[0007] In another aspect, provided herein are methods of treating muscle atrophy or myotonic dystrophy in a subject in need thereof, the method comprising: providing the conjugate disclosed herein; and administering to the subject the conjugate, wherein the conjugate mediates RNA interference against a target mRNA in the subject, thereby treating muscle atrophy or mytonic dystrophy in the subject.

[0007a] In one aspect, the present disclosure refers to use of the conjugate as described herein in the manufacture of a medicament for modulating mRNA expression levels of a gene in a subject, wherein the conjugate is to be administered to the subject, wherein the conjugate decreases mRNA expression levels of the gene in the subject.

[0007b] In another aspect, the present disclosure refers to use of the conjugate as described herein in the manufacture of a medicament for treating muscle atrophy or myotonic dystrophy in a subject in need thereof, wherein the conjugate is to be administered to the subject, wherein the conjugate mediates RNA interference against a target mRNA in the subject, thereby treating muscle atrophy or mytonic dystrophy in the subject.

[0007c] In another aspect, the present disclosure refers to the conjugate as described herein for use in therapy.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present disclosure. The disclosure may be better understood by reference to one or more of these drawings in combination with the detailed description of specific embodiments presented herein.

[0009] Fig. 1 shows a SAX chromatogram for DAR2 conjugates (DAR2 AOC) having myostatin (MSTN) siRNA modified with 8 phosphoryl guanidine (PG) linkages (R3668).

[0010] Fig. 2 shows a SAX chromatogram for DAR2 conjugates (DAR2 AOC) having MSTN siRNA modified with 12 PG linkages (R3669).

[0011] Fig. 3 shows mass spectrometry data of molecular weight (MW) for MSTN passenger strand (PS) with 8 PG linkages.

[0012] Fig. 4 shows mass spectrometry data of MW for MSTN PS with 12 PG linkages.

[0013] Fig. 5 shows mass spectrometry data of MW for MSTN guide strand (GS) with vinyl phosphonate vpUq.

[0014] Fig. 6 shows ion-pair reverse phase (IP-RP) chromatogram of MSTN GS with vinyl phosphonate vpUq.

[0015] Fig. 7 shows an IP-RP chromatogram of MSTN PS with 8 PG linkages.

[0016] Fig. 8 shows an IP-RP chromatogram of MSTN PS with 12 PG linkages.

[0017] Fig. 9 shows a non-denaturing IP-RP of MSTN duplex with 8 PG linkages.

[0018] Fig. 10 shows a non-denaturing IP-RP of MSTN duplex with 12 PG linkages.

[0019] Fig. 11 shows SAX-HPLC of MSTN duplex with 8 PG linkages.

[0020] Fig. 12 shows SAX-HPLC of MSTN duplex with 12 PG linkages.

[0021] Figs. 13A and **13B** show the *in vivo* dose response of MSTN mRNA expression levels in the gastrocnemius muscle of mice administered with increasing concentrations of DAR2 AOC with PG modified siRNA (2, 4, 8, and 15 mg/kg of mAb) at Day 28 (**Fig. 13A**) and the *in vivo* time-dependent response of MSTN mRNA expression levels in the gastrocnemius muscle in mice administered with a dose of DAR2 AOC with PG modified siRNA (7.5 mg/kg of mAb) at Day 14, 28, and 56 (**Fig. 13B**).