CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising a cationic peptide-linked morpholino antisense oligonucleotide comprising:

    (a) a morpholino antisense oligonucleotide sequence complementary to at least 3 polyCUG repeat sequences in a 3' untranslated region (UTR) of a dystrophia myotonica protein kinase (DMPK) RNA transcript target; and

    (b) a cationic peptide that is 8-30 amino acid residues in length,

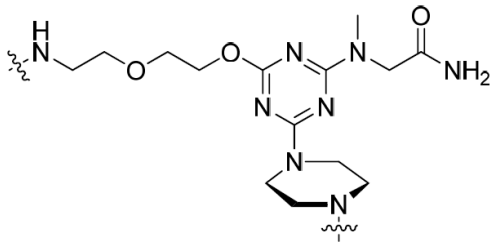
        wherein the cationic peptide comprises one or more subsequences selected from the group consisting of RXR, RX, RB, and RBR,

            wherein R is arginine, B is β-alanine, and each X is independently –NH–$(CHR^1)_n$– C(O)–, and

            wherein n is 4-6 and each R^1 is independently H or methyl such that at most two R^1s are methyl.

2. The pharmaceutical composition of claim 1, wherein the cationic peptide is separated from the morpholino antisense oligonucleotide by a spacer moiety linked at the 5' end of the morpholino antisense oligonucleotide.

3. The pharmaceutical composition of claim 2, wherein the spacer moiety comprises

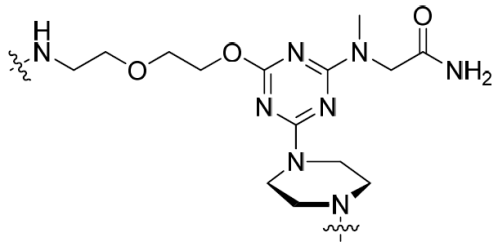


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4. A pharmaceutical composition comprising a cationic peptide-linked morpholino antisense oligonucleotide comprising:

(a) a morpholino antisense oligonucleotide sequence complementary to at least 3 polyCUG repeat sequences in a 3' untranslated region (UTR) of a dystrophia myotonica protein kinase (DMPK) RNA transcript target;

(b) a spacer moiety linking the morpholino antisense oligonucleotide and a cationic peptide, the spacer moiety comprising



; and

(c) the cationic peptide that is 8-30 amino acid residues in length.

5. The pharmaceutical composition of claim 4, wherein the spacer moiety is linked to the morpholino antisense oligonucleotide at the 5' end of the morpholino antisense oligonucleotide.

6. The pharmaceutical composition of claim 4 or 5, wherein the cationic peptide comprises one or more subsequences selected from the group consisting of RXR, RX, RB, and RBR,

wherein R is arginine, B is β-alanine, and each X is independently $–NH–(CHR^1)_n–C(O)–$,

wherein n is 4-6 and each R^1 is independently H or methyl such that at most two R^1s are methyl.

7. The pharmaceutical composition of any one of claims 1-6, wherein the cationic peptide comprises the amino acid sequence $Ac(RXRRBR)_2XB–$.

8. The pharmaceutical composition of any one of claims 1-6, wherein the cationic peptide comprises the amino acid sequence $Ac(RXR)_4XB–$.

9. The pharmaceutical composition of any one of claims 1-8, wherein the morpholino antisense oligonucleotide comprises the sequence 5' $–(AGC)_n–$ 3', 5' $–(GCA)_n–$ 3', or 5' $–(CAG)_n–$ 3', wherein n is any of about 5-25.

10. The pharmaceutical composition of claim 9, wherein the morpholino antisense oligonucleotide further comprises 1 to 2 additional morpholino nucleotides on the 5' and/or the 3' end of the oligonucleotide.

11. The pharmaceutical composition of any one of claims 1-10, wherein the morpholino antisense oligonucleotide comprises the sequence: 5' – AGCAGCAGCAGCAGCAGCAGCA– 3'.

12. The pharmaceutical composition of claim 11, wherein the morpholino antisense oligonucleotide further comprises a 5' amine modification.

13. The pharmaceutical composition of any one of claims 1-12, wherein the morpholino antisense oligonucleotide is a phosphorodiamidate morpholino antisense oligonucleotide.

14. The pharmaceutical composition of any one of claims 1-13, wherein the cationic peptide-linked morpholino antisense oligonucleotide is capable of penetrating into cells of the tibialis anterior muscle, the quadriceps muscle, and/or the gastrocnemius muscle.

15. The pharmaceutical composition of any one of claims 1-14, further comprising a pharmaceutically acceptable excipient.