

CLAIMS

WHAT IS CLAIMED IS:

1. ~~A polynucleic acid~~ A small interfering RNA (siRNA) molecule conjugate comprising:
an anti-transferrin receptor antibody or antigen binding fragment thereof conjugated to a
polynucleic acid molecule that hybridizes to a target sequence of DMPK mRNA;
wherein an antisense strand of the polynucleic acid siRNA molecule ~~having a sense strand~~
having comprises a sequence ~~at least 80% identical to~~ selected from the group
consisting of SEQ ID NO: ~~4~~ NOs: 4, 6, 8, 10, 12, 14, and ~~an antisense strand~~
~~having a sequence at least 80% identical to~~ SEQ ID NO: 216; and
wherein the ~~polynucleic acid siRNA~~ molecule conjugate mediates RNA interference
against the DMPK mRNA.
2. The ~~polynucleic acid molecule siRNA molecule~~ conjugate of claim 1, wherein the ~~anti-~~
~~transferrin receptor antibody or antigen binding fragment thereof~~ sense strand of the siRNA
molecule comprises a ~~variable heavy chain (VH) region and a variable light chain (VL)~~
~~region, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 17;~~
~~HCDR2 sequence EINPIX₁GRSNYAX₂KFQG, wherein X₁ is selected from N or Q and X₂ is~~
~~selected from Q or E; and HCDR3 sequence comprising SEQ ID NO: 19~~ the group consisting
of SEQ ID Nos: 3, 5, 7, 9, 11, 13, and 15.
3. The ~~polynucleic acid siRNA~~ molecule conjugate of claim 1 or 2, wherein the VH region
comprises HCDR1 sequence comprising SEQ ID NO: 17, HCDR2 sequence comprising one
of SEQ ID NO: ~~18~~ 20, SEQ ID NO: ~~20~~ 18, SEQ ID NO: 21, and HCDR3 sequence comprising
SEQ ID NO: 19.
4. ~~The polynucleic acid molecule conjugate of any one of claim 2-3, wherein the VL region~~
~~comprises LCDR1 sequence RTSENIYX₃NLA, LCDR2 sequence AX₄TNLAX₅, and~~
~~LCDR3 sequence QHFWGTPLTX₆, wherein X₃ is selected from N or S, X₄ is selected from~~
~~A or G, X₅ is selected from D or E, and X₆ is present or absence, and if present, is F.~~
5. ~~The polynucleic acid molecule conjugate of any one of claims 2-4, wherein the VL region~~
~~comprises LCDR1 sequence comprising SEQ ID NO: 22, LCDR2 sequence AATNLAX₅,~~

and LCDR3 sequence QHFWGTPLTX₆, wherein X₅ is selected from D or E and X₆ is present or absence, and if present, is F.

- ~~6.4. The polynucleic acid molecule conjugate of any one of claims 2-5~~The siRNA molecule conjugate of claim 3, wherein the VL region comprises LCDR1 sequence comprising SEQ ID NO: 22 or SEQ ID NO: 27, LCDR2 sequence comprising SEQ ID NO: 23, SEQ ID NO: 25, or SEQ ID NO: 28, and LCDR3 sequence comprising SEQ ID NO: 24 or SEQ ID NO: 26.
- ~~7. The polynucleic acid molecule conjugate of any one of claims 2-6, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 17, HCDR2 sequence comprising SEQ ID NO: 18, and HCDR3 sequence comprising SEQ ID NO: 19; and the VL region comprises LCDR1 sequence comprising SEQ ID NO: 22, LCDR2 sequence comprising SEQ ID NO: 23, and LCDR3 sequence comprising SEQ ID NO: 24.~~
- ~~8.5. The polynucleic acid molecule conjugate of any one of claims 2-6~~The siRNA molecule conjugate of any one of claims 3-4, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 17, HCDR2 sequence comprising SEQ ID NO: 20, and HCDR3 sequence comprising SEQ ID NO: 19; and the VL region comprises LCDR1 sequence comprising SEQ ID NO: 22, LCDR2 sequence comprising SEQ ID NO: 23, and LCDR3 sequence comprising SEQ ID NO: 24.
- ~~9. The polynucleic acid molecule conjugate of any one of claims 2-6, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 17, HCDR2 sequence comprising SEQ ID NO: 21, and HCDR3 sequence comprising SEQ ID NO: 19; and the VL region comprises LCDR1 sequence comprising SEQ ID NO: 22, LCDR2 sequence comprising SEQ ID NO: 25, and LCDR3 sequence comprising SEQ ID NO: 26.~~
- ~~10. The polynucleic acid molecule conjugate of any one of claims 2-6, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 17, HCDR2 sequence comprising SEQ ID NO: 20, and HCDR3 sequence comprising SEQ ID NO: 19; and the VL region comprises LCDR1 sequence comprising SEQ ID NO: 27, LCDR2 sequence comprising SEQ ID NO: 28, and LCDR3 sequence comprising SEQ ID NO: 26.~~

- ~~11. The polynucleic acid molecule conjugate of any one of claims 2-10, wherein the VH region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to a sequence selected from SEQ ID NOs: 29-33.~~
- ~~12. The polynucleic acid molecule conjugate of any one of claims 2-11, wherein the VL region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to a sequence selected from SEQ ID NOs: 34-38.~~
- ~~13.6.~~ The polynucleic acid molecule conjugate of any one of claims 2-12The siRNA molecule conjugate of any one of claims 3-5, wherein the VH region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to SEQ ID NO: 30, and wherein the VL region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to SEQ ID NO: 34.
- ~~14.7.~~ The polynucleic acidsiRNA molecule conjugate of any one of claims 1-~~136~~, wherein the anti-transferrin receptor antibody comprises a humanized antibody, or antigen binding fragment thereof or a chimeric antibody or antigen binding fragment thereof, or a multi-specific antibody or antigen binding fragment thereof.
- ~~15.8.~~ The polynucleic acidsiRNA molecule conjugate of any one of claims 1-~~147~~, wherein the anti-transferrin receptor antibody comprises an IgG-scFv, nanobody, BiTE, diabody, DART, TandAb, scDiabody, scDiabody-CH3, triple body, mini-antibody, minibody, TriBi minibody, scFv-CH3 KIH, Fab-scFv-Fc KIH, Fab-scFv, scFv-CH-CL-scFv, F(ab')₂, F(ab')₂-scFv₂, scFv-KIH, Fab-scFv-Fc, tetravalent HCAb, scDiabody-Fc, diabody-Fc, tandem scFv-Fc, or intrabody.
- ~~16. The polynucleic acidsiRNA molecule conjugate of any one of claims 1-15, wherein the anti-transferrin receptor antibody comprises an IgG1 framework.~~
- ~~17. The polynucleic acid molecule conjugate of any one of claims 1-15, wherein the anti-transferrin receptor antibody comprises an IgG2 framework.~~
- ~~18. The polynucleic acid molecule conjugate of claim 17, wherein the IgG2 framework is IgG2b framework.~~

- ~~19. The polynucleic acid molecule conjugate of any one of claims 1-15, wherein the anti-transferrin receptor antibody comprises IgG4 framework.~~
- ~~20. The polynucleic acid molecule conjugate of any one of claims 1-19~~8~~, wherein the anti-transferrin receptor antibody further comprises at least one mutation in the Fc region.~~
- ~~21. The polynucleic acid molecule conjugate of any one of claims 1-20, wherein the at least one mutation modulates effector function.~~
- ~~22. The polynucleic acid molecule conjugate of any one of claims 20-21, wherein the at least one mutation attenuates or eliminates Fe- γ receptor binding.~~
- 23.9. ~~The polynucleic acid molecule conjugate of any one of claims 20-22, and~~ wherein the at least one mutation is at residue position D265, N297, K322, L328, or P329, wherein the residue position is in reference to IgG1.
- ~~24. The polynucleic acid molecule conjugate of any one of claims 20-23, wherein the Fc region comprises two or more, three or more, or four or more mutations.~~
- ~~25. The polynucleic acid molecule conjugate of any one of claims 20-24, wherein the Fc region comprises mutations at L233 and L234, wherein the residues correspond to position 233 and 234 of SEQ ID NO: 39.~~
- ~~26. The polynucleic acid molecule conjugate of any one of claims 20-25, wherein the Fc region comprises mutations at D265 and N297.~~
- ~~27. The polynucleic acid siRNA molecule conjugate of any one of claims 1-26, wherein the anti-transferrin receptor antibody comprises a heavy chain (HC) sequence selected from SEQ ID NOs: 39-62 and a light chain (LC) sequence selected from SEQ ID NOs: 63-66.~~
- ~~28. The polynucleic acid molecule conjugate of any one of claims 1-27~~9~~, wherein the anti-transferrin receptor antibody specifically binds to human transferrin receptor (TfR).~~

10.

- ~~29. The polynucleic acid siRNA molecule conjugate of any one of claims 1-28, wherein the sense strand and the antisense strand each independently comprises at least one 2' modified nucleotide, at least one modified internucleotide linkage, or at least one inverted abasic moiety.~~
- ~~30. The polynucleic acid molecule conjugate of any one of claims 1-29, wherein the sense strand comprises a 2'-O-methyl modified nucleotide at the 5'-end.~~
- ~~31. The polynucleic acid molecule conjugate of any one of claims 1-30, wherein the sense strand comprises at least two consecutive 2'-O-methyl modified nucleotides at the 5'-end.~~
- ~~32. The polynucleic acid molecule conjugate of any one of claims 1-31, wherein the sense strand comprises at least three, four, five, or six consecutive 2'-O-methyl modified nucleotides at the 5'-end.~~
- ~~33. The polynucleic acid molecule conjugate of any one of claims 1-32, wherein the sense strand comprises six consecutive 2'-O-methyl modified nucleotides at the 5'-end.~~
- ~~34. The polynucleic acid molecule conjugate of any one of claims 1-33, wherein the sense strand comprises at least one 2'-F modified nucleotides.~~
- ~~35. The polynucleic acid molecule conjugate of any one of claims 1-33, wherein the sense strand comprises at least two, at least three 2'-F modified nucleotides.~~
- ~~36. The polynucleic acid molecule conjugate of any one of claims 1-33, wherein the sense strand comprises at least two, at least three consecutive 2'-F modified nucleotides.~~
- ~~37. The polynucleic acid molecule conjugate of any one of claims 1-36, wherein the sense strand comprises a 2'-O-methyl modified nucleotide at the 3'-end.~~
- ~~38. The polynucleic acid molecule conjugate of any one of claims 1-37, wherein the sense strand comprises at least two consecutive 2'-O-methyl modified nucleotides at the 3'-end.~~

- ~~39. The polynucleic acid molecule conjugate of any one of claims 1-38, wherein the sense strand comprises at least three, four, five, six, seven, eight, nine, or ten consecutive 2'-O-methyl modified nucleotides at the 3'-end.~~
- ~~40. The polynucleic acid molecule conjugate of any one of claims 1-39, wherein the sense strand comprises ten consecutive 2'-O-methyl modified nucleotides at the 3'-end.~~
- ~~41. The polynucleic acid molecule conjugate of any one of claims 1-40, wherein the sense strand comprises at least two phosphorothioate internucleotide linkages.~~
- ~~42. The polynucleic acid molecule conjugate of any one of claims 1-41, wherein the sense strand has a sequence of SEQ ID NO: 3, 5, 7, 9, 11, 13 or 15.~~
- ~~43. The polynucleic acid molecule conjugate of any one of claims 1-42, wherein the antisense strand comprises a 2'-O-methyl modified nucleotide at the 5'-end.~~
- ~~44. The polynucleic acid molecule conjugate of any one of claims 1-43, wherein the antisense strand comprises a 2'-O-methyl modified nucleotide at the 3'-end.~~
- ~~45. The polynucleic acid molecule conjugate of any one of claims 1-44, wherein the antisense strand comprises at least two, at least three, at least four, at least five consecutive 2'-O-methyl modified nucleotide at the 3'-end.~~
- ~~46. The polynucleic acid molecule conjugate of any one of claims 1-45, wherein the antisense strand comprises five consecutive 2'-O-methyl modified nucleotide at the 3'-end.~~
- ~~47. The polynucleic acid molecule conjugate of any one of claims 1-46, wherein the antisense strand comprises at least one, at least two, at least three, at least four 2'-F modified nucleotides.~~
- ~~48. The polynucleic acid molecule conjugate of any one of claims 1-47, wherein the antisense strand comprises four 2'-F modified nucleotides, wherein any two of the four 2'-F modified nucleotides are not consecutive.~~

- ~~49. The polynucleic acid molecule conjugate of any one of claims 1-48, wherein the antisense strand comprises two overhang nucleotides at the 3'-end.~~
- ~~50. The polynucleic acid molecule conjugate of any one of claims 1-49, wherein the antisense strand comprises at least two, at least three phosphorothioate internucleotide linkages.~~
- ~~51. The polynucleic acid molecule conjugate of any one of claims 1-50, wherein the antisense strand has a sequence of SEQ ID NO: 4, 6, 8, 10, 12, 14, or 16.~~
- ~~52.11. The polynucleic acid molecule conjugate of any one of claims 1-51, wherein the polynucleic acid molecule conjugate comprises a linker connecting anti-transferrin receptor antibody or antigen binding fragment thereof to the polynucleic acid molecule.~~
- ~~53. The polynucleic acid siRNA molecule conjugate of claim 52, wherein the linker is C6 linker.~~
- ~~54.12. The polynucleic acid molecule conjugate of claim 53.11, wherein the C6 linker is a 6-Amino-1-hexanol linker.~~
- ~~55. The polynucleic acid siRNA molecule conjugate of claim 52, wherein the linker is a homobifunctional linker or heterobifunctional linker, a maleimide group, a dipeptide moiety, a benzoic acid group, or its derivative thereof.~~
- ~~56.13. The polynucleic acid molecule conjugate of any one of claims 52-55.11, wherein the linker comprises 4-(N-maleimidomethyl) cyclohexane -1-amidate (SMCC).~~
- ~~57.14. The polynucleic acid siRNA molecule conjugate of any one of claims 52-56.11-13, wherein the linker is coupled to the 5'-end of the sense strand.~~
- ~~58.15. The polynucleic acid siRNA molecule conjugate of any one of claims 52-57.11-14, wherein the polynucleic acid siRNA molecule is conjugated to a cysteine residue of the anti-transferrin receptor antibody or antigen binding fragment thereof.~~
- ~~59. The polynucleic acid molecule conjugate of claim 58, wherein the cysteine residue is in the Fe domain of the anti-transferrin receptor antibody or antigen binding fragment thereof.~~

~~60.16.~~ The polynucleic acid siRNA molecule conjugate of any one of claims 1-~~59~~15, wherein a ratio between the polynucleic acid siRNA -molecule and the anti-transferrin receptor antibody or antigen binding fragment thereof is about 1:1, 2:1, 3:1, or 4:1.

~~61. The polynucleic acid molecule conjugate of any one of claims 1-60, wherein the polynucleic acid moiety mediates RNA interference against the human DMPK gene modulates muscle atrophy in a subject.~~

~~62. The polynucleic acid molecule conjugate of claim 61, wherein the RNA interference comprises reducing expression of the mRNA transcript of DMPK gene at least 50%, at least 60%, or at least 70% compared to a quantity of the mRNA transcript of DMPK gene in a cell affected by a muscle dystrophy.~~

~~63. The polynucleic acid molecule conjugate of any one of claims 61-62, wherein the muscle dystrophy is myotonic dystrophy type 1 (DM1).~~

~~64. A polynucleic acid molecule conjugate comprising:~~

~~an anti-transferrin receptor antibody or antigen binding fragment thereof conjugated to a polynucleic acid molecule that hybridizes to a target sequence of *DMPK*;~~

~~wherein the polynucleic acid molecule having a sense strand having a sequence of SEQ ID NO: 3, 5, 7, 9, 11, 13, or 15 and an antisense strand having a sequence of SEQ ID NO: 4, 6, 8, 10, 12, 14, or 16;~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof comprises a variable heavy chain (VH) region and a variable light chain (VL) region, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 17, HCDR2 sequence comprising SEQ ID NO: 20, and HCDR3 sequence comprising SEQ ID NO: 19; and the VL region comprises LCDR1 sequence comprising SEQ ID NO: 22, LCDR2 sequence comprising SEQ ID NO: 23, and LCDR3 sequence comprising SEQ ID NO: 24; and~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof and the polynucleic acid molecule is conjugated via a linker comprising 4-(N-maleimidomethyl) cyclohexane-1 amidate (SMCC).~~

~~65. A polynucleic acid molecule conjugate comprising:~~

~~an anti-transferrin receptor antibody or antigen binding fragment thereof conjugated to a polynucleic acid molecule that hybridizes to a target sequence of *DMPK*;~~

~~wherein the polynucleic acid molecule having a sense strand having a sequence of SEQ ID NO: 3, 5, 7, 9, 11, 13, or 15 and an antisense strand having a sequence of SEQ ID NO: 4, 6, 8, 10, 12, 14, or 16;~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof comprises a variable heavy chain (VH) region and a variable light chain (VL) region, wherein the VH region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to SEQ ID NO: 30, and wherein the VL region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to SEQ ID NO: 34; and~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof and the polynucleic acid molecule is conjugated via a maleimide linker.~~

~~66. A polynucleic acid molecule conjugate comprising:~~

~~an anti-transferrin receptor antibody or antigen binding fragment thereof conjugated to a polynucleic acid molecule that hybridizes to a target sequence of *DMPK*;~~

~~wherein the polynucleic acid molecule having a sense strand having a sequence of SEQ ID NO: 1 and an antisense strand having a sequence of SEQ ID NO: 2;~~

~~wherein the sense strand comprises at least three, four, five, or six consecutive 2'-O-methyl modified nucleotides at the 5'-end and at least two, at least three 2'-F modified nucleotides;~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof comprises a variable heavy chain (VH) region and a variable light chain (VL) region, wherein the VH region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to SEQ ID NO: 30, and wherein the VL region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to SEQ ID NO: 34; and~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof and the polynucleic acid molecule is conjugated via a maleimide linker.~~

~~67. A polynucleic acid molecule conjugate comprising:~~

~~an anti-transferrin receptor antibody or antigen binding fragment thereof conjugated to a polynucleic acid molecule that hybridizes to a target sequence of *DMPK*;~~

~~wherein the polynucleic acid molecule having a sense strand having a sequence of SEQ ID NO: 1 and an antisense strand having a sequence of SEQ ID NO: 2;~~

~~wherein the antisense strand comprises at least two, at least three, at least four, at least five consecutive 2'-O-methyl-modified nucleotide at the 3'-end, and at least one, at least two, at least three, at least four 2'-F-modified nucleotides;~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof comprises a variable heavy chain (VH) region and a variable light chain (VL) region, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 17, HCDR2 sequence comprising SEQ ID NO: 20, and HCDR3 sequence comprising SEQ ID NO: 19; and the VL region comprises LCDR1 sequence comprising SEQ ID NO: 22, LCDR2 sequence comprising SEQ ID NO: 23, and LCDR3 sequence comprising SEQ ID NO: 24; and~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof and the polynucleic acid molecule is conjugated via a maleimide linker.~~

~~68. A polynucleic acid molecule conjugate comprising:~~

~~an anti-transferrin receptor antibody or antigen binding fragment thereof conjugated to a polynucleic acid molecule that hybridizes to a target sequence of *DMPK*;~~

~~wherein the polynucleic acid molecule having a sense strand having a sequence of SEQ ID NO: 1 and an antisense strand having a sequence of SEQ ID NO: 2;~~

~~wherein the antisense strand comprises 2'-O-methyl-modified nucleotides at the 5'-end and at the 3'-end;~~

~~wherein the anti-transferrin receptor antibody or antigen binding fragment thereof comprises a variable heavy chain (VH) region and a variable light chain (VL) region, wherein the VH region comprises HCDR1 sequence comprising SEQ ID NO: 17, HCDR2 sequence comprising SEQ ID NO: 18, and HCDR3 sequence comprising SEQ ID NO: 19; and the VL region comprises LCDR1 sequence~~

~~comprising SEQ ID NO: 22, LCDR2 sequence comprising SEQ ID NO: 23, and LCDR3 sequence comprising SEQ ID NO: 24; and wherein the anti-transferrin receptor antibody or antigen binding fragment thereof and the polynucleic acid molecule is conjugated via a maleimide linker.~~

~~69. A polynucleic acid molecule conjugate comprising:~~

~~an anti-transferrin receptor antibody or antigen binding fragment thereof conjugated to a polynucleic acid molecule that hybridizes to a target sequence of *DMPK*; wherein the polynucleic acid molecule having a sense strand having a sequence of SEQ ID NO: 1 and an antisense strand having a sequence of SEQ ID NO: 2; wherein the antisense strand comprises at least five consecutive 2'-O-methyl modified nucleotide at the 3'-end and four 2'-F modified nucleotides, wherein any two of the four 2'-F modified nucleotides are not consecutive; wherein the anti-transferrin receptor antibody or antigen binding fragment thereof comprises a variable heavy chain (VH) region and a variable light chain (VL) region, and the VH region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to SEQ ID NO: 30, and wherein the VL region comprises at least 80%, 85%, 90%, 95%, 99%, or 100% sequence identity to SEQ ID NO: 34; and wherein the anti-transferrin receptor antibody or antigen binding fragment thereof and the polynucleic acid molecule is conjugated via a 6-Amino-1-hexanol linker.~~

~~70.17.~~ A pharmaceutical composition comprising:

~~a polynucleic acid-small interfering RNA (siRNA) molecule conjugate of any one of claims 1-~~69~~16; and a pharmaceutically acceptable excipient.~~

~~71. The pharmaceutical composition of claim 70, wherein the pharmaceutical composition is formulated as a nanoparticle formulation.~~

~~72.18.~~ ~~The pharmaceutical composition of any one of claims 70-~~71~~17,~~ wherein the pharmaceutical composition is formulated for intravenous, parenteral, oral, intranasal, buccal, rectal, or transdermal administration.

- ~~73. A method for treating muscular dystrophy in a subject in need thereof, comprising:~~
~~providing a polynucleic acid conjugate of any one of claims 1-69 or a pharmaceutical composition of any one of claims 70-72; and~~
~~administering the polynucleic acid conjugate to the subject in need thereof to treat the muscular dystrophy, wherein the polynucleic acid conjugate reduces a quantity of the mRNA transcript of human *DMPK*.~~
- ~~74. The method of claim 73, wherein the polynucleic acid moiety mediates RNA interference against the human *DMPK* modulates muscle atrophy in a subject.~~
- ~~75. The method of any one of claims 73-74, wherein the muscular dystrophy is myotonic dystrophy type 1 (DM1).~~
- 76.19. Use of the ~~polynucleic acid~~small interfering RNA (siRNA) molecule conjugate of any one of claims 1-~~69~~16 or the pharmaceutical composition of any one of claims ~~70-72~~for17-18 in the manufacture of a medicament for treating ~~in~~ a subject diagnosed with or suspected to have ~~myotoniemuscular~~ dystrophy ~~type 1 (DM1).~~.
- 77.20. Use~~The use~~ of the ~~polynucleic acid molecule~~siRNA molecule conjugate of ~~any one of claims 1-69 or~~claim 19, wherein the ~~pharmaceutical composition of any one of claims 70-72 for manufacturing a medicament for treating in a subject diagnosed with or suspected to have~~muscular dystrophy ~~is~~ myotonic dystrophy type 1 (DM1).
- ~~78. A kit comprising a polynucleic acid molecule conjugate of claims 1-69 or the pharmaceutical composition of any one of claims 70-72.~~
21. The siRNA molecule conjugate of any one of claims 1-16 or the pharmaceutical composition of any one of claims 17-18 for use in therapy.