WE CLAIM:

1. A pharmaceutical composition comprising:

(a) a DNA-directed RNA interference (ddRNAi) construct comprising a nucleic acid comprising a DNA sequence encoding a hairpin RNA interference (RNAi) molecule comprising an effector sequence of at least 17 contiguous nucleotides and an effector complement sequence, wherein the effector sequence is substantially complementary to a region of corresponding length in a RNA transcript corresponding to a PABPN1 protein, wherein the region of the RNA transcript is set forth in SEQ ID NO: 3;

(b) a nucleic acid encoding a functional PABPN1 protein having a mRNA transcript which is not targeted by the RNAi agent encoded by the nucleic acid in the ddRNAi construct, wherein said nucleic acid encoding the functional PABPN1 protein is codon optimised; and

(c) a pharmaceutically acceptable carrier or diluent.

2. The pharmaceutical composition according to claim 1, wherein the hairpin RNAi molecule comprises an effector sequence set forth in SEQ ID NO:8 and an effector complement sequence which is substantially complementary to the sequence set forth in SEQ ID NO:8.

3. The pharmaceutical composition according to claim 1, wherein the hairpin RNAi molecule comprises an effector sequence set forth in SEQ ID NO:8 and an effector complement sequence set forth in SEQ ID NO:9.

4. The pharmaceutical composition according to claim 1, comprising a loop sequence positioned between the effector sequence and the effector complement sequence.

5. The pharmaceutical composition according to claim 4, wherein the hairpin RNA molecule is a short hairpin RNA (shRNA) comprising a sequence set forth in SEQ IDNO: 20 or 21.

6. The pharmaceutical composition according to claim 1, wherein the hairpin RNA molecule comprises a primary miRNA (pri-miRNA) backbone.

7. The pharmaceutical composition according to claim 6, wherein the hairpin RNA molecule is a short hairpin microRNA (shmiR) molecule.

8. The pharmaceutical composition according to any one of claims 1 to 7, wherein the DNA sequence encoding a hairpin RNAi molecule within the ddRNAi construct is operably linked to a muscle-specific promoter.

9. The pharmaceutical composition of claim 8, wherein the ddRNAi construct comprises at least one further nucleic acid comprising a DNA sequence encoding a hairpin RNAi molecule comprising an effector sequence of at least 17 contiguous nucleotides and an effector complement sequence, wherein the effector sequence is substantially complementary to a region of corresponding length in a RNA transcript corresponding to a PABPN1 protein,

wherein the hairpin RNAi molecules encoded by the nucleic acids within the ddRNAi construct comprise different effector sequences.

10. The pharmaceutical composition according to claim 9, wherein each DNA sequence encoding a hairpin RNAi molecule within the ddRNAi construct is operably linked to a muscle-specific promoter.

11 The pharmaceutical composition according to any one of claims 1 to 7, wherein:

(i) the functional PABPN1 protein comprises a sequence set forth in SEQ ID NO: 25; or

(ii) the ddRNAi construct and/or the nucleic acid encoding the functional PABPN1 protein is comprised within an expression vector; or

(iii) the nucleic acid encoding the functional PABPN1 protein is set forth in SEQ ID NO: 24; or

(iv) any combination of (i) to (iii).

12. The pharmaceutical composition according to claim 11, wherein the nucleic acid encoding the functional PABPN1 protein is comprised within the same expression vector as the ddRNAi construct.

13. The pharmaceutical composition according to claim 11, wherein the nucleic acid encoding the functional PABPN1 protein and the ddRNAi construct are comprised within different expression vectors.

14. The pharmaceutical composition according to claim 11, wherein:

(i) the expression vector is a viral vector selected from an adeno-associated viral (AAV) vector, a retroviral vector, an adenoviral vector and a lentiviral vector; or

(ii) each DNA sequence encoding a hairpin RNAi molecule within the ddRNAi construct is operably linked to a promoter; or

(iii) each DNA sequence encoding a hairpin RNAi molecule within the ddRNAi construct is operably linked to a muscle-specific promoter; or

(iv) any combination of (i), (ii) and (iii).

15. The pharmaceutical composition according to claim 12, wherein:

(i) the expression vector is a viral vector selected from an adeno-associated viral (AAV) vector, a retroviral vector, an adenoviral vector and a lentiviral vector; or

(ii) each DNA sequence encoding a hairpin RNAi molecule within the ddRNAi construct is operably linked to a promoter; or

(iii) the nucleic acid encoding the functional PABPN1 protein is operably linked to a promoter; or

(iv) the nucleic acid encoding the functional PABPN1 protein, and each DNA sequence encoding a hairpin RNAi molecule within the ddRNAi construct, are operably linked to the same promoter; or

(v) any combination of (ii), (iii) and (iv), wherein the or each promoter is a muscle specific promoter; or

(vi) any combination of (i)-(v).

16. The pharmaceutical composition according to claim 13, wherein:

(i) the expression vector is a viral vector selected from an adeno-associated viral (AAV) vector, a retroviral vector, an adenoviral vector and a lentiviral vector; or

(ii) each DNA sequence encoding a hairpin RNAi molecule within the ddRNAi construct is operably linked to a promoter; or

(iii) the nucleic acid encoding the functional PABPN1 protein is operably linked to a promoter; or

(iv) any combination of (ii) and (iii), wherein each promoter is a muscle specific promoter; or

(v) any combination of (i)-(iv).

17. Use of a DNA-directed RNA interference (ddRNAi) construct and a nucleic acid encoding a functional PABPN1 protein in the preparation of a medicament for treatment of oculopharyngeal muscular dystrophy (OPMD), wherein

(a) the ddRNAi construct a nucleic acid comprising a DNA sequence encoding a hairpin RNA interference (RNAi) molecule comprising an effector sequence of at least 17 contiguous nucleotides and an effector complement sequence, wherein the effector sequence is substantially complementary to a region of corresponding length in a RNA transcript corresponding to a PABPN1 protein, wherein the region of the RNA transcript is set forth in SEQ ID NO: 3; and

(b) a nucleic acid encoding a functional PABPN1 protein having a mRNA transcript which is not targeted by the RNAi agent encoded by the nucleic acid in the ddRNAi construct, wherein said nucleic acid encoding the functional PABPN1 protein is codon optimised.

18. The use according to claim 17, wherein the medicament is a pharmaceutical composition according to any one of claims 1 to 16.