

What is Claimed is:

1. A nucleic acid molecule comprising a nucleotide sequence, which encodes a miniaturized dystrophin polypeptide comprising a modified spectrin repeat 16 (R16) domain, wherein a part of the R16 domain is replaced by a corresponding part of a spectrin repeat 2 (R2) domain, and wherein the miniaturized dystrophin polypeptide comprises an amino acid sequence at least about 98% identical to the amino acid sequence set forth as SEQ ID NO: 83.
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2. The nucleic acid molecule of claim 1, wherein the miniaturized dystrophin polypeptide comprises an amino acid sequence set forth as SEQ ID NO: 83.
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3. The nucleic acid molecule of claim 1, comprising a nucleotide sequence comprising in order a C5-12(T) promoter, an SV40 intron, a coding sequence for the miniaturized dystrophin polypeptide comprising the amino acid sequence set forth as SEQ ID NO: 83, a 3' UTR, and a polyA sequence.
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4. The nucleic acid molecule of claim 1, comprising a nucleotide sequence comprising in order a C5-12(T) promoter having the nucleotide sequence set forth as SEQ ID NO: 109, an SV40 intron having the nucleotide sequence set forth as SEQ ID NO: 110, a coding sequence for the miniaturized dystrophin polypeptide having the nucleotide sequence set forth as SEQ ID NO: 111, a 3' UTR having the nucleotide sequence set forth as SEQ ID NO: 112, and a polyA sequence having the nucleotide sequence set forth as SEQ ID NO: 113.
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5. The nucleic acid molecule of claim 4, which further comprises a first inverted terminal repeat (ITR) and a second ITR both from adeno-associated virus (AAV).
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6. A host cell comprising the nucleic acid molecule of claim 5.
7. A vector comprising the nucleic acid molecule of claim 5.
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8. A pharmaceutical composition comprising (a) the vector of claim 7; and (b) a pharmaceutically acceptable excipient.

9. A recombinant adeno-associated virus (rAAV) vector particle comprising an AAV capsid and a nucleic acid molecule comprising a nucleotide sequence, which encodes a miniaturized dystrophin polypeptide comprising a modified R16 domain, wherein a part of the R16 domain is replaced by a corresponding part of a R2 domain, and wherein the miniaturized dystrophin polypeptide comprises an amino acid sequences at least about 98% identical to the amino acid sequence set forth as SEQ ID NO: 83.

10. The rAAV vector particle of claim 9, wherein the miniaturized dystrophin polypeptide comprises an amino acid sequence set forth as SEQ ID NO: 83.

11. The rAAV vector particle of claim 9, wherein the nucleotide sequence comprises in order a C5-12(T) promoter, an SV40 intron, a coding sequence for the miniaturized dystrophin polypeptide comprising the amino acid sequence set forth as SEQ ID NO: 83, a 3' UTR, and a polyA sequence.

12. The rAAV vector particle of claim 9, wherein the nucleotide sequence comprises in order a C5-12(T) promoter having the nucleotide sequence set forth as of SEQ ID NO: 109, an SV40 intron having the nucleotide sequence set forth as SEQ ID NO: 110, a coding sequence for the miniaturized dystrophin polypeptide having the nucleotide sequence set forth as SEQ ID NO: 111, a 3' UTR having the nucleotide sequence set forth as SEQ ID NO: 112, and a polyA sequence having the nucleotide sequence set forth as SEQ ID NO: 113.

13. The rAAV vector particle of claim 12, wherein the nucleic acid molecule further comprises a first ITR and a second ITR both from AAV.

14. The rAAV vector particle of claim 13, wherein the first ITR and the second ITR are from the genome of AAV2.

15. The rAAV vector particle of claim 14, wherein the AAV capsid is from AAV8.

16. The rAAV vector particle of claim 14, wherein the AAV capsid is from AAV9.

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17. The rAAV vector particle of claim 12, wherein the AAV capsid is from AAV8 or AAV9.

18. The rAAV vector particle of claim 12, wherein the AAV capsid is from AAV8.

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19. The rAAV vector particle of claim 12, wherein the AAV capsid is from AAV9.

20. A rAAV vector particle comprising an AAV capsid and a nucleic acid molecule comprising a nucleotide sequence comprising in order a C5-12(T) promoter having the nucleotide sequence set forth as of SEQ ID NO: 109, an SV40 intron having the nucleotide sequence set forth as SEQ ID NO: 110, a coding sequence for a miniaturized dystrophin polypeptide having the nucleotide sequence set forth as SEQ ID NO: 111, a 3' UTR having the nucleotide sequence set forth as SEQ ID NO: 112, and a polyA sequence having the nucleotide sequence set forth as SEQ ID NO: 113, wherein the nucleic acid molecule further comprises a first ITR and a second ITR both from the genome of AAV2 flanking the nucleotide sequence, and wherein the AAV capsid is from AAV8 or AAV9.

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21. The rAAV vector particle of claim 20, wherein the AAV capsid is from AAV8.

22. A pharmaceutical composition comprising (a) the rAAV vector particle of claim 21; and (b) a pharmaceutically acceptable excipient.

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23. A kit comprising the pharmaceutical composition of claim 22, and instructions for administering the pharmaceutical composition to a subject in need thereof.

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24. The rAAV vector particle of claim 20, wherein the AAV capsid is from AAV9.

25. A pharmaceutical composition comprising (a) the rAAV vector particle of claim 24; and (b) a pharmaceutically acceptable excipient.
- 5 26. A kit comprising the pharmaceutical composition of claim 25, and instructions for administering the pharmaceutical composition to a subject in need thereof.