SUPPLEMENTAL INFORMATION INVENTORY

**Supplemental Experimental Procedures**

Vectors and Sequences

Sequence-structure analysis

Transmission electron microscopy of AAV vectors

Analytical ultracentrifugation of AAV vectors

Thermal stability assessment

Tissue Histology

Tissue DNA Biodistribution and RNA quantitation

Quantification of human alpha1-antitrypsin (hA1AT)

Neutralizing antibody assay

Blood count and serum biochemistry

Cytokines measurements

**Supplemental Figure Legends and Figures**

**Figure S1** eGFP Expression after Viral Vector Intramuscular Injection, related to Figure 4.

**Figure S2** Multiple Sequence Alignment of AAV Isolates used in Ancestral Sequence Reconstruction, related to Figure 1 and 6.

**Figure S3** Full Phylogeny and Reconstructed Nodes of AAV Evolutionary Lineage, related to Figure 1.

**Supplemental Table Legends**

**Table S1** Vector Genomes (GC) distribution in Mouse Liver, Heart, Spleen, Kidney and Lung, related to Figure 4.

**Table S2** Characteristic and Previous Clinical History of Rhesus Macaques Treated with Viral Vectors Injected Via Saphenous Vein, related to Figure 4.

**Table S3** Complete Blood Count Values for Mice Injected with AAV8 and Anc80L65, related to Figure 4.

**Table S4** Serum Biochemistry Values for Mice Injected with AAV8 and Anc80L65, related to Figure 4.

**Table S5** Levels of Serum Cytokines Measured at Different Time points in Mice Injected with Saline, AAV8 and Anc80L65, related to Figure 4.

**Table S6** Complete Blood Count Values from Non-Human Primates Injected with AAV8 and Anc80L65, related to Figure 4.

**Table S7** Serum Biochemistry Values from Non-Human Primates Injected with AAV8 and Anc80L65, related to Figure 4.