CLAIMS

1. A polynucleotide comprising a nucleic acid sequence encoding a palmitoyl-protein thioesterase-1(PPT1) polypeptide, wherein said PPT1 polypeptide comprises a PPT1 amino acid sequence having at least 95% identity to the sequence of SEQ ID NO: 1, wherein:

(a) said PPT1 polypeptide further comprises a signal sequence of any of SEQ ID NOs: 16-27 or a variant thereof having a one amino acid substitution, deletion or insertion; and/or

(b) said PPT1 amino acid sequence comprises a glycine (G), valine (V) or leucine (L) substitution for aspartic acid (D) at its amino terminus; and/or

(c) said PPT1 sequence comprises the amino acid sequence leucine-glutamine histidine-leucine at its N-terminus; and/or

(d) said nucleic acid sequence comprises a PPT1 encoding sequence having at least 85% identity to any of SEQ ID NOs: 61-94.

2. The polynucleotide of claim 1, wherein said PPT1 polypeptide further comprises said signal sequence comprising the sequence of any of SEQ ID NOs: 16-27.

3. The polynucleotide of claim 2, wherein said signal sequence comprises the sequence of SEQ ID NO: 16 and said nucleic acid sequence comprises the signal encoding sequence of SEQ ID NO: 43; or said signal peptide comprises the sequence of SEQ ID NO: 19 and said nucleic acid sequence comprises the signal encoding sequence of SEQ ID NO: 50.

4. The polynucleotide of claim 1, wherein said PPT1 amino acid sequence comprises a G, V, or L substitution for aspartic acid D at its amino terminus and said PPT1 amino acid sequence has at least 97% identity to the sequence of SEQ ID NO: 1.

5. The polynucleotide of claim 4, wherein said PPT1 amino acid sequence comprises the sequence of SEQ ID NO: 2, wherein X is G.

6. The polynucleotide of claim 3, wherein said PPT1 amino acid sequence comprises a G substitution for aspartic acid D at its amino terminus and said PPT1 amino acid sequence has at least 97% identity to the sequence of SEQ ID NO: 1.

7. The polynucleotide of claim 1, wherein said nucleic acid comprises a sequence having at least 85% identity to any of SEQ ID NOs: 61-94.

8. The polynucleotide of claim 1, wherein said PPT1 polypeptide comprises the sequence of SEQ ID NO: 31 or SEQ ID NO: 34.

9. The polynucleotide of claim 15, wherein said PPT1 polypeptide comprises the sequence of SEQ ID NO: 31 wherein X is G and said nucleic acid comprises a sequence having at least 85% identity with the sequence of any of SEQ ID NOs: 107-125 and 168.

10. The polynucleotide of claim 9, wherein said nucleic acid comprises the sequence of any of SEQ ID NOs: 107-125 and 168.

11. The polynucleotide of claim 8, wherein said PPT1 polypeptide comprises the sequence of SEQ ID NO: 34 wherein X is G and said nucleic acid comprises a sequence having at least 95% identity with the sequence of any of SEQ ID NOs: 126-140 and 161-167.

12. A palmitoyl-protein thioesterase-1(PPT1) polypeptide comprising a PPT1 amino acid sequence having at least 95% identity to the sequence of SEQ ID NO: 1, wherein:

(a) said PPT1 polypeptide further comprises a signal sequence of any of SEQ ID NOs: 16-27 or a variant thereof having a one amino acid substitution, deletion or insertion; and/or

(b) said PPT1 amino acid sequence comprises a glycine (G), valine (V) or leucine (L) substitution for aspartic acid (D) at its amino terminus; and/or

(c) said PPT1 sequence comprises the amino acid sequence leucine-glutamine- histidine-leucine at its N-terminus.

13. The polypeptide of claim 12, wherein said signal sequence comprises the sequence of any of SEQ ID NOs: 16 or 19.

14. The polypeptide of claim 13, wherein said PPT1 amino acid sequence comprises a G, V, or L substitution for aspartic acid D at its amino terminus and said PPT1 amino acid sequence has at least 97% identity to the sequence of SEQ ID NO: 1.

15. The polypeptide of claim 14, wherein said PPT1 amino acid sequence comprises the sequence of SEQ ID NO: 2, wherein X is G.

16. The polypeptide of claim 12, wherein said PPT1 polypeptide comprises the sequence of SEQ ID NO: 31 wherein X is G, SEQ ID NO: 34 wherein X is G, or SEQ ID NO: 38.

17. A polynucleotide comprising a PPT1 polypeptide encoding nucleic acid sequence, wherein said PPT1 encoding nucleic acid sequence encodes the PPT1 polypeptide of claim 12.

18. The polynucleotide of any one of claims 1-11 and 17, wherein said polynucleotide is an expression cassette comprising one or more expression control elements operably linked to said nucleic acid encoding said PPT1 polypeptide,

wherein said nucleic acid encoding said PPT1 polypeptide is operably linked to an upstream promoter and a downstream polyadenylation signal.

19. The polynucleotide of claim 18, wherein said expression cassette comprises 5’ to 3’, operably linked to said nucleic acid encoding said PPT1 polypeptide, a promoter, a kozak sequence, said PPT1 polypeptide encoding nucleic acid sequence, and a polyadenylation signal.

20. The polynucleotide of claim 18, wherein said polynucleotide is DNA.

21. A recombinant viral vector nucleic acid comprising the polynucleotide of claim 18, and 5’ and/or 3’ viral elements providing for viral packaging and replication, wherein said recombinant viral vector nucleic acid is DNA and comprises an adeno-associated virus (AAV) inverted repeat (ITR) flanking the 5’ terminus of said polynucleotide and an AAV ITR flanking the 3’ terminus of said polynucleotide.

22.A recombinant AAV vector comprising the recombinant viral vector nucleic acid of claim 21 and a capsid.

23. A pharmaceutical composition comprising the recombinant viral vector of claim 22, and a pharmaceutically acceptable carrier.

24. Use of the recombinant viral vector of 22 for the preparation of a medicament for treating Neuronal Ceroid Lipofuscinosis 1 in a subject, wherein said subject is a human.