CLAIMS

1. An expression construct comprising a mutated Woodchuck Hepatitis Virus (WHV) Posttranscriptional Regulatory Element (WPRE) sequence, and an α galactosidase A (α-Gal A) transgene encoding at least one α-Gal A protein.

2. The expression construct of claim 1, wherein the expression construct comprises a wild-type α-Gal A sequence or a codon optimized α-Gal A sequence.

3. The expression construct of claim 1 or 2, wherein the expression construct further comprises one or more of the following: an enhancer, a promoter, an intron, a signal peptide and/or a polyadenylation (polyA) signal, sequence wherein the mutated WPRE sequence, and the α-Gal A transgene encoding at least one α-Gal A protein are located between the signal peptide and the polyA signal sequence.

4. The expression construct of any one of claims 1-3, wherein the mutated WPRE sequence is a mut6 mutated WRPE sequence.

5. The expression construct of any one of claims 1-4, wherein the expression construct comprises an apolipoprotein E (APOE) enhancer operably linked to an alpha 1-antitrypsin (hAAT) promoter, a human hemoglobin beta (HBB)-IGG intron, an α-Gal A signal peptide, the mutated WPRE sequence, and a bovine growth hormone poly A signal sequence.

6. The expression construct of claim 3, wherein the expression construct comprises one or more of the following: the enhancer comprising the nucleotide sequence as set forth in SEQ ID NO: 2, the promoter comprising the nucleotide sequence as set forth in SEQ ID NO: 3, the intron comprising the nucleotide sequence as set forth in SEQ ID NO: 4, the α-GalA transgene comprising nucleic acids 1052-2341 of SEQ ID NO: 9, the mutated WPRE sequence comprising the nucleotide sequence as set forth in SEQ ID NO:

6, and/or the poly A signal sequence comprising the nucleotide sequence as set forth in SEQ ID NO: 7.

7. The expression construct of any one of claims 1-6, wherein the expression construct comprises the nucleotide sequence as set forth in SEQ ID NO: 9.

8. The expression construct of any one of claims 1-7, wherein the expression construct is an adeno-associated virus (AAV) expression construct .

9. The expression construct of claim 8, wherein the AAV expression construct serotype is AAV2/6.

10. An expression construct comprising an enhancer comprising the nucleotide sequence as set forth in SEQ ID NO: 2, a promoter comprising the nucleotide sequence as set forth in SEQ ID NO: 3, an intron comprising the nucleotide sequence as set forth in SEQ ID NO: 4, an α-GalA transgene comprising nucleic acids 1052-2341 of SEQ ID NO: 9, a mutated WPRE sequence comprising the nucleotide sequence as set forth in SEQ ID NO: 6, and a poly A signal sequence comprising the nucleotide sequence as set forth in SEQ ID NO: 7.

11. A composition, comprising the expression construct of any one of claims 1-10.

12. The composition of claim 11, further comprising a pharmaceutically acceptable carrier.

13. The composition of claim 12, wherein the pharmaceutically acceptable carrier comprises $CaCl_2$, $MgCl_2$, NaCl, Sucrose, and Kolliphor (Poloxamer) P 188.

14. An *in vitro* method of expressing at least one α-Gal A protein in a cell, the method comprising administering the expression construct of any one of claims 1-10 to the cell such that the α-Gal A protein is expressed in the cell.

15. A genetically modified cell comprising the expression construct of any one of claims 1-10.

16. The genetically modified cell of claim 14, wherein the cell is made by the method of claim 14.

17. The genetically modified cell of claim 15 or 16, wherein (a) the cell is a stem cell or a precursor cell; or (b) the cell is a liver or muscle cell.

18. Use of the expression construct of any one of claims 1-10, the composition of any one of claims 11-13, or the cell of any one of claims 15-17, for the manufacture of a medicament for use in preventing, inhibiting, or treating Fabry disease or one or more symptoms associated with Fabry disease.

19. The use of claim 18, wherein the symptoms comprise one or more of Gb3 levels above normal, lyso-Gb3 levels above normal, renal disease, cardiac disease, acroparesthesia, angiokeratomas, GI tract pain, corneal and lenticular opacities, or cerebrovascular disease.

20. The use of claim 18 or 19, wherein the expression construct is administered to a subject by intravenous infusion.

21. The use of claim 20, wherein only one dose of the expression construct is administered to the subject.

22. The use of claim 20 or 21, wherein the subject is administered an immunosuppressant prior to and/or during administration of the expression construct.

23. The use of claim 22, wherein the immunosuppressant comprises prednisone.

24. The use of any one of claims 20-23, wherein expression of the at least one α-Gal A protein is sustained for at least 3 months, at least 9 months, or at least 12 months.

25. The use of any one of claims 20-24, wherein the α-Gal A protein expressed from the transgene decreases the amount of glycospingolipids in the subject by at least about 2-fold.

26. The use of any one of claims 20-25, wherein the α-Gal A protein expressed from the transgene decreases the amount of glycospingolipids in the subject by at least about 80%.

27. The use of any one of claims 20-26, wherein the α-Gal A protein expressed from the transgene decreases the amount of glycospingolipids in one or more of the subject's plasma, liver, heart, kidney, or spleen.

28. The use of any one of claims 20-27, wherein the expression construct manufactured in a HEK293 cell system provides the α-Gal A protein levels in the subject at about 21-fold higher as compared to the α-Gal A protein levels in subjects administered the expression construct manufactured in a Sf9 cell system.

29. The use of any one of claims 20-28, wherein the α-Gal A protein activity in the subject is between about 100-fold higher to 1,500-fold higher than physiologial normal/wild type.

30. The use of any one of claims 20-29, wherein the α-Gal A protein expressed from the transgene is active in kidneys, liver, and/or heart of the subject.

31. An *in vitro* method of producing an α-Gal A protein for the treatment of Fabry disease, the method comprising expressing the α-Gal A protein in an isolated cell

according to the method of claim 14, and isolating the α-Gal A protein produced by the cell.