heart or muscle without increasing overall dose to the patient. By reducing the overall dose required to achieve a therapeutic benefit, fewer viral antigens are delivered to the patient, ideally resulting in reduced immune responses to the vector and increased safety. Manufacturing enough gene therapy drug product to conduct late stage clinical trials is a major hurdle in further development. Reducing the dose requirements to achieve therapeutic benefit will result in reduced manufacturing requirements, reduced costs of manufacturing, faster clinical trial development and greater ability to treat more patients.

[0009a] In one aspect, provided herein is a modified AAVrh74 VP1 capsid protein comprising one or more modifications selected from the group of a substitution of isoleucine for asparagine at amino acid position 502, a substitution of tryptophan to arginine at amino acid 505 of the VP1 of AAVrh74, and an insertion of the peptide YIG or YIGSR (SEQ ID NO: 2) at amino acid position 591 of the VP1 of AAVrh74, or an equivalent of each thereof.

[0009b] In one aspect, provided herein is a recombinant viral particle comprising the modified AAVrh74 VP1 as described herein.

[0009c] In one aspect, provided herein is a polynucleotide encoding the modified AAVrh74 VP1 as described herein and/or the recombinant viral particle as described herein, that is optionally contained within a vector.

[0009d] In one aspect, provided herein is a recombinant expression system for producing the recombinant viral particle as described herein, optionally comprising the vector as described herein.

[0009e] In one aspect, provided herein is a host cell comprising the polynucleotide or vector as described herein.

~~**[0009f]** In one aspect, provided herein is a method for modifying a polynucleotide and/or protein in a cell comprising delivering to the cell an effective amount of a recombinant viral particle that comprises the modified capsid protein as described herein, or the viral particle as described herein.~~

[~~0009g~~0009f] In one aspect, provided herein is a use of a recombinant viral particle that comprises the modified capsid protein as described herein, or the viral particle as described herein in the manufacture of a medicament for modifying a polynucleotide and/or protein in a subject, wherein the medicament is to be administered to the subject having a disease, disorder or condition, wherein the disease, disorder or condition is selected from the group consisting of hemophilia, muscular dystrophy, multiple sclerosis, alpha-1-antitrypsin,

amyotrophic lateral sclerosis, Alzheimer's, spinal muscular atrophy, cystic fibrosis, HIV, thalassemia, choroideremia, Parkinson's, Leber congenital amaurosis, macular degeneration, aromatic amino acid decarboxylase deficiency, achromatopsia, Crigler Najjar syndrome, Pompe disease, X-linked retinoschisis, homozygous familial hypercholesteremia, Batten disease, retinal degeneration, ornithine transcarbamylase deficiency, mucopolysarccharidosis (I-IX), hepatitis B, and hepatitis C.

[~~0009h~~0009g] In one aspect, provided herein is a kit comprising a recombinant viral particle that comprises the modified capsid protein as described herein, or the viral particle as described herein.

[~~0009i~~0009h] In one aspect, provided herein is a modified capsid protein as described herein, or the viral particle as described herein for use in therapy.

[0010] Accordingly, this disclosure relates to modified capsid proteins, isolated polynucleotides, methods for the preparation of modified capsid proteins, recombinant viral particles and recombinant expression systems for the generation of modified viral particles. One aspect of the disclosure relates to a modified viral capsid protein that comprises, or alternatively consists essentially of, or yet further consists of, a viral capsid protein modified by amino acid substitution or insertion of between 1 to 7 amino acid. In some embodiments, viral capsid protein is a VP1, optionally of AAVrh74. In further embodiments, the modification comprises the substitution of isoleucine for asparagine at amino acid position 502 of the VP1 of AAVrh74 or an equivalent modification. In some embodiments, the modification comprises the substitution of tryptophan to arginine at amino acid 505 of the VP1 of AAVrh74. In some embodiments, the modification targets a receptor found primarily on satellite cells, optionally muscle stem cells. In some embodiments, the modification is an insertion of the peptide YIG or YIGSR (Tyr–Ile–Gly–Ser–Arg) (SEQ ID NO: 2) at amino acid position 591 of the VP1 of AAVrh74 or an equivalent thereof. In some embodiments, this peptide has a has a high affinity for Alpha 7 beta 1 integrin and/or is positioned in a region that is likely to alter normal rh74 receptor binding.

[0011] Also disclosed herein is an isolated polynucleotide encoding a modified viral capsid protein that comprises, or alternatively consists essentially of, or yet further consists of, a modified viral capsid protein modified by amino acid substitution or insertion of between 1 to 7 amino acid. In some embodiments, viral capsid protein is a VP1, optionally of AAVrh74. In further embodiments, the modification comprises the substitution of isoleucine for

asparagine at amino acid position 502 of the VP1 of AAVrh74 or an equivalent modification. In some embodiments, the modification comprises the substitution of tryptophan to arginine at amino acid 505 of the VP1 of AAVrh74. In some embodiments, the modification targets a receptor found primarily on satellite cells,

WHAT IS CLAIMED IS:

1. A modified AAVrh74 VP1 capsid protein comprising one or more modifications selected from the group of a substitution of isoleucine for asparagine at amino acid position 502, a substitution of tryptophan to arginine at amino acid 505 of the VP1 of AAVrh74, and an insertion of the peptide YIG or YIGSR (SEQ ID NO: 2) at amino acid position 591 of the VP1 of AAVrh74, or an equivalent of each thereof.

2. A recombinant viral particle comprising the modified AAVrh74 VP1 of claim 1.

3. The recombinant viral particle of claim 2, wherein the recombinant viral particle is a modified AAVrh74.

4. The recombinant viral particle of any of claims 2~~1~~-3, further comprising a transgene or CRISPR system.

5. A polynucleotide encoding the modified AAVrh74 VP1 of claim 1 and/or the recombinant viral particle of claims 2 or 3, that is optionally contained within a vector.

6. A recombinant expression system for producing the recombinant viral particle of claim 3, optionally comprising the vector of claim 5.

7. A host cell comprising the polynucleotide or vector of claim 5.

~~8. A method for modifying a polynucleotide and/or protein in a cell comprising delivering to the cell an effective amount of a recombinant viral particle that comprises the modified capsid protein of claim 1 or 4, or the viral particle of claim 2.~~

~~9. The method of claim 8, wherein the cell is a mammalian cell.~~

~~10. The method of claim 9, wherein the mammalian cell is a human cell.~~

8~~11~~. Use of a recombinant viral particle that comprises the modified capsid protein of claim 1 or 4, or the viral particle of claim 2 in the manufacture of a medicament for modifying a polynucleotide and/or protein in a subject, wherein the medicament is to be administered to the subject having a disease, disorder or condition, wherein the disease, disorder or condition is selected from the group consisting of hemophilia, muscular dystrophy, multiple sclerosis, alpha-1-antitrypsin, amyotrophic lateral sclerosis, Alzheimer's, spinal muscular atrophy, cystic fibrosis, HIV, thalassemia, choroideremia, Parkinson's, Leber congenital amaurosis, macular degeneration, aromatic amino acid decarboxylase deficiency, achromatopsia, Crigler Najjar syndrome, Pompe disease, X-linked retinoschisis, homozygous

familial hypercholesteremia, Batten disease, retinal degeneration, ornithine transcarbamylase deficiency, mucopolysarccharidosis (I-IX), hepatitis B, and hepatitis C.

912. The use of claim 811, wherein the subject is a mammal.

1013. The use of claim 912, wherein the mammalian is a human.

1114. The use of any one of claims 811-103, wherein the administration is local or systemic.

1215. A kit comprising a recombinant viral particle that comprises the modified capsid protein of claim 1 or 4, or the viral particle of claim 2.

1316. The modified capsid protein of claim 1 or 4, or the viral particle of claim 2 for use in therapy.