CLAIMS

1. A CRISPR-Cas system comprising one or more vectors encoding a composition, the composition comprising:

(a) a first guide RNA (gRNA) molecule targeting intron 44 of dystrophin;

(b) a second gRNA molecule targeting intron 55 of dystrophin; and

(c) a Cas9 protein; and

(d) one or more Cas9 gRNA scaffolds.

2. The system of claim 1, wherein the first gRNA targets the polynucleotide of SEQ ID NO:2 or a 5' truncation thereof and the second gRNA targets the polynucleotide of SEQ ID NO:3 or a 5' truncation thereof,

or wherein the first gRNA targets the polynucleotide of SEQ ID NO:2 or a 5' truncation thereof,

or wherein the second gRNA targets the polynucleotide of SEQ ID NO:3 or a 5' truncation thereof.

3. The system of any one of claims 1-2, wherein the one or more vectors comprises at least one bidirectional promoter,

wherein the bidirectional promoter comprises:

a first promoter driving expression of the first gRNA molecule and/or the second gRNA molecule; and

a second promoter driving expression of the Cas9 protein.

4. The system of any one of claims 1-3, wherein the expression of the Cas9 protein is driven by a constitutive promoter or a muscle-specific promoter.

5. The system of any one of claims 1-4, wherein the system comprises a single vector,

wherein the single vector encodes the first gRNA molecule, the second gRNA molecule, and the Cas9 protein.

6. The system of any one of claims 1-4, wherein the system comprises two or more vectors, wherein the two or more vectors comprises a first vector and a second vector.

7. The system of claim 6, wherein (a) the first vector encodes the first gRNA molecule and the second gRNA molecule and (b) the second vector encodes the Cas9 protein,

or wherein (a) the first vector encodes the first gRNA molecule and (b) the second vector encodes the second gRNA molecule.

8. The system of claim 7, wherein the first vector further encodes the Cas9 protein, or wherein the second vector further encodes the Cas9 protein.

9. The system of any one of claims 1-8, wherein the Cas9 protein is SpCas9, SaCas9, or St1Cas9 protein.

10. The system of claim 9, wherein the Cas9 protein is a SaCas9 protein encoded by the polynucleotide of SEQ ID NO:11.

11. The system of any one of claims 1-10, wherein the Cas9 gRNA scaffold is a SaCas9 gRNA scaffold.

12. The system of claim 11, wherein the SaCas9 gRNA scaffold comprises or is encoded by the polynucleotide of SEQ ID NO:4.

13. The system of any one of claims 1-12, wherein the vector comprises at least one polynucleotide selected from SEQ ID NOs: 1-24, 29-30, and 41-42, or wherein the vector comprises a polynucleotide sequence at least 95% identical to a sequence selected from SEQ ID NOs: 1-24, 29-30, and 41-42.

14. The system of any one of claims 1-12, wherein the vector is a viral vector.

15. The system of claim14, wherein the vector is an Adeno-associated virus (AAV) vector.

16. The system of any one of claims 1-15, wherein the vector comprises a ubiquitous promoter or a tissue-specific promoter operably linked to the polynucleotide sequence encoding the first gRNA molecule, the second gRNA molecule, and/or the Cas9 protein.

17. The system of claim 16, wherein the tissue-specific promoter is a muscle specific promoter.

18. A cell comprising the system of any one of claims 1-17.

19. A kit comprising the system of any one of claims 1-17.

20. A system of any one of claims 1-17, for use in correcting or genome editing a mutant dystrophin gene in a cell, wherein the system is administered to the cell.

21. A system of any one of claims 1-17, for use in treating a subject having a mutant dystrophin gene, wherein the system is administered to the subject.