

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)2/8 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 transgene encoding GAA is operably linked to a muscle creatine kinase (MCK) promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In a first 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 AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In another example, 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 AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In a further example, 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, or 5×10^{13} vg/kg.

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 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 AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In another 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.

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 AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In another 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 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 in an 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, $3.1 \times$

eleven months, or twelve months of age). In some examples, 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 examples, 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 examples, 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 examples, the patient has not previously received GAA enzyme replacement therapy. In some examples, the patient has previously received GAA enzyme replacement therapy.

In some examples, 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 examples, 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 to 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 example, 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 examples of the disclosure.

In one aspect, the disclosure provides use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In another example, 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, or 9×10^{13} vg/kg.

5 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.

10 In another aspect, the disclosure provides use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In another example, the disclosure features a use of an AAV vector containing a

15 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

20 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.

40 In another aspect, the disclosure provides use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In another 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

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 yet another aspect, the disclosure provides use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg. In another example, the disclosure features a use of an AAV vector containing 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 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 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.

In one aspect, the disclosure provides use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1 x 10¹³ vg/kg to 3 x 10¹⁴ vg/kg. In another example, 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 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.

Claims

1. Use of an adeno-associated viral (AAV)2/8 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 transgene encoding GAA is operably linked to a muscle creatine kinase (MCK) promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

2. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

3. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

4. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

5. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the AAV2/8 vector is to be administered to the patient in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

6. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

7. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

8. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

9. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.

10. Use of an AAV2/8 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 transgene encoding GAA is operably linked to an MCK promoter, and wherein the medicament comprises the AAV2/8 vector in an amount of from 1×10^{13} vg/kg to 3×10^{14} vg/kg.