CLAIMS

1. A recombinant adeno-associated virus (AAV) vector comprising an expression cassette, said expression cassette comprising a nucleic acid molecule encoding a truncated acid-alpha glucosidase (GAA) polypeptide, said truncated GAA polypeptide comprising a deletion of 1 to 75 consecutive amino acids from its N-terminal end as compared to a parent GAA polypeptide,

wherein said parent GAA polypeptide corresponds to a precursor form of a GAA polypeptide devoid of its signal peptide, and

wherein said truncated GAA polypeptide further comprises a signal peptide fused to its N-terminal end.

2. The recombinant AAV vector of claim 1, wherein said truncated GAA polypeptide has 6, 7, 8, 9, 10, 40, 41, 42, 43, 44, 45 or 46 consecutive amino acids deleted at its N-terminal end as compared to said parent GAA polypeptide, in particular 8, 42 or 43 consecutive amino acids truncated at its N-terminal end as compared to said parent GAA polypeptide.

3. The recombinant AAV vector of claim 1 or 2, wherein said parent polypeptide is a human GAA (hGAA), in particular hGAA having the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:33, in particular SEQ ID NO:1, or is a functional variant of hGAA having the amino acid sequence shown of SEQ ID NO:1 or SEQ ID NO:33, in particular SEQ ID NO:1.

4. The recombinant AAV vector of any of claims 1 to 3, wherein said truncated GAA polypeptide has the amino acid sequence of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO: 34 or SEQ ID NO:35.

5. The recombinant AAV vector of any of claims 1 to 4, wherein said fused signal peptide has the amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 and SEQ ID NO:7, in particular the signal peptide has the amino acid sequence of SEQ ID NO:3.

6. The recombinant AAV vector of any of claims 1 to 4, wherein said fused signal peptide is a functional derivative having an amino acid sequence comprising from 1 to 5, in particular from 1 to 4, in particular from 1 to 3, in particular from 1 to 2, in particular 1 amino acid deletion(s), insertion(s) or substitution(s) as compared to the sequences of SEQ ID NOs:3 to 7.

7. The recombinant AAV vector of any of claims 1 to 6, wherein said nucleic acid molecule encoding a truncated GAA polypeptide is optimized to improve the expression of and/or improve immune

tolerance to said truncated GAA polypeptide *in vivo*, said nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50 or SEQ ID NO:51.

8. The recombinant AAV vector of any of claims 1 to 7, wherein said nucleic acid molecule is operably linked to a promoter, in particular a promoter that is a liver-specific promoter preferably selected from the group consisting of the alpha-1 antitrypsin promoter (hAAT), the transthyretin promoter, the albumin promoter and the thyroxine-binding globulin (TBG) promoter, wherein said expression cassette further optionally comprises an intron, in particular an intron selected from the group consisting of a human beta globin b2 (HBB2) intron, a FIX intron, a chicken beta-globin intron, and a SV40 intron, wherein said intron is optionally a modified intron such as a modified HBB2 intron of SEQ ID NO:17, a modified FIX intron of SEQ ID NO:19, or a modified chicken beta-globin intron of SEQ ID NO:21.

9. The recombinant AAV vector of any of claims 1 to 8,wherein said expression cassette comprises, preferably in this order: an enhancer; an intron; a promoter, in particular a liver-specific promoter; said nucleic acid molecule encoding said truncated GAA polypeptide; and a polyadenylation signal, said expression cassette comprising preferably, in this order: an ApoE control region; a HBB2 intron, in particular a modified HBB2 intron; a hAAT promoter; said nucleic acid molecule encoding said truncated GAA polypeptide; and a bovine growth hormone polyadenylation signal, said expression cassette more particularly comprising the nucleotide sequence of any one of SEQ ID NO:22 to 26.

10. The recombinant AAV vector of any of claims 1 to9, wherein said recombinant AAV vector is a single-stranded or double-stranded self-complementary AAV vector, preferably an AAV vector with an AAV-derived capsid, such as an AAV1, AAV2, variant AAV2, AAV3, variant AAV3, AAV3B, variant AAV3B, AAV4, AAV5, AAV6, variant AAV6, AAV7, AAV8, AAV9, AAV10 such as AAVcy10 and AAVrh10, AAVrh74, AAVdj, AAV-Anc80, AAV-LK03, AAV2i8, and porcine AAV, such as AAVpo4 and AAVpo6 capsid or with a chimeric capsid.

11. The recombinant AAV vector of any of claims 1 to10, wherein said recombinant AAV vector has an AAV8, AAV9, AAVrh74 or AAV2i8 capsid, in particular an AAV8, AAV9 or AAVrh74 capsid, more particularly an AAV8 capsid.

12. The recombinant AAV vector of any of claims 1 to 11, wherein said nucleic acid molecule encoding said truncated GAA polypeptide is about 70 percent, about 80 percent, about 90 percent, about 95 percent, about 97 percent, about 98 percent, or about 99 percent identical to nucleotides 82-2859 of SEQ ID NO:8; or has at least 75 percent, at least 80 percent, or at least 82 percent sequence

identity to a nucleotide sequence encoding SEQ ID NO:1 or SEQ ID NO:33; or has at least 85 percent, at least 90 percent, at least 92 percent, at least 95 percent, at least 98 percent, at least 99 percent or 100 percent identity to the nucleotide sequence of SEQ ID NO:10 or SEQ ID NO:11.

13. The recombinant AAV vector of any of claims 1 to 12, comprising an expression cassette and a modified capsid, said expression cassette comprising a nucleic acid molecule encoding a truncated acid alpha-glucosidase (GAA) polypeptide comprising the amino acid sequence of SEQ ID NO:27, said truncated GAA polypeptide further comprising a signal peptide fused to its N-terminal end, said signal peptide having the amino acid sequence of SEQ ID NO:3, and said modified capsid comprising one or more variant VP capsid proteins derived from AAVrh74, or selected from the group consisting of RHM4-1, RHM15-1, RHM15-2, RHM15-3/RHM15-5, RHM15-4 and RHM15-6.

14. A cell transformed with the recombinant AAV vector of any one of claims 1 to 13, wherein said cell is in particular a liver cell or a muscle cell.

15. A pharmaceutical composition, comprising, in a pharmaceutically acceptable carrier, , the recombinant AAV vector of any one of claims 1 to 13, or the cell of claim 14.

16. The recombinant AAV vector of any one of claims 1 to 13, or the cell according to claim 14, or the pharmaceutical composition of claim 15 for use as a medicament.

17. Use of the recombinant AAV vector of any of claims 1 to 13, or the cell of claim 14, or the pharmaceutical composition of claim 15 in the manufacture of a medicament for treating a GAA deficiency, a glycogen storage disease, such as GSDI (von Gierke's disease), GSDII (Pompe disease), GSDIII (Cori disease), GSDIV, GSDV, GSDVI, GSDVII, GSDVIII and lethal congenital glycogen storage disease of the heart, more particularly GSDI, GSDII or GSDIII, even more particularly GSDII and GSDIII, and most particularly GSDII.

18. Use of the recombinant AAV vector of any of claims 1 to 13, the cell of claim 14, or the pharmaceutical composition of claim 15, in the manufacture of a medicament for treating a glycogen storage disease, while reducing immunogenicity of said truncated GAA polypeptide.