CLAIMS

1. A recombinant adeno-associated virus (rAAV) vector, comprising in its genome:
    (a) a 5’ inverted terminal repeat (ITR) and a 3’ ITR; and
    (b) located between the 5’ ITR and 3’ ITR, a liver-specific promoter operably linked to a nucleic acid, comprising:
        (i) a nucleotide sequence encoding a BM40 signal peptide; and
        (ii) a nucleotide sequence encoding an alpha-glucosidase (GAA) polypeptide comprising residues 57-952 of SEQ ID NO: 1, or an amino acid sequence at least 80%, at least 85%, or at least 90% identical thereto;

    wherein the BM40 signal peptide and the GAA polypeptide are expressed in a single fusion polypeptide.
2. The rAAV vector of claim 1, wherein the GAA polypeptide lacks an endogenous GAA signal peptide.
3. The rAAV vector of any one of the preceding claims, wherein the nucleotide sequence encoding the GAA polypeptide comprises:
    a) SEQ ID NO: 28; or
    b) a nucleotide sequence with at least 80%, at least 85%, or at least 90% sequence identity to SEQ ID NO: 28.
4. The rAAV vector of any one of the preceding claims, wherein: the nucleotide sequence encoding the GAA polypeptide is codon optimized; and/or the nucleotide sequence encoding the BM40 signal peptide is codon optimized.
5. The rAAV vector of any one of the preceding claims, wherein the liver specific promoter comprises a nucleotide sequence of one of SEQ ID NOs: 24, 60-78, 84-249, or 256-258, or a nucleotide sequence at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.
6. The rAAV vector of any one of the preceding claims, wherein the nucleotide sequence encoding the BM40 signal peptide comprises:
    (a) SEQ ID NO: 27;
    (b) a codon optimized version of SEQ ID NO: 27;
    (c) a nucleotide sequence that is at least 80%, at least 85%, or at least 90% identical to SEQ ID NO: 27; or
    (d) a fragment of (a), (b), or (c) which encodes a polypeptide with signal peptide activity.

7. The rAAV vector of any one of the preceding claims, wherein the nucleic acid has a nucleotide sequence comprising:
    (a) SEQ ID NO: 26;
    (b) a nucleotide sequence having at least 80%, or at least 85%, or at least 90% sequence identity to SEQ ID NO: 26; or
    (c) a functional fragment of (a) or (b).
8. The rAAV vector of any one of the preceding claims, wherein the genome further comprises at least one un-translated region (UTR);
    wherein the at least one UTR is a 5' UTR and/or a 3' UTR.
9. The rAAV vector of any one of the preceding claims, wherein the genome comprises a nucleotide sequence of SEQ ID NO: 22, or a nucleotide sequence at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto, or a functional fragment thereof.
10. The rAAV vector of any one of the preceding claims, wherein the genome comprises, in the 5' to 3' direction:
    (a) the 5' ITR;
    (b) the liver-specific promoter;
    (c) a 5' UTR;
    (d) the nucleic acid comprising, from 5' to 3':
        (i) the nucleotide sequence encoding the BM40 signal peptide;
        (ii) the nucleotide sequence encoding the GAA polypeptide, wherein the GAA polypeptide comprises amino acid residues 57-952 of SEQ ID NO: 1;
    (e) a 3' UTR;
    (f) a polyA signal sequence;
    and
    (g) the 3' ITR.
11. The rAAV vector of any one of the preceding claims, which is manufactured from a nucleotide sequence comprising SEQ ID NO: 20 or a nucleotide sequence having at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity thereto; and/or
    which is manufactured from a nucleotide sequence comprising SEQ ID NO: 21 or a nucleotide sequence having at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity thereto.
12. The rAAV vector of any one of the preceding claims, which is a virus particle with a capsid.

13. The rAAV vector of claim 12, wherein the capsid is from serotype AAV843/XL32.1.
14. The rAAV vector of claim 12, wherein the capsid is from serotype AAV6.
15. A pharmaceutical composition comprising the rAAV vector of any one of claims 1-14 in a pharmaceutically acceptable carrier.
16. Use of the rAAV vector of any one of claims 1-14 in the manufacture of a medicament for treating a subject with Pompe Disease, a glycogen storage disease type II (GSD II, Acid Maltase Deficiency), or a deficiency in alpha-glucosidase (GAA) polypeptide.
17. The use of claim 16, wherein the therapeutically effective amount of the rAAV vector is $1.0x10^{11}$ vector genomes per kilogram of the subject (vg/kg) to $5.0x10^{13}$ vg/kg.
18. The use of any one of claims 16-17, wherein the therapeutically effective amount of the rAAV vector is $5.0x10^{12}$ vg/kg to $2.0x10^{13}$ vg/kg.
19. A cell comprising the rAAV vector of any one of claims 1-14.
20. The cell of claim 19, which is a liver cell.