexamples of any of the above aspects of the disclosure, the AAV vector is administered to the patient in an amount of 2×10^{14} vg/kg.

In some embodimentexamples of any of the above aspects of the disclosure, the AAV vector is administered to the patient in a single dose containing the specified amount. In some

embodimentexamples, the AAV vector is administered to the patient in two or more doses that, together, total the specified amount. For example, the AAV vector may be administered to the patient in from two to ten doses that, together, total the specified amount (e.g., in two, three, four, five, six, seven, eight, nine, or ten doses that, together, total the specified amount). In some embodimentexamples, the AAV vector is administered to the patient in two, three, or four doses that, together, total the specified amount. In some embodimentexamples, the AAV vector is administered to the patient in two doses that, together, total the specified amount.

In some embodimentexamples, the two or more doses of the AAV vector that, together, total the specified amount are separated from one another, for example, by a year or more. In some

embodimentexamples, the two or more doses are administered to the patient within about 12 months of one another (e.g., within about 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, 19 weeks, 20 weeks, 21 weeks, 22 weeks, 23 weeks, 24 weeks, 25 weeks, 26 weeks, 27 weeks, 28 weeks, 29 weeks, 30 weeks, 31 weeks, 32 weeks, 33 weeks, 34 weeks, 35 weeks, 36 weeks, 37 weeks, 38 weeks, 39 weeks, 40 weeks, 41 weeks, 42 weeks, 43 weeks, 44 weeks, 45 weeks, 46 weeks, 47 weeks, 48 weeks, 49 weeks, 50 weeks, 51 weeks, or 52 weeks of one another). For example, in some embodimentexamples, the two or more doses are administered to the patient within from about one week to about 48 weeks of one another (e.g., within about 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, 19 weeks, 20 weeks, 21 weeks, 22 weeks, 23 weeks, 24 weeks, 25 weeks, 26 weeks, 27 weeks, 28 weeks, 29 weeks, 30 weeks, 31 weeks, 32 weeks, 33 weeks, 34 weeks, 35 weeks, 36 weeks, 37 weeks, 38 weeks, 39 weeks, 40 weeks, 41 weeks, 42 weeks, 43 weeks, 44 weeks, 45 weeks, 46 weeks, 47 weeks, or 48 weeks of one another). In some embodimentexamples, the two or more doses are administered to the patient within from about two weeks to about 44 weeks of one another (e.g., within about 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, 19 weeks, 20 weeks, 21 weeks, 22 weeks, 23 weeks,

24 weeks, 25 weeks, 26 weeks, 27 weeks, 28 weeks, 29 weeks, 30 weeks, 31 weeks, 32 weeks, 33 weeks, 34 weeks, 35 weeks, 36 weeks, 37 weeks, 38 weeks, 39 weeks, 40 weeks, 41 weeks, 42 weeks, 43 weeks, or 44 weeks of one another). In some [embodimentexamples](#), the two or more doses are administered to the patient within from about three weeks to about 40 weeks of one another (e.g., within about 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, 19 weeks, 20 weeks, 21 weeks, 22 weeks, 23 weeks, 24 weeks, 25 weeks, 26 weeks, 27 weeks, 28 weeks, 29 weeks, 30 weeks, 31 weeks, 32 weeks, 33 weeks, 34 weeks, 35 weeks, 36 weeks, 37 weeks, 38 weeks, 39 weeks, or 40 weeks of one another). In some [embodimentexamples](#), the two or more doses are administered to the patient within from about four weeks to about 36 weeks of one another (e.g., within about 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, 19 weeks, 20 weeks, 21 weeks, 22 weeks, 23 weeks, 24 weeks, 25 weeks, 26 weeks, 27 weeks, 28 weeks, 29 weeks, 30 weeks, 31 weeks, 32 weeks, 33 weeks, 34 weeks, 35 weeks, or 36 weeks of one another). In some [embodimentexamples](#), the two or more doses are administered to the patient within from about five weeks to about 32 weeks of one another (e.g., within about 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, 19 weeks, 20 weeks, 21 weeks, 22 weeks, 23 weeks, 24 weeks, 25 weeks, 26 weeks, 27 weeks, 28 weeks, 29 weeks, 30 weeks, 31 weeks, or 32 weeks of one another). In some [embodimentexamples](#), the two or more doses are administered to the patient within from about six weeks to about 24 weeks of one another (e.g., within about 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 11 weeks, 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, 19 weeks, 20 weeks, 21 weeks, 22 weeks, 23 weeks, or 24 weeks of one another). In some [embodimentexamples](#), the two or more doses are administered to the patient within from about 12 weeks to about 20 weeks of one another (e.g., within about 12 weeks, 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, 19 weeks, or 20 weeks of one another). In some [embodimentexamples](#), the two or more doses are administered to the patient within about 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, or 19 weeks of one another.

In some [embodimentexamples](#), the AAV vector is administered to the patient in two or more doses that each, individually, contain the specified amount. For example, the AAV vector may be administered to the patient in from two to ten doses that each, individually, contain the specified amount (e.g., in two, three, four, five, six, seven, eight, nine, or ten doses that each, individually, contain the specified amount). In some [embodimentexamples](#), the AAV vector is administered to the patient in two, three, or four doses that each, individually, contain the specified amount. In some [embodimentexamples](#), the AAV vector is administered to the patient in two doses that each, individually, contain the specified amount.

In some [embodimentexamples](#), the AAV vector is administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral, intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration. For example, the AAV vector may be administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, and/or intramuscular administration. In some [embodimentexamples](#), the AAV vector is administered to the patient

by way of intravenous and/or intrathecal administration. some embodimentexamples, the AAV vector is administered to the patient by way of intravenous administration.

In some embodimentexamples, the AAV is an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAVrh74, AAVrh.8, or AAVrh.10 serotype. The AAV may be a pseudotyped AAV, such as an AAV2/8 or AAV2/9. In some embodimentexamples, the AAV contains a recombinant capsid protein.

In some embodimentexamples, the transgene encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell. The promoter may be, for example, a muscle creatine kinase (MCK) promoter, desmin promoter, chicken beta actin promoter, cytomegalovirus (CMV) promoter, myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.

In some embodimentexamples, the promoter is a MCK promoter. The MCK promoter may have, for example, a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is 100% identical to SEQ ID NO: 1.

In some embodimentexamples, the transgene encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell. For example, the transgene encoding GAA may be operably linked to a CMV enhancer, a myocyte enhancer factor 2 (MEF2) enhancer, or a MyoD enhancer.

In some embodimentexamples, the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In

some embodimentexamples, the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexample, the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2. In some embodimentexamples, the GAA differs from human wild-type GAA only by way of one or more conservative amino acid substitutions. In some embodimentexamples, the GAA differs from human wild-type GAA by way of one or more non-conservative amino acid substitutions.

In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is 100% identical to SEQ ID NO: 3.

In some embodimentexamples, the patient has infantile-onset Pompe disease. The patient may be, for example, from about one month to about one year of age (e.g., about one month, two months, three months, four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, or twelve months of age). In some embodimentexamples, the patient is from about one month to about six months of age (e.g., about month, two months, three months, four months, five months, or six months of age).

In some embodimentexamples, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.

In some embodimentexamples, the patient has late-onset Pompe disease. The patient may exhibit, for example, endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

In some embodimentexamples, the patient has not previously received GAA enzyme replacement therapy. In some embodimentexamples, the patient has previously received GAA enzyme replacement therapy.

In some embodimentexamples, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

In some embodimentexamples, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.

In one aspect, the disclosure provides use of an agent that increases GAA expression in the manufacture of a medicament for treating Pompe disease in a human patient in need thereof, wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter. In another aspectexample, the disclosure

features a method of treating Pompe disease in a human patient in need thereof by administering to the patient an agent that increases GAA expression. In accordance with this aspectexample, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector containing a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg (e.g., in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg), wherein the transgene encoding GAA is operably linked to a MCK promoter. For example, the agent may be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index upon administration to the subject of the AAV vector in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg.

vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

In another aspect, the disclosure provides use of an agent that increases GAA expression in the manufacture of a medicament for improving muscle function in a human patient diagnosed as having Pompe disease, wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

In another aspect, the disclosure features a method of improving muscle function in a human patient diagnosed as having Pompe disease by administering to the patient an agent that increases GAA expression. In accordance with this aspect, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector containing a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg (e.g., in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg), wherein the transgene encoding GAA is operably linked to a MCK promoter. For example, the agent may be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index upon administration to the subject of the AAV vector in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

In yet another aspect, the disclosure provides use of an agent that increases GAA expression in the manufacture of a medicament for reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

In another aspect, the disclosure features a method of reducing glycogen accumulation in a human patient diagnosed as having Pompe disease by administering to the patient an agent that increases GAA expression. In accordance with this aspect, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA

activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector containing a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg (e.g., in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg), wherein the transgene encoding GAA is operably linked to a MCK promoter. For

5 example, the agent may be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index upon administration to the subject of the AAV vector in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg. In some
30 embodiment examples of this aspect, administration of the agent to the patient reduces glycogen accumulation in muscle tissue (e.g., in cardiac and/or skeletal muscle tissue) and/or in neuronal tissue.

In one aspect, the disclosure provides use of an agent that increases GAA expression in the manufacture of a medicament for improving pulmonary function in a human patient diagnosed as having Pompe disease, wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter. In another aspect example, the disclosure features a method of improving pulmonary function in a human
35 a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter. In another aspect example, the disclosure features a method of improving pulmonary function in a human patient diagnosed as having Pompe disease by administering to the patient an agent that increases GAA expression. In accordance with this aspect example, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector containing a transgene encoding GAA in an amount of
40 from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg (e.g., in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg), wherein the transgene encoding GAA is operably linked to a MCK promoter. For

example, the agent may be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index upon administration to the subject of the AAV vector in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

In another aspect, the disclosure provides use of an agent that increases GAA expression in the manufacture of a medicament for increasing GAA expression in a human patient diagnosed as having Pompe disease, wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter. In another ~~aspect~~ example, the disclosure features a method of increasing GAA expression in a human patient diagnosed as having Pompe disease by administering to the patient an agent that increases GAA expression. In accordance with this ~~aspect~~ example, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector containing a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg (e.g., in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg), wherein the transgene encoding GAA is operably linked to a MCK promoter. For example, the agent may be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index upon administration to the subject of the AAV vector in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13}

5 vg/kg, 2.8 x 10¹³ vg/kg, 2.9 x 10¹³ vg/kg, 3 x 10¹³ vg/kg, 3.1 x 10¹³ vg/kg, 3.2 x 10¹³ vg/kg, 3.3 x 10¹³ vg/kg, 3.4 x 10¹³ vg/kg, 3.5 x 10¹³ vg/kg, 3.6 x 10¹³ vg/kg, 3.7 x 10¹³ vg/kg, 3.8 x 10¹³ vg/kg, 3.9 x 10¹³ vg/kg, 4 x 10¹³ vg/kg, 4.1 x 10¹³ vg/kg, 4.2 x 10¹³ vg/kg, 4.3 x 10¹³ vg/kg, 4.4 x 10¹³ vg/kg, 4.5 x 10¹³ vg/kg, 4.6 x 10¹³ vg/kg, 4.7 x 10¹³ vg/kg, 4.8 x 10¹³ vg/kg, 4.9 x 10¹³ vg/kg, 5 x 10¹³ vg/kg, 5.1 x 10¹³ vg/kg, 5.2 x 10¹³ vg/kg, 5.3 x 10¹³ vg/kg, 5.4 x 10¹³ vg/kg, 5.5 x 10¹³ vg/kg, 5.6 x 10¹³ vg/kg, 5.7 x 10¹³ vg/kg, 5.8 x 10¹³ vg/kg, 5.9 x 10¹³ vg/kg, 6 x 10¹³ vg/kg, 6.1 x 10¹³ vg/kg, 6.2 x 10¹³ vg/kg, 6.3 x 10¹³ vg/kg, 6.4 x 10¹³ vg/kg, 6.5 x 10¹³ vg/kg, 6.6 x 10¹³ vg/kg, 6.7 x 10¹³ vg/kg, 6.8 x 10¹³ vg/kg, 6.9 x 10¹³ vg/kg, 7 x 10¹³ vg/kg, 7.1 x 10¹³ vg/kg, 7.2 x 10¹³ vg/kg, 7.3 x 10¹³ vg/kg, 7.4 x 10¹³ vg/kg, 7.5 x 10¹³ vg/kg, 7.6 x 10¹³ vg/kg, 7.7 x 10¹³ vg/kg, 7.8 x 10¹³ vg/kg, 7.9 x 10¹³ vg/kg, 8 x 10¹³ vg/kg, 8.1 x 10¹³ vg/kg, 8.2 x 10¹³ vg/kg, 8.3 x 10¹³ vg/kg, 8.4 x 10¹³ vg/kg, 8.5 x 10¹³ vg/kg, 8.6 x 10¹³ vg/kg, 8.7 x 10¹³ vg/kg, 8.8 x 10¹³ vg/kg, 8.9 x 10¹³ vg/kg, 9 x 10¹³ vg/kg, 9.1 x 10¹³ vg/kg, 9.2 x 10¹³ vg/kg, 9.3 x 10¹³ vg/kg, 9.4 x 10¹³ vg/kg, 9.5 x 10¹³ vg/kg, 9.6 x 10¹³ vg/kg, 9.7 x 10¹³ vg/kg, 9.8 x 10¹³ vg/kg, 9.9 x 10¹³ vg/kg, 1 x 10¹⁴ vg/kg, 1.1 x 10¹⁴ vg/kg, 1.2 x 10¹⁴ vg/kg, 1.3 x 10¹⁴ vg/kg, 1.4 x 10¹⁴ vg/kg, 1.5 x 10¹⁴ vg/kg, 1.6 x 10¹⁴ vg/kg, 1.7 x 10¹⁴ vg/kg, 1.8 x 10¹⁴ vg/kg, 1.9 x 10¹⁴ vg/kg, 2 x 10¹⁴ vg/kg, 2.1 x 10¹⁴ vg/kg, 2.2 x 10¹⁴ vg/kg, 2.3 x 10¹⁴ vg/kg, 2.4 x 10¹⁴ vg/kg, 2.5 x 10¹⁴ vg/kg, 2.6 x 10¹⁴ vg/kg, 2.7 x 10¹⁴ vg/kg, 2.8 x 10¹⁴ vg/kg, 2.9 x 10¹⁴ vg/kg, 3 x 10¹⁴ vg/kg, 3.1 x 10¹⁴ vg/kg, 3.2 x 10¹⁴ vg/kg, 3.3 x 10¹⁴ vg/kg, 3.4 x 10¹⁴ vg/kg, 3.5 x 10¹⁴ vg/kg, 3.6 x 10¹⁴ vg/kg, 3.7 x 10¹⁴ vg/kg, 3.8 x 10¹⁴ vg/kg, 3.9 x 10¹⁴ vg/kg, 4 x 10¹⁴ vg/kg, 4.1 x 10¹⁴ vg/kg, 4.2 x 10¹⁴ vg/kg, 4.3 x 10¹⁴ vg/kg, 4.4 x 10¹⁴ vg/kg, 4.5 x 10¹⁴ vg/kg, 4.6 x 10¹⁴ vg/kg, 4.7 x 10¹⁴ vg/kg, 4.8 x 10¹⁴ vg/kg, 4.9 x 10¹⁴ vg/kg, or 5 x 10¹⁴ vg/kg.

20 In some **embodimentexamples** of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 2 x 10¹³ vg/kg to about 2 x 10¹⁴ vg/kg, such as an in amount of about 2 x 10¹³ vg/kg, 2.1 x 10¹³
 25 vg/kg, 2.2 x 10¹³ vg/kg, 2.3 x 10¹³ vg/kg, 2.4 x 10¹³ vg/kg, 2.5 x 10¹³ vg/kg, 2.6 x 10¹³ vg/kg, 2.7 x 10¹³ vg/kg, 2.8 x 10¹³ vg/kg, 2.9 x 10¹³ vg/kg, 3 x 10¹³ vg/kg, 3.1 x 10¹³ vg/kg, 3.2 x 10¹³ vg/kg, 3.3 x 10¹³ vg/kg, 3.4 x 10¹³ vg/kg, 3.5 x 10¹³ vg/kg, 3.6 x 10¹³ vg/kg, 3.7 x 10¹³ vg/kg, 3.8 x 10¹³ vg/kg, 3.9 x 10¹³ vg/kg, 4 x 10¹³ vg/kg, 4.1 x 10¹³ vg/kg, 4.2 x 10¹³ vg/kg, 4.3 x 10¹³ vg/kg, 4.4 x 10¹³ vg/kg, 4.5 x 10¹³ vg/kg, 4.6 x 10¹³ vg/kg, 4.7 x 10¹³ vg/kg, 4.8 x 10¹³ vg/kg, 4.9 x 10¹³ vg/kg, 5 x 10¹³ vg/kg, 5.1 x 10¹³
 30 vg/kg, 5.2 x 10¹³ vg/kg, 5.3 x 10¹³ vg/kg, 5.4 x 10¹³ vg/kg, 5.5 x 10¹³ vg/kg, 5.6 x 10¹³ vg/kg, 5.7 x 10¹³ vg/kg, 5.8 x 10¹³ vg/kg, 5.9 x 10¹³ vg/kg, 6 x 10¹³ vg/kg, 6.1 x 10¹³ vg/kg, 6.2 x 10¹³ vg/kg, 6.3 x 10¹³ vg/kg, 6.4 x 10¹³ vg/kg, 6.5 x 10¹³ vg/kg, 6.6 x 10¹³ vg/kg, 6.7 x 10¹³ vg/kg, 6.8 x 10¹³ vg/kg, 6.9 x 10¹³ vg/kg, 7 x 10¹³ vg/kg, 7.1 x 10¹³ vg/kg, 7.2 x 10¹³ vg/kg, 7.3 x 10¹³ vg/kg, 7.4 x 10¹³ vg/kg, 7.5 x 10¹³ vg/kg, 7.6 x 10¹³ vg/kg, 7.7 x 10¹³ vg/kg, 7.8 x 10¹³ vg/kg, 7.9 x 10¹³ vg/kg, 8 x 10¹³ vg/kg, 8.1 x 10¹³
 35 vg/kg, 8.2 x 10¹³ vg/kg, 8.3 x 10¹³ vg/kg, 8.4 x 10¹³ vg/kg, 8.5 x 10¹³ vg/kg, 8.6 x 10¹³ vg/kg, 8.7 x 10¹³ vg/kg, 8.8 x 10¹³ vg/kg, 8.9 x 10¹³ vg/kg, 9 x 10¹³ vg/kg, 9.1 x 10¹³ vg/kg, 9.2 x 10¹³ vg/kg, 9.3 x 10¹³ vg/kg, 9.4 x 10¹³ vg/kg, 9.5 x 10¹³ vg/kg, 9.6 x 10¹³ vg/kg, 9.7 x 10¹³ vg/kg, 9.8 x 10¹³ vg/kg, 9.9 x 10¹³ vg/kg, 1 x 10¹⁴ vg/kg, 1.1 x 10¹⁴ vg/kg, 1.2 x 10¹⁴ vg/kg, 1.3 x 10¹⁴ vg/kg, 1.4 x 10¹⁴ vg/kg, 1.5 x 10¹⁴ vg/kg, 1.6 x 10¹⁴ vg/kg, 1.7 x 10¹⁴ vg/kg, 1.8 x 10¹⁴ vg/kg, 1.9 x 10¹⁴ vg/kg, or 2 x 10¹⁴ vg/kg. In some

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embodimentexamples, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 2×10^{13} vg/kg to about 7×10^{13} vg/kg, such as in an amount of from about 2×10^{13} vg/kg to about 4×10^{13} vg/kg (e.g., about 3×10^{13} vg/kg) or in an amount of from about 5×10^{13} vg/kg to about 7×10^{13} vg/kg (e.g., about 6×10^{13} vg/kg).

In some embodimentexamples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg, such as an in amount of about 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, or 2×10^{14} vg/kg.

In some embodimentexamples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 4×10^{13} vg/kg to about 2×10^{14} vg/kg, such as an in amount of about 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13}

vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, or 2×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 5×10^{13} vg/kg to about 2×10^{14} vg/kg, such as an in amount of 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, or 2×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 6×10^{13} vg/kg to about 2×10^{14} vg/kg, such as an in amount of about 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, or 2×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 7×10^{13} vg/kg to about 2×10^{14} vg/kg, such as an in amount of about 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13}

vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, or 2×10^{14} vg/kg.

In some ~~embodiment~~examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 8×10^{13} vg/kg to about 2×10^{14} vg/kg, such as an in amount of about 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, or 2×10^{14} vg/kg.

In some ~~embodiment~~examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 9×10^{13} vg/kg to about 2×10^{14} vg/kg, such as an in amount of about 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, or 2×10^{14} vg/kg.

In some ~~embodiment~~examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 1×10^{14} vg/kg to about 2×10^{14} vg/kg, such as an in amount of about 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, or 2×10^{14} vg/kg.

In some ~~embodiment~~examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 6×10^{13} vg/kg.

In some ~~embodiment~~examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body

mass index as the patient upon administration to the subject of the AAV vector in an amount of about 7×10^{13} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 8×10^{13} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 9×10^{13} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.1×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.2×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.3×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.4×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is

equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.5×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.6×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.7×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.8×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.9×10^{14} vg/kg.

In some embodiment examples of any of the preceding five aspects of the disclosure, the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 2×10^{14} vg/kg.

In some embodiment examples, the agent is administered to the patient in a single dose. In some embodiment examples, the agent is administered to the patient in two or more doses.

In some embodiment examples, the agent is administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral, intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration.

In some embodiment examples, the agent contains (i) a nucleic acid molecule encoding GAA, (ii) one or more interfering RNA molecules that collectively increase expression of endogenous GAA, (iii) one or more nucleic acid molecules encoding the one or more interfering RNA molecules, (iv) a GAA protein, and/or (v) one or more small molecules that collectively increase expression of endogenous GAA. For

example, the agent may be one that contains one or more interfering RNA molecules that comprise short interfering RNA (siRNA), short hairpin RNA (shRNA), and/or micro RNA (miRNA).

In some [embodimentexamples](#), the agent contains a nucleic acid molecule encoding GAA. The nucleic acid molecule encoding GAA may be provided to the patient, for example, by administering to the patient a viral vector that contains the nucleic acid molecule. The viral vector may be, for example, an AAV, an adenovirus, a parvovirus, a coronavirus, a rhabdovirus, a paramyxovirus, a picornavirus, an alphavirus, a herpes virus, a poxvirus, or a Retroviridae family virus.

In some [embodimentexamples](#), the nucleic acid molecule encoding GAA is provided to the patient by administering to the patient an AAV containing the nucleic acid molecule. The AAV may have, for example, a serotype selected from AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, and AAVrh74. In some [embodimentexamples](#), the AAV is a pseudotyped AAV. In some [embodimentexamples](#), the pseudotyped AAV is AAV2/8. In some [embodimentexamples](#), the AAV is a pseudotyped AAV. In some [embodimentexamples](#), the pseudotyped AAV is AAV2/9. In some [embodimentexamples](#), the AAV contains a recombinant capsid protein.

In some [embodimentexamples](#), the nucleic acid molecule encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell. The promoter may be, for example, a MCK promoter, desmin promoter, chicken beta actin promoter, CMV promoter, myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.

In some [embodimentexamples](#), the promoter is a MCK promoter. The MCK promoter may have, for example, a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some [embodimentexamples](#), the MCK promoter has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some [embodimentexamples](#), the MCK promoter has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some [embodimentexamples](#), the MCK promoter has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some [embodimentexamples](#), the MCK promoter has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 1). In some [embodimentexamples](#), the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 1). In some [embodimentexamples](#), the MCK promoter has a nucleic acid sequence that is 100% identical to SEQ ID NO: 1.

In some [embodimentexamples](#), the nucleic acid molecule encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell. For example, the

nucleic acid molecule encoding GAA may be operably linked to a CMV enhancer, a MEF2 enhancer, or a MyoD enhancer.

In some embodimentexamples, the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2. In some embodimentexamples, the GAA differs from human wild-type GAA only by way of one or more conservative amino acid substitutions. In some embodimentexample, the GAA differs from human wild-type GAA by way of one or more non-conservative amino acid substitutions.

In some embodimentexamples, the nucleic acid molecule encoding GAA has a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the nucleic acid molecule encoding GAA has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the nucleic acid molecule encoding GAA has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the nucleic acid molecule encoding GAA has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the nucleic acid molecule encoding GAA has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the nucleic acid molecule encoding GAA has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the nucleic acid molecule encoding GAA has a nucleic acid sequence that is 100% identical to SEQ ID NO: 3.

In some embodimentexample, the patient has infantile-onset Pompe disease. The patient may be, for example, from about one month to about one year of age (e.g., about one month, two months, three months, four months, five months, six months, seven months, eight months, nine months, ten months,

eleven months, or twelve months of age). In some embodimentexamples, the patient is from about one month to about six months of age (e.g., about month, two months, three months, four months, five months, or six months of age).

In some embodimentexamples, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.

In some embodimentexamples, the patient has late-onset Pompe disease. The patient may exhibit, for example, endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

In some embodimentexamples, the patient has not previously received GAA enzyme replacement therapy. In some embodimentexamples, the patient has previously received GAA enzyme replacement therapy.

In some embodimentexamples, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

In some embodimentexamples, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.

In one aspect, the disclosure provides a kit comprising an AAV vector comprising a transgene encoding GAA and a package insert, wherein the package insert instructs a user of the kit to administer the AAV vector a human patient in accordance with the use disclosed herein. In one aspect, the disclosure provides a kit comprising an agent that increases GAA expression and a package insert, wherein the package insert instructs a user of the kit to administer the agent to a human patient in accordance with the use disclosed herein. In another aspectexample, the disclosure features a kit containing (i) an AAV vector containing a transgene encoding GAA, e.g., in an amount specified above, or (ii) an agent that increases GAA expression, e.g., in an amount specified above. The kit may further contain, for example, a package insert that instructs a user of the kit to administer the AAV vector or agent to a human patient in accordance with the method of any of the above aspectexamples of the disclosure.

In one aspect, the disclosure provides use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for treating Pompe disease in a human patient in need thereof, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. In another aspectexample, the disclosure features a use of an AAV vector containing a transgene encoding GAA in the manufacture of a medicament for treating Pompe disease in a human patient in need thereof, wherein the medicament contains the AAV vector in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg (e.g., in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg). For example, the medicament may contain the AAV vector in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13}

vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

In another aspect, the disclosure provides use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for improving muscle function in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. In another ~~aspect~~example, the disclosure features a use of an AAV vector containing a transgene encoding GAA in the manufacture of a medicament for improving muscle function in a human patient diagnosed as having Pompe disease, wherein the medicament contains the AAV vector in an amount of from about 1×10^{13} vg/kg to about 5×10^{14} vg/kg (e.g., in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg). For example, the medicament may contain the AAV vector in an amount of about 1×10^{13} vg/kg, 1.1×10^{13} vg/kg, 1.2×10^{13} vg/kg, 1.3×10^{13} vg/kg, 1.4×10^{13} vg/kg, 1.5×10^{13} vg/kg, 1.6×10^{13} vg/kg, 1.7×10^{13} vg/kg, 1.8×10^{13} vg/kg, 1.9×10^{13} vg/kg, 2×10^{13} vg/kg, 2.1×10^{13} vg/kg, 2.2×10^{13} vg/kg, 2.3×10^{13} vg/kg, 2.4×10^{13} vg/kg, 2.5×10^{13} vg/kg, 2.6×10^{13} vg/kg, 2.7×10^{13} vg/kg, 2.8×10^{13} vg/kg, 2.9×10^{13} vg/kg, 3×10^{13} vg/kg, 3.1×10^{13} vg/kg, 3.2×10^{13} vg/kg, 3.3×10^{13} vg/kg, 3.4×10^{13} vg/kg, 3.5×10^{13} vg/kg, 3.6×10^{13} vg/kg, 3.7×10^{13} vg/kg, 3.8×10^{13} vg/kg, 3.9×10^{13} vg/kg, 4×10^{13} vg/kg, 4.1×10^{13} vg/kg, 4.2×10^{13} vg/kg, 4.3×10^{13} vg/kg, 4.4×10^{13} vg/kg, 4.5×10^{13} vg/kg, 4.6×10^{13} vg/kg, 4.7×10^{13} vg/kg, 4.8×10^{13} vg/kg, 4.9×10^{13} vg/kg, 5×10^{13} vg/kg, 5.1×10^{13} vg/kg, 5.2×10^{13} vg/kg, 5.3×10^{13} vg/kg, 5.4×10^{13} vg/kg, 5.5×10^{13} vg/kg, 5.6×10^{13} vg/kg, 5.7×10^{13} vg/kg, 5.8×10^{13} vg/kg, 5.9×10^{13} vg/kg, 6×10^{13} vg/kg, 6.1×10^{13} vg/kg, 6.2×10^{13} vg/kg, 6.3×10^{13} vg/kg, 6.4×10^{13} vg/kg, 6.5×10^{13} vg/kg, 6.6×10^{13} vg/kg, 6.7×10^{13} vg/kg, 6.8×10^{13} vg/kg, 6.9×10^{13} vg/kg, 7×10^{13} vg/kg, 7.1×10^{13} vg/kg, 7.2×10^{13} vg/kg, 7.3×10^{13} vg/kg, 7.4×10^{13} vg/kg, 7.5×10^{13} vg/kg, 7.6×10^{13} vg/kg, 7.7×10^{13} vg/kg, 7.8×10^{13} vg/kg, 7.9×10^{13} vg/kg, 8×10^{13} vg/kg, 8.1×10^{13} vg/kg, 8.2×10^{13} vg/kg, 8.3×10^{13} vg/kg, 8.4×10^{13} vg/kg, 8.5×10^{13} vg/kg, 8.6×10^{13} vg/kg, 8.7×10^{13} vg/kg, 8.8×10^{13} vg/kg, 8.9×10^{13} vg/kg, 9×10^{13} vg/kg, 9.1×10^{13} vg/kg, 9.2×10^{13} vg/kg, 9.3×10^{13} vg/kg, 9.4×10^{13} vg/kg, 9.5×10^{13} vg/kg, 9.6×10^{13} vg/kg, 9.7×10^{13} vg/kg, 9.8×10^{13} vg/kg, 9.9×10^{13} vg/kg, 1×10^{14} vg/kg, 1.1×10^{14} vg/kg, 1.2×10^{14} vg/kg, 1.3×10^{14} vg/kg, 1.4×10^{14} vg/kg, 1.5×10^{14} vg/kg, 1.6×10^{14} vg/kg, 1.7×10^{14} vg/kg, 1.8×10^{14} vg/kg, 1.9×10^{14} vg/kg, 2×10^{14} vg/kg, 2.1×10^{14} vg/kg, 2.2×10^{14} vg/kg, 2.3×10^{14} vg/kg, 2.4×10^{14} vg/kg, 2.5×10^{14} vg/kg, 2.6×10^{14} vg/kg, 2.7×10^{14} vg/kg, 2.8×10^{14} vg/kg, 2.9×10^{14} vg/kg, 3×10^{14} vg/kg, 3.1×10^{14} vg/kg, 3.2×10^{14} vg/kg, 3.3×10^{14} vg/kg, 3.4×10^{14} vg/kg, 3.5×10^{14} vg/kg, 3.6×10^{14} vg/kg, 3.7×10^{14} vg/kg, 3.8×10^{14} vg/kg, 3.9×10^{14} vg/kg, 4×10^{14} vg/kg, 4.1×10^{14} vg/kg, 4.2×10^{14} vg/kg, 4.3×10^{14} vg/kg, 4.4×10^{14} vg/kg, 4.5×10^{14} vg/kg, 4.6×10^{14} vg/kg, 4.7×10^{14} vg/kg, 4.8×10^{14} vg/kg, 4.9×10^{14} vg/kg, or 5×10^{14} vg/kg.

In another aspect, the disclosure provides use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg. In another ~~aspect~~example, the disclosure features a use of an AAV vector containing a transgene encoding GAA in the manufacture of a medicament for reducing glycogen accumulation (e.g., in muscle and/or neuronal tissue) in a human patient diagnosed as having Pompe disease, wherein the

5 vg/kg, 6.5 x 10¹³ vg/kg, 6.6 x 10¹³ vg/kg, 6.7 x 10¹³ vg/kg, 6.8 x 10¹³ vg/kg, 6.9 x 10¹³ vg/kg, 7 x 10¹³ vg/kg, 7.1 x 10¹³ vg/kg, 7.2 x 10¹³ vg/kg, 7.3 x 10¹³ vg/kg, 7.4 x 10¹³ vg/kg, 7.5 x 10¹³ vg/kg, 7.6 x 10¹³ vg/kg, 7.7 x 10¹³ vg/kg, 7.8 x 10¹³ vg/kg, 7.9 x 10¹³ vg/kg, 8 x 10¹³ vg/kg, 8.1 x 10¹³ vg/kg, 8.2 x 10¹³ vg/kg, 8.3 x 10¹³ vg/kg, 8.4 x 10¹³ vg/kg, 8.5 x 10¹³ vg/kg, 8.6 x 10¹³ vg/kg, 8.7 x 10¹³ vg/kg, 8.8 x 10¹³ vg/kg, 8.9 x 10¹³ vg/kg, 9 x 10¹³ vg/kg, 9.1 x 10¹³ vg/kg, 9.2 x 10¹³ vg/kg, 9.3 x 10¹³ vg/kg, 9.4 x 10¹³ vg/kg, 9.5 x 10¹³ vg/kg, 9.6 x 10¹³ vg/kg, 9.7 x 10¹³ vg/kg, 9.8 x 10¹³ vg/kg, 9.9 x 10¹³ vg/kg, 1 x 10¹⁴ vg/kg, 1.1 x 10¹⁴ vg/kg, 1.2 x 10¹⁴ vg/kg, 1.3 x 10¹⁴ vg/kg, 1.4 x 10¹⁴ vg/kg, 1.5 x 10¹⁴ vg/kg, 1.6 x 10¹⁴ vg/kg, 1.7 x 10¹⁴ vg/kg, 1.8 x 10¹⁴ vg/kg, 1.9 x 10¹⁴ vg/kg, 2 x 10¹⁴ vg/kg, 2.1 x 10¹⁴ vg/kg, 2.2 x 10¹⁴ vg/kg, 2.3 x 10¹⁴ vg/kg, 2.4 x 10¹⁴ vg/kg, 2.5 x 10¹⁴ vg/kg, 2.6 x 10¹⁴ vg/kg, 2.7 x 10¹⁴ vg/kg, 2.8 x 10¹⁴ vg/kg, 2.9 x 10¹⁴ vg/kg, 3 x 10¹⁴ vg/kg, 3.1 x 10¹⁴ vg/kg, 3.2 x 10¹⁴ vg/kg, 3.3 x 10¹⁴ vg/kg, 3.4 x 10¹⁴ vg/kg, 3.5 x 10¹⁴ vg/kg, 3.6 x 10¹⁴ vg/kg, 3.7 x 10¹⁴ vg/kg, 3.8 x 10¹⁴ vg/kg, 3.9 x 10¹⁴ vg/kg, 4 x 10¹⁴ vg/kg, 4.1 x 10¹⁴ vg/kg, 4.2 x 10¹⁴ vg/kg, 4.3 x 10¹⁴ vg/kg, 4.4 x 10¹⁴ vg/kg, 4.5 x 10¹⁴ vg/kg, 4.6 x 10¹⁴ vg/kg, 4.7 x 10¹⁴ vg/kg, 4.8 x 10¹⁴ vg/kg, 4.9 x 10¹⁴ vg/kg, or 5 x 10¹⁴ vg/kg.

15 In one aspect, the disclosure provides use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for increasing GAA expression in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1 x 10¹³ vg/kg to about 3 x 10¹⁴ vg/kg. In another aspectexample, the disclosure features a use of an AAV vector containing a transgene encoding GAA in the manufacture of a medicament for increasing GAA expression in a human patient diagnosed as having Pompe disease, wherein the medicament

20 contains the AAV vector in an amount of from about 1 x 10¹³ vg/kg to about 5 x 10¹⁴ vg/kg (e.g., in an amount of from about 1 x 10¹³ vg/kg to about 3 x 10¹⁴ vg/kg). For example, the medicament may contain the AAV vector in an amount of about 1 x 10¹³ vg/kg, 1.1 x 10¹³ vg/kg, 1.2 x 10¹³ vg/kg, 1.3 x 10¹³ vg/kg, 1.4 x 10¹³ vg/kg, 1.5 x 10¹³ vg/kg, 1.6 x 10¹³ vg/kg, 1.7 x 10¹³ vg/kg, 1.8 x 10¹³ vg/kg, 1.9 x 10¹³ vg/kg, 2 x 10¹³ vg/kg, 2.1 x 10¹³ vg/kg, 2.2 x 10¹³ vg/kg, 2.3 x 10¹³ vg/kg, 2.4 x 10¹³ vg/kg, 2.5 x 10¹³ vg/kg, 2.6 x 10¹³ vg/kg, 2.7 x 10¹³ vg/kg, 2.8 x 10¹³ vg/kg, 2.9 x 10¹³ vg/kg, 3 x 10¹³ vg/kg, 3.1 x 10¹³ vg/kg, 3.2 x 10¹³ vg/kg, 3.3 x 10¹³ vg/kg, 3.4 x 10¹³ vg/kg, 3.5 x 10¹³ vg/kg, 3.6 x 10¹³ vg/kg, 3.7 x 10¹³ vg/kg, 3.8 x 10¹³ vg/kg, 3.9 x 10¹³ vg/kg, 4 x 10¹³ vg/kg, 4.1 x 10¹³ vg/kg, 4.2 x 10¹³ vg/kg, 4.3 x 10¹³ vg/kg, 4.4 x 10¹³ vg/kg, 4.5 x 10¹³ vg/kg, 4.6 x 10¹³ vg/kg, 4.7 x 10¹³ vg/kg, 4.8 x 10¹³ vg/kg, 4.9 x 10¹³ vg/kg, 5 x 10¹³ vg/kg, 5.1 x 10¹³ vg/kg, 5.2 x 10¹³ vg/kg, 5.3 x 10¹³ vg/kg, 5.4 x 10¹³ vg/kg, 5.5 x 10¹³ vg/kg, 5.6 x 10¹³ vg/kg, 5.7 x 10¹³ vg/kg, 5.8 x 10¹³ vg/kg, 5.9 x 10¹³ vg/kg, 6 x 10¹³ vg/kg, 6.1 x 10¹³ vg/kg, 6.2 x 10¹³ vg/kg, 6.3 x 10¹³ vg/kg, 6.4 x 10¹³ vg/kg, 6.5 x 10¹³ vg/kg, 6.6 x 10¹³ vg/kg, 6.7 x 10¹³ vg/kg, 6.8 x 10¹³ vg/kg, 6.9 x 10¹³ vg/kg, 7 x 10¹³ vg/kg, 7.1 x 10¹³ vg/kg, 7.2 x 10¹³ vg/kg, 7.3 x 10¹³ vg/kg, 7.4 x 10¹³ vg/kg, 7.5 x 10¹³ vg/kg, 7.6 x 10¹³ vg/kg, 7.7 x 10¹³ vg/kg, 7.8 x 10¹³ vg/kg, 7.9 x 10¹³ vg/kg, 8 x 10¹³ vg/kg, 8.1 x 10¹³ vg/kg, 8.2 x 10¹³ vg/kg, 8.3 x 10¹³ vg/kg, 8.4 x 10¹³ vg/kg, 8.5 x 10¹³ vg/kg, 8.6 x 10¹³ vg/kg, 8.7 x 10¹³ vg/kg, 8.8 x 10¹³ vg/kg, 8.9 x 10¹³ vg/kg, 9 x 10¹³ vg/kg, 9.1 x 10¹³ vg/kg, 9.2 x 10¹³ vg/kg, 9.3 x 10¹³ vg/kg, 9.4 x 10¹³ vg/kg, 9.5 x 10¹³ vg/kg, 9.6 x 10¹³ vg/kg, 9.7 x 10¹³ vg/kg, 9.8 x 10¹³ vg/kg, 9.9 x 10¹³ vg/kg, 1 x 10¹⁴ vg/kg, 1.1 x 10¹⁴ vg/kg, 1.2 x 10¹⁴ vg/kg, 1.3 x 10¹⁴ vg/kg, 1.4 x 10¹⁴ vg/kg, 1.5 x 10¹⁴ vg/kg, 1.6 x 10¹⁴ vg/kg, 1.7 x 10¹⁴ vg/kg, 1.8 x 10¹⁴ vg/kg, 1.9 x 10¹⁴ vg/kg, 2 x 10¹⁴ vg/kg, 2.1 x 10¹⁴ vg/kg, 2.2 x 10¹⁴ vg/kg, 2.3 x 10¹⁴ vg/kg, 2.4 x 10¹⁴ vg/kg, 2.5 x 10¹⁴ vg/kg, 2.6 x 10¹⁴ vg/kg, 2.7 x 10¹⁴ vg/kg, 2.8 x 10¹⁴ vg/kg, 2.9 x 10¹⁴ vg/kg, 3 x 10¹⁴ vg/kg, 3.1 x 10¹⁴ vg/kg, 3.2 x 10¹⁴ vg/kg, 3.3 x 10¹⁴ vg/kg, 3.4 x 10¹⁴ vg/kg, 3.5 x 10¹⁴ vg/kg, 3.6 x 10¹⁴ vg/kg, 3.7 x 10¹⁴ vg/kg, 3.8 x 10¹⁴ vg/kg, 3.9 x 10¹⁴ vg/kg, 4 x 10¹⁴ vg/kg.

In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 1.2×10^{14} vg/kg.

In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 1.3×10^{14} vg/kg.

5 In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 1.4×10^{14} vg/kg.

In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 1.5×10^{14} vg/kg.

10 In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 1.6×10^{14} vg/kg.

In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 1.7×10^{14} vg/kg.

In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 1.8×10^{14} vg/kg.

15 In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 1.9×10^{14} vg/kg.

In some embodimentexamples of any of the preceding five aspects of the disclosure, the medicament contains the AAV vector in an amount of about 2×10^{14} vg/kg.

20 In some embodimentexamples, the AAV vector is formulated for administration to the patient in a single dose containing the amount. In some embodimentexamples, the AAV vector is formulated for administration to the patient in two or more doses that, together, total the specified amount (e.g., in two, three, four, five, six, seven, eight, nine, or ten doses that, together, total the specified amount). In some embodimentexamples, the AAV vector is formulated for administration to the patient in two or more doses that each, individually, contain the specified amount (e.g., in two, three, four, five, six, seven, eight, nine, or ten doses that each, individually, contain the specified amount).

30 In some embodimentexamples, the AAV vector is formulated for intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral, intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration to the patient. For example, the AAV vector may be formulated for intravenous, intrathecal, intracisternal, intracerebroventricular, and/or intramuscular administration to the patient. In some embodimentexamples, the AAV vector is formulated for intravenous and/or intrathecal administration to the patient. The AAV vector may be, for example, formulated for intravenous administration to the patient.

35 In some embodimentexamples, the AAV is an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAVrh74, AAVrh.8, or AAVrh.10 serotype. In some embodimentexamples, the AAV is a pseudotyped AAV, such as an AAV2/8 or AAV2/9. In some embodimentexamples, the AAV contains a recombinant capsid protein.

40 In some embodimentexamples, the transgene encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell. The promoter may be, for example, a MCK promoter, desmin promoter, chicken beta actin promoter, CMV promoter, myosin light chain-2 promoter,

alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.

In some embodimentexamples, the promoter is a MCK promoter. The MCK promoter may have, for example, a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1 (e.g., a nucleic acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 1). In some embodimentexamples, the MCK promoter has a nucleic acid sequence that is 100% identical to SEQ ID NO: 1.

In some embodimentexamples, the transgene encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell. For example, the transgene encoding GAA may be operably linked to a CMV enhancer, a MEF2 enhancer, or a MyoD enhancer.

In some embodimentexamples, the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2 (e.g., an amino acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 2). In some embodimentexamples, the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2. In some embodimentexamples, the GAA differs from human wild-type GAA only by way of one or more conservative amino acid substitutions. In some embodimentexamples, the GAA differs from human wild-type GAA by way of one or more non-conservative amino acid substitutions.

In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 97%, 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 98%, 99%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 3 (e.g., a nucleic acid sequence that is 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8%, 99.9%, or 100% identical to SEQ ID NO: 3). In some embodimentexamples, the transgene encoding GAA has a nucleic acid sequence that is 100% identical to SEQ ID NO: 3.

In some embodimentexamples, the patient has infantile-onset Pompe disease. The patient may be, for example, from about one month to about one year of age (e.g., about one month, two months, three months, four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, or twelve months of age). In some embodimentexamples, the patient is from about one month to about six months of age (e.g., about month, two months, three months, four months, five months, or six months of age).

In some embodimentexamples, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.

In some embodimentexamples, the patient has late-onset Pompe disease. The patient may exhibit, for example, endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

In some embodimentexamples, the patient has not previously received GAA enzyme replacement therapy. In some embodimentexamples, the patient has previously received GAA enzyme replacement therapy.

In some embodimentexamples, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.

In some embodimentexamples, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.

Brief Description of the Drawings

FIGS. 1A and 1B are graphs showing changes in acid alpha-glucosidase (GAA) protein expression and enzymatic activity levels, respectively, in muscles of mice treated with an AAV2/8 vector

Claims

1. Use of an adeno-associated viral (AAV) vector comprising a transgene encoding acid alpha-glucosidase (GAA) in the manufacture of a medicament for ~~A method of~~ treating Pompe disease in a human patient in need thereof, ~~the method comprising administering to the patient an adeno-associated viral (AAV) vector comprising a transgene encoding acid alpha-glucosidase (GAA),~~ wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
2. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for ~~A method of~~ improving muscle function in a human patient diagnosed as having Pompe disease, ~~the method comprising administering to the patient an AAV vector comprising a transgene encoding GAA,~~ wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
3. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for ~~A method of~~ reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, ~~the method comprising administering to the patient an AAV vector comprising a transgene encoding GAA,~~ wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
4. ~~The method of claim 3, wherein administration of the AAV vector to the patient reduces glycogen accumulation in muscle tissue and/or in neuronal tissue.~~
- 5.4. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for ~~A method of~~ improving pulmonary function in a human patient diagnosed as having Pompe disease, ~~the method comprising administering to the patient an AAV vector comprising a transgene encoding GAA,~~ wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
- 6.5. Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for ~~A method of~~ increasing GAA expression in a human patient diagnosed as having Pompe disease, ~~the method comprising administering to the patient an AAV vector comprising a transgene encoding GAA,~~ wherein the AAV vector is to be administered to the patient in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.
7. ~~The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of from about 2×10^{13} vg/kg to about 2×10^{14} vg/kg.~~
8. ~~The method of claim 7, wherein the AAV vector is administered to the patient in an amount of from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg.~~
9. ~~The method of claim 8, wherein the AAV vector is administered to the patient in an amount of from about 4×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

10. — The method of claim 9, wherein the AAV vector is administered to the patient in an amount of from about 5×10^{13} vg/kg to about 2×10^{14} vg/kg.

11. — The method of claim 10, wherein the AAV vector is administered to the patient in an amount of from about 6×10^{13} vg/kg to about 2×10^{14} vg/kg.

12. — The method of claim 11, wherein the AAV vector is administered to the patient in an amount of from about 7×10^{13} vg/kg to about 2×10^{14} vg/kg.

13. — The method of claim 12, wherein the AAV vector is administered to the patient in an amount of from about 8×10^{13} vg/kg to about 2×10^{14} vg/kg.

14. — The method of claim 13, wherein the AAV vector is administered to the patient in an amount of from about 9×10^{13} vg/kg to about 2×10^{14} vg/kg.

15. — The method of claim 14, wherein the AAV vector is administered to the patient in an amount of from about 1×10^{14} vg/kg to about 2×10^{14} vg/kg.

16. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 3×10^{13} vg/kg.

17. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 4×10^{13} vg/kg.

18. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 5×10^{13} vg/kg.

19. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 6×10^{13} vg/kg.

20. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 7×10^{13} vg/kg.

21. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 8×10^{13} vg/kg.

22. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 9×10^{13} vg/kg.

23. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1×10^{14} vg/kg.

24. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.1×10^{14} vg/kg.

25. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.2×10^{14} vg/kg.

~~26. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.3×10^{14} vg/kg.~~

~~27. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.4×10^{14} vg/kg.~~

~~28. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.5×10^{14} vg/kg.~~

~~29. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.6×10^{14} vg/kg.~~

~~30. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.7×10^{14} vg/kg.~~

~~31. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.8×10^{14} vg/kg.~~

~~32. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 1.9×10^{14} vg/kg.~~

~~33. — The method of any one of claims 1-6, wherein the AAV vector is administered to the patient in an amount of about 2×10^{14} vg/kg.~~

~~34. — The method of any one of claims 1-33, wherein the AAV vector is administered to the patient in a single dose comprising the amount.~~

~~35. — The method of any one of claims 1-33, wherein the AAV vector is administered to the patient in two or more doses that, together, comprise the amount.~~

~~36. — The method of claim 35, wherein the AAV vector is administered to the patient in from two doses to ten doses that, together, comprise the amount.~~

~~37. — The method of claim 36, wherein the AAV vector is administered to the patient in two, three, or four doses that, together, comprise the amount.~~

~~38. — The method of claim 37, wherein the AAV vector is administered to the patient in two doses that, together, comprise the amount.~~

~~39. — The method of any one of claims 35-38, wherein the two or more doses are separated from one another by one year or more.~~

~~40. — The method of any one of claims 35-38, wherein the two or more doses are administered to the patient within about 12 months of one another.~~

~~41. — The method of claim 40, wherein the two or more doses are administered to the patient within from about one week to about 48 weeks of one another.~~

~~42. — The method of claim 41, wherein the two or more doses are administered to the patient within from about two weeks to about 44 weeks of one another.~~

~~43. — The method of claim 42, wherein the two or more doses are administered to the patient within from about three weeks to about 40 weeks of one another.~~

~~44. — The method of claim 43, wherein the two or more doses are administered to the patient within from about four weeks to about 36 weeks of one another.~~

~~45. — The method of claim 44, wherein the two or more doses are administered to the patient within from about five weeks to about 32 weeks of one another.~~

~~46. — The method of claim 45, wherein the two or more doses are administered to the patient within from about six weeks to about 24 weeks of one another.~~

~~47. — The method of claim 46, wherein the two or more doses are administered to the patient within from about 12 weeks to about 20 weeks of one another.~~

~~48. — The method of claim 47, wherein the two or more doses are administered to the patient within about 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, or 19 weeks of one another.~~

~~49. — The method of any one of claims 1-33, wherein the AAV vector is administered to the patient in two or more doses that each, individually, comprise the amount.~~

~~50. — The method of claim 49, wherein the AAV vector is administered to the patient in from two doses to ten doses that each, individually, comprise the amount.~~

~~51. — The method of claim 50, wherein the AAV vector is administered to the patient in two, three, or four doses that each, individually, comprise the amount.~~

~~52. — The method of claim 51, wherein the AAV vector is administered to the patient in two doses that each, individually, comprise the amount.~~

~~53. — The method of any one of claims 49-52, wherein the two or more doses are separated from one another by one year or more.~~

~~54. — The method of any one of claims 49-52, wherein the two or more doses are administered to the patient within about 12 months of one another.~~

~~55. — The method of claim 54, wherein the two or more doses are administered to the patient within from about one week to about 48 weeks of one another.~~

~~56. — The method of claim 55, wherein the two or more doses are administered to the patient within from about two weeks to about 44 weeks of one another.~~

~~57. — The method of claim 56, wherein the two or more doses are administered to the patient within from about three weeks to about 40 weeks of one another.~~

~~58. — The method of claim 57, wherein the two or more doses are administered to the patient within from about four weeks to about 36 weeks of one another.~~

~~59. — The method of claim 58, wherein the two or more doses are administered to the patient within from about five weeks to about 32 weeks of one another.~~

~~60. — The method of claim 59, wherein the two or more doses are administered to the patient within from about six weeks to about 24 weeks of one another.~~

~~61. — The method of claim 60, wherein the two or more doses are administered to the patient within from about 12 weeks to about 20 weeks of one another.~~

~~62. — The method of claim 61, wherein the two or more doses are administered to the patient within about 13 weeks, 14 weeks, 15 weeks, 16 weeks, 17 weeks, 18 weeks, or 19 weeks of one another.~~

~~63. — The method of any one of claims 1-62, wherein the AAV vector is administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral, intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration.~~

~~64. — The method of claim 63, wherein the AAV vector is administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, and/or intramuscular administration.~~

~~65. — The method of claim 64, wherein the AAV vector is administered to the patient by way of intravenous and/or intrathecal administration.~~

~~66. — The method of claim 65, wherein the AAV vector is administered to the patient by way of intravenous administration.~~

~~67. — The method of any one of claims 1-66, wherein the AAV is an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAVrh74, AAVrh.8, or AAVrh.10 serotype.~~

~~68. — The method of claim 67, wherein the AAV is a pseudotyped AAV.~~

~~69. — The method of claim 68, wherein the pseudotyped AAV is AAV2/8.~~

~~70. — The method of claim 69, wherein the pseudotyped AAV is AAV2/9.~~

~~71. The method of any one of claims 1-66, wherein the AAV comprises a recombinant capsid protein.~~

~~72. The method of any one of claims 1-71, wherein the transgene encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell.~~

~~73. The method of claim 72, wherein the promoter is a muscle creatine kinase (MCK) promoter, desmin promoter, chicken beta actin promoter, cytomegalovirus (CMV) promoter, myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺-exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.~~

~~74. The method of claim 73, wherein the promoter is a MCK promoter.~~

~~75. The method of claim 74, wherein the MCK promoter has a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 1.~~

~~76. The method of claim 75, wherein the MCK promoter has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 1.~~

~~77. The method of claim 76, wherein the MCK promoter has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 1.~~

~~78. The method of claim 77, wherein the MCK promoter has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 1.~~

~~79. The method of claim 78, wherein the MCK promoter has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 1.~~

~~80. The method of claim 79, wherein the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1.~~

~~81. The method of claim 80, wherein the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1.~~

~~82. The method of claim 81, wherein the MCK promoter has a nucleic acid sequence that is 100% identical to SEQ ID NO: 1.~~

~~83. The method of any one of claims 1-82, wherein the transgene encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell.~~

~~84. The method of claim 83, wherein the enhancer is a CMV enhancer, a myocyte enhancer factor 2 (MEF2) enhancer, or a MyoD enhancer.~~

~~85. The method of any one of claims 1-84, wherein the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2.~~

~~86. The method of claim 85, wherein the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2.~~

~~87. The method of claim 86, wherein the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2.~~

~~88. The method of claim 87, wherein the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2.~~

~~89. The method of claim 88, wherein the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2.~~

~~90. The method of claim 89, wherein the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2.~~

~~91. The method of claim 90, wherein the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2.~~

~~92. The method of any one of claims 1-91, wherein the patient has infantile-onset Pompe disease.~~

~~93. The method of claim 92, wherein the patient is from about one month to about one year of age.~~

~~94. The method of claim 93, wherein the patient is from about one month to about six months of age.~~

~~95. The method of any one of claims 92-94, wherein, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.~~

~~96. The method of any one of claims 1-91, wherein the patient has late-onset Pompe disease.~~

~~97. The method of claim 96, wherein the patient exhibits endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.~~

~~98. The method of any one of claims 1-97, wherein the patient has not previously received GAA enzyme replacement therapy.~~

~~99. The method of any one of claims 1-98, wherein the patient has previously received GAA enzyme replacement therapy.~~

~~100. The method of any one of claims 1-99, wherein, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.~~

~~101. The method of any one of claims 1-100, wherein, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.~~

102.6. Use of an agent that increases GAA expression in the manufacture of a medicament for A~~method of~~ treating Pompe disease in a human patient in need thereof, ~~the method comprising administering to the patient an agent that increases GAA expression,~~ wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

103.7. Use of an agent that increases GAA expression in the manufacture of a medicament for A~~method of~~ improving muscle function in a human patient diagnosed as having Pompe disease, ~~the method comprising administering to the patient an agent that increases GAA expression,~~ wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

104.8. Use of an agent that increases GAA expression in the manufacture of a medicament for A~~method of~~ reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, ~~the method comprising administering to the patient an agent that increases GAA expression,~~ wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

~~105. The method of claim 104, wherein administration of the agent to the patient reduces glycogen accumulation in muscle tissue and/or in neuronal tissue.~~

106.9. Use of an agent that increases GAA expression in the manufacture of a medicament for A~~method of~~ improving pulmonary function in a human patient diagnosed as having Pompe disease, ~~the~~

~~method comprising administering to the patient an agent that increases GAA expression,~~ wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

~~107.10. Use of an agent that increases GAA expression in the manufacture of a medicament for A method of~~ increasing GAA expression in a human patient diagnosed as having Pompe disease, ~~the method comprising administering to the patient an agent that increases GAA expression,~~ wherein the agent is to be administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in a human subject of the same gender and similar body mass index as the patient upon administration to the subject of an AAV2/8 vector comprising a transgene encoding GAA in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg, wherein the transgene encoding GAA is operably linked to a MCK promoter.

~~108. The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 2×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~109. The method of claim 108, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~110. The method of claim 109, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 4×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~111. The method of claim 110, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 5×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~112. The method of claim 111, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon~~

administration to the subject of the AAV vector in an amount of from about 6×10^{13} vg/kg to about 2×10^{14} vg/kg.

113. — The method of claim 112, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 7×10^{13} vg/kg to about 2×10^{14} vg/kg.

114. — The method of claim 113, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 8×10^{13} vg/kg to about 2×10^{14} vg/kg.

115. — The method of claim 114, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 9×10^{13} vg/kg to about 2×10^{14} vg/kg.

116. — The method of claim 115, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of from about 1×10^{14} vg/kg to about 2×10^{14} vg/kg.

117. — The method of any one of claims 102–107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 3×10^{13} vg/kg.

118. — The method of any one of claims 102–107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 4×10^{13} vg/kg.

119. — The method of any one of claims 102–107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA

activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 5×10^{13} vg/kg.

120. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 6×10^{13} vg/kg.

121. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 7×10^{13} vg/kg.

122. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 8×10^{13} vg/kg.

123. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 9×10^{13} vg/kg.

124. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1×10^{14} vg/kg.

125. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.1×10^{14} vg/kg.

126. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.2×10^{14} vg/kg.

127. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA

activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.3×10^{14} vg/kg.

128. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.4×10^{14} vg/kg.

129. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.5×10^{14} vg/kg.

130. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.6×10^{14} vg/kg.

131. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.7×10^{14} vg/kg.

132. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.8×10^{14} vg/kg.

133. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 1.9×10^{14} vg/kg.

134. — The method of any one of claims 102-107, wherein the agent is administered to the patient in an amount sufficient to achieve a level of GAA activity in the patient that is equivalent to a level of GAA activity observed in the human subject of the same gender and similar body mass index as the patient upon administration to the subject of the AAV vector in an amount of about 2×10^{14} vg/kg.

135. — The method of any one of claims 102-134, wherein the agent is administered to the patient in a single dose.

~~136. —The method of any one of claims 102-134, wherein the agent is administered to the patient in two or more doses.~~

~~137. —The method of any one of claims 102-136, wherein the agent is administered to the patient by way of intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral, intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration.~~

~~138. —The method of any one of claims 102-137, wherein the agent comprises (i) a nucleic acid molecule encoding GAA, (ii) one or more interfering RNA molecules that collectively increase expression of endogenous GAA, (iii) one or more nucleic acid molecules encoding the one or more interfering RNA molecules, (iv) a GAA protein, and/or (v) one or more small molecules that collectively increase expression of endogenous GAA.~~

~~139. —The method of claim 138, wherein the one or more interfering RNA molecules comprise short interfering RNA (siRNA), short hairpin RNA (shRNA), and/or micro RNA (miRNA).~~

~~140. —The method of claim 139, wherein the agent comprises a nucleic acid molecule encoding GAA.~~

~~141. —The method of claim 140, wherein the nucleic acid molecule is provided to the patient by administering to the patient a viral vector that comprises the nucleic acid molecule.~~

~~142. —The method of claim 141, wherein the viral vector is an AAV, an adenovirus, a parvovirus, a coronavirus, a rhabdovirus, a paramyxovirus, a picornavirus, an alphavirus, a herpes virus, a poxvirus, or a Retroviridae family virus.~~

~~143. —The method of claim 142, wherein the viral vector is an AAV.~~

~~144. —The method of claim 143, wherein the AAV has a serotype selected from AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, and AAVrh74.~~

~~145. —The method of claim 143, wherein the AAV is a pseudotyped AAV.~~

~~146. —The method of claim 145, wherein the pseudotyped AAV is AAV2/8.~~

~~147. —The method of claim 145, wherein the pseudotyped AAV is AAV2/9.~~

~~148. —The method of claim 143, wherein the AAV comprises a recombinant capsid protein.~~

~~149. —The method of any one of claims 138-148, wherein the nucleic acid molecule encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell.~~

~~150. The method of claim 149, wherein the promoter is a muscle MCK promoter, desmin promoter, chicken beta actin promoter, CMV promoter, myosin light chain-2 promoter, alpha actin promoter, troponin 1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.~~

~~151. The method of any one of claims 138-150, wherein the nucleic acid molecule encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell.~~

~~152. The method of claim 151, wherein the enhancer is a CMV enhancer, a MEF2 enhancer, or a MyoD enhancer.~~

~~153. The method of any one of claims 102-152, wherein the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2.~~

~~154. The method of claim 153, wherein the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2.~~

~~155. The method of claim 154, wherein the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2.~~

~~156. The method of claim 155, wherein the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2.~~

~~157. The method of claim 156, wherein the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2.~~

~~158. The method of claim 157, wherein the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2.~~

~~159. The method of claim 158, wherein the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2.~~

~~160. The method of any one of claims 102-159, wherein the patient has infantile-onset Pompe disease.~~

~~161. The method of claim 160, wherein the patient is from about one month to about one year of age.~~

~~162. The method of claim 161, wherein the patient is from about one month to about six months of age.~~

~~163. The method of any one of claims 160-162, wherein, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.~~

~~164. The method of any one of claims 102-159, wherein the patient has late-onset Pompe disease.~~

~~165. The method of claim 164, wherein the patient exhibits endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.~~

~~166. The method of any one of claims 102-165, wherein the patient has not previously received GAA enzyme replacement therapy.~~

~~167. The method of any one of claims 102-166, wherein the patient has previously received GAA enzyme replacement therapy.~~

~~168. The method of any one of claims 102-167, wherein, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.~~

~~169. The method of any one of claims 102-168, wherein, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.~~

~~170.11.~~ A kit comprising an AAV vector comprising a transgene encoding GAA and a package insert, wherein the package insert instructs a user of the kit to administer the AAV vector a human patient in accordance with the ~~method-use~~ of any one of claims 1-~~5101~~.

~~171.12.~~ A kit comprising an agent that increases GAA expression and a package insert, wherein the package insert instructs a user of the kit to administer the agent to a human patient in accordance with the ~~method-use~~ of any one of claims ~~6102-1069~~.

~~172.13.~~ Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for treating Pompe disease in a human patient in need thereof, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

~~173.14.~~ Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for improving muscle function in a human patient diagnosed as having Pompe disease,

wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

~~174.15.~~ Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for reducing glycogen accumulation in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

~~175.— The use of claim 174, wherein administration of the AAV vector to the patient reduces glycogen accumulation in muscle tissue and/or in neuronal tissue.~~

~~176.16.~~ Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for improving pulmonary function in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

~~177.17.~~ Use of an AAV vector comprising a transgene encoding GAA in the manufacture of a medicament for increasing GAA expression in a human patient diagnosed as having Pompe disease, wherein the medicament comprises the AAV vector in an amount of from about 1×10^{13} vg/kg to about 3×10^{14} vg/kg.

~~178.— The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of from about 2×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~179.— The use of claim 178, wherein the medicament comprises the AAV vector in an amount of from about 3×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~180.— The use of claim 179, wherein the medicament comprises the AAV vector in an amount of from about 4×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~181.— The use of claim 180, wherein the medicament comprises the AAV vector in an amount of from about 5×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~182.— The use of claim 181, wherein the medicament comprises the AAV vector in an amount of from about 6×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~183.— The use of claim 182, wherein the medicament comprises the AAV vector in an amount of from about 7×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~184.— The use of claim 183, wherein the medicament comprises the AAV vector in an amount of from about 8×10^{13} vg/kg to about 2×10^{14} vg/kg.~~

~~185. — The use of claim 184, wherein the medicament comprises the AAV vector in an amount of from about $9 \times 10^{+3}$ vg/kg to about $2 \times 10^{+4}$ vg/kg.~~

~~186. — The use of claim 185, wherein the medicament comprises the AAV vector in an amount of from about $1 \times 10^{+4}$ vg/kg to about $2 \times 10^{+4}$ vg/kg.~~

~~187. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $3 \times 10^{+3}$ vg/kg.~~

~~188. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $4 \times 10^{+3}$ vg/kg.~~

~~189. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $5 \times 10^{+3}$ vg/kg.~~

~~190. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $6 \times 10^{+3}$ vg/kg.~~

~~191. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $7 \times 10^{+3}$ vg/kg.~~

~~192. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $8 \times 10^{+3}$ vg/kg.~~

~~193. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $9 \times 10^{+3}$ vg/kg.~~

~~194. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $1 \times 10^{+4}$ vg/kg.~~

~~195. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $1.1 \times 10^{+4}$ vg/kg.~~

~~196. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $1.2 \times 10^{+4}$ vg/kg.~~

~~197. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $1.3 \times 10^{+4}$ vg/kg.~~

~~198. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $1.4 \times 10^{+4}$ vg/kg.~~

~~199. — The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about $1.5 \times 10^{+4}$ vg/kg.~~

~~200.—The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.6×10^{14} vg/kg.~~

~~201.—The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.7×10^{14} vg/kg.~~

~~202.—The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.8×10^{14} vg/kg.~~

~~203.—The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 1.9×10^{14} vg/kg.~~

~~204.—The use of any one of claims 172-177, wherein the medicament comprises the AAV vector in an amount of about 2×10^{14} vg/kg.~~

~~205.—The use of any one of claims 172-204, wherein the AAV vector is formulated for administration to the patient in a single dose comprising the amount.~~

~~206.—The use of any one of claims 172-204, wherein the AAV vector is formulated for administration to the patient in two or more doses that, together, comprise the amount.~~

~~207.—The use of claim 206, wherein the AAV vector is formulated for administration to the patient in from two doses to ten doses that, together, comprise the amount.~~

~~208.—The use of claim 207, wherein the AAV vector is formulated for administration to the patient in two, three, or four doses that, together, comprise the amount.~~

~~209.—The use of claim 208, wherein the AAV vector is formulated for administration to the patient in two doses that, together, comprise the amount.~~

~~210.—The use of any one of claims 172-204, wherein the AAV vector is formulated for administration to the patient in two or more doses that each, individually, comprise the amount.~~

~~211.—The use of claim 210, wherein the AAV vector is formulated for administration to the patient in in from two doses to ten doses that each, individually, comprise the amount.~~

~~212.—The use of claim 211, wherein the AAV vector is formulated for administration to the patient in two, three, or four doses that each, individually, comprise the amount.~~

~~213.—The use of claim 212, wherein the AAV vector is formulated for administration to the patient in two doses that each, individually, comprise the amount.~~

~~214.—The use of any one of claims 172-213, wherein the AAV vector is formulated for intravenous, intrathecal, intracisternal, intracerebroventricular, intramuscular, intradermal, transdermal, parenteral,~~

~~intranasal, subcutaneous, percutaneous, intratracheal, intraperitoneal, intraarterial, intravascular, inhalation, perfusion, lavage, and/or oral administration to the patient.~~

~~215. — The use of claim 214, wherein the AAV vector is formulated for intravenous, intrathecal, intracisternal, intracerebroventricular, and/or intramuscular administration to the patient.~~

~~216. — The use of claim 215, wherein the AAV vector is formulated for intravenous and/or intrathecal administration to the patient.~~

~~217. — The use of claim 216, wherein the AAV vector is formulated for intravenous administration to the patient.~~

~~218. — The use of any one of claims 172-217, wherein the AAV is an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAVrh74, AAVrh.8, or AAVrh.10 serotype.~~

~~219. — The use of claim 218, wherein the AAV is a pseudotyped AAV.~~

~~220. — The use of claim 219, wherein the pseudotyped AAV is AAV2/8.~~

~~221. — The use of claim 219, wherein the pseudotyped AAV is AAV2/9.~~

~~222. — The use of any one of claims 172-217, wherein the AAV comprises a recombinant capsid protein.~~

~~223. — The use of any one of claims 172-222, wherein the transgene encoding GAA is operably linked to a promoter that induces expression of the transgene in a muscle and/or neuronal cell.~~

~~224. — The use of claim 223, wherein the promoter is a MCK promoter, desmin promoter, chicken beta-actin promoter, CMV promoter, myosin light chain-2 promoter, alpha-actin promoter, troponin-1 promoter, Na⁺/Ca²⁺ exchanger promoter, dystrophin promoter, alpha7 integrin promoter, brain natriuretic peptide promoter, alpha-B-crystallin/small heat shock protein promoter, alpha myosin heavy chain promoter, or atrial natriuretic factor promoter.~~

~~225. — The use of claim 224, wherein the promoter is a MCK promoter.~~

~~226. — The use of claim 225, wherein the MCK promoter has a nucleic acid sequence that is at least 85% identical to SEQ ID NO: 1.~~

~~227. — The use of claim 226, wherein the MCK promoter has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 1.~~

~~228. — The use of claim 227, wherein the MCK promoter has a nucleic acid sequence that is at least 95% identical to SEQ ID NO: 1.~~

~~229. — The use of claim 228, wherein the MCK promoter has a nucleic acid sequence that is at least 97% identical to SEQ ID NO: 1.~~

~~230. — The use of claim 229, wherein the MCK promoter has a nucleic acid sequence that is at least 98% identical to SEQ ID NO: 1.~~

~~231. — The use of claim 230, wherein the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1.~~

~~232. — The use of claim 231, wherein the MCK promoter has a nucleic acid sequence that is at least 99% identical to SEQ ID NO: 1.~~

~~233. — The use of claim 232, wherein the MCK promoter has a nucleic acid sequence that is 100% identical to SEQ ID NO: 1.~~

~~234. — The use of any one of claims 172-233, wherein the transgene encoding GAA is operably linked to an enhancer that induces expression of the transgene in a muscle and/or neuronal cell.~~

~~235. — The use of claim 234, wherein the enhancer is a CMV enhancer, a MEF2 enhancer, or a MyoD enhancer.~~

~~236. — The use of any one of claims 172-235, wherein the GAA has an amino acid sequence that is at least 85% identical to SEQ ID NO: 2.~~

~~237. — The use of claim 236, wherein the GAA has an amino acid sequence that is at least 90% identical to SEQ ID NO: 2.~~

~~238. — The use of claim 237, wherein the GAA has an amino acid sequence that is at least 95% identical to SEQ ID NO: 2.~~

~~239. — The use of claim 238, wherein the GAA has an amino acid sequence that is at least 97% identical to SEQ ID NO: 2.~~

~~240. — The use of claim 239, wherein the GAA has an amino acid sequence that is at least 98% identical to SEQ ID NO: 2.~~

~~241. — The use of claim 240, wherein the GAA has an amino acid sequence that is at least 99% identical to SEQ ID NO: 2.~~

~~242. — The use of claim 241, wherein the GAA has an amino acid sequence that is 100% identical to SEQ ID NO: 2.~~

~~243. — The use of any one of claims 172-242, wherein the patient has infantile-onset Pompe disease.~~

~~244. The use of claim 243, wherein the patient is from about one month to about one year of age.~~

~~245. The use of claim 244, wherein the patient is from about one month to about six months of age.~~

~~246. The use of any one of claims 242-245, wherein, prior to administration of the AAV vector to the patient, the patient exhibits a symptom selected from feeding difficulties, failure to thrive, hypotonia, progressive weakness, respiratory distress, severe enlargement of the tongue, and thickening of the heart muscle.~~

~~247. The use of any one of claims 172-242, wherein the patient has late-onset Pompe disease.~~

~~248. The use of claim 247, wherein the patient exhibits endogenous GAA activity of from about 1% to about 40% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.~~

~~249. The use of any one of claims 172-248, wherein the patient has not previously received GAA enzyme replacement therapy.~~

~~250. The use of any one of claims 172-248, wherein the patient has previously received GAA enzyme replacement therapy.~~

~~251. The use of any one of claims 172-250, wherein, following administration of the AAV vector to the patient, the patient exhibits endogenous GAA activity of from about 50% to about 200% of the endogenous GAA activity of a human of the same gender and similar body mass index that does not have Pompe disease.~~

~~252. The use of any one of claims 172-251, wherein, following administration of the AAV vector to the patient, the patient exhibits a reduction in glycogen in skeletal muscle, cardiac muscle, and/or neuronal tissue.~~