

CLAIMS:

1. An RNAi agent for inhibiting expression of a double homeobox 4 (*DUX4*) gene, comprising:
 - i. an antisense strand comprising at least 17 contiguous nucleotides differing by 0 or 1 nucleotides from any one of the sequences provided in Table 2, Table 3, or Table 5.4; and
 - ii. a sense strand comprising a nucleotide sequence that is at least partially complementary to the antisense strand.
2. The RNAi agent of claim 1, wherein the antisense strand comprises nucleotides 2-18 of any one of the sequences provided in Table 2, Table 3, or Table 5.4.
3. The RNAi agent of claim 1 or claim 2, wherein the sense strand comprises a nucleotide sequence of at least 17 contiguous nucleotides differing by 0 or 1 nucleotides from any one of the sequences provided in Table 2, Table 4.1, Table 4.2, Table 4.3, Table 4.4, Table 4.5, Table 4.6, or Table 5.4, and wherein the sense strand has a region of at least 85% complementarity over the 17 contiguous nucleotides to the antisense strand.
- ~~4. The RNAi agent of any one of claims 1-3, wherein at least one nucleotide of the DUX4 RNAi agent is a modified nucleotide or includes a modified internucleoside linkage.~~
- ~~5. The RNAi agent of any one of claims 1-3, wherein all or substantially all of the nucleotides are modified nucleotides.~~
- ~~6. The RNAi agent of any one of claims 4-5, wherein the modified nucleotide is selected from the group consisting of: 2'-O-methyl nucleotide, 2'-fluoro nucleotide, 2'-deoxy nucleotide, 2',3'-seco nucleotide mimic, locked nucleotide, 2'-F-arabino nucleotide, 2'-methoxyethyl nucleotide, abasic nucleotide, ribitol, inverted nucleotide, inverted 2'-O-methyl nucleotide, inverted 2'-deoxy nucleotide, 2'-amino-modified nucleotide, 2'-alkyl~~

~~modified nucleotide, morpholino nucleotide, vinyl phosphonate-containing nucleotide, cyclopropyl phosphonate-containing nucleotide, and 3' O-methyl nucleotide.~~

~~7. The RNAi agent of claim 5, wherein all or substantially all of the modified nucleotides are 2' O-methyl nucleotides, 2' fluoro nucleotides, or combinations thereof.~~

~~8.4. The RNAi agent of any one of claims 1-37, wherein the antisense strand comprises the nucleotide sequence of any one of the modified sequences provided in Table 3.~~

~~9.5. The RNAi agent of any one of claims 1-48, wherein the sense strand comprises the nucleotide sequence of any one of the modified sequences provided in Table 4.1, Table 4.2, Table 4.3, Table 4.4, Table 4.5, Table 4.6, or Table 5.4.~~

~~10.6. _____ The RNAi agent of claim 1, wherein the antisense strand comprises the nucleotide sequence of any one of the modified sequences provided in Table 3 and the sense strand comprises the nucleotide sequence of any one of the modified sequences provided in Table 4.1, Table 4.2, Table 4.3, Table 4.4, Table 4.5, Table 4.6, or Table 5.4.~~

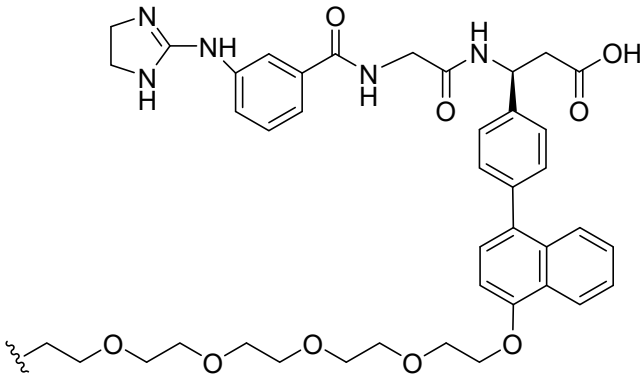
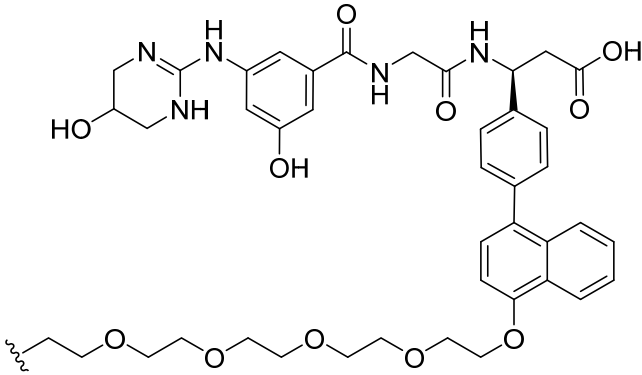
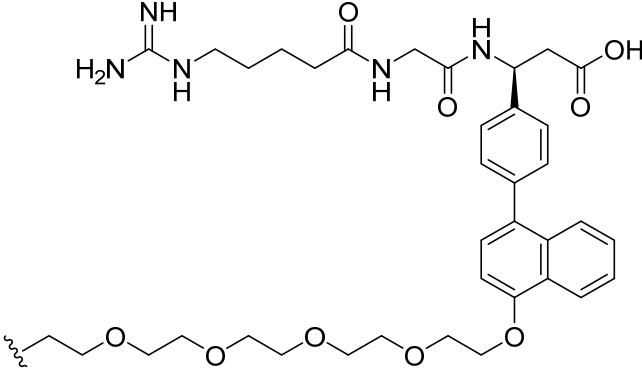
~~11.7. _____ The RNAi agent of any one of claims 1-610, wherein the RNAi agent is linked to a targeting ligand.~~

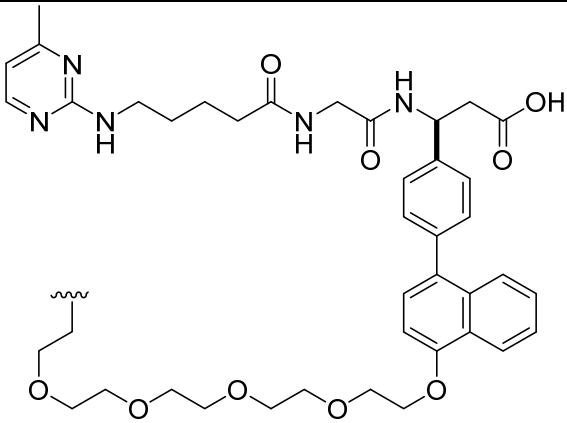
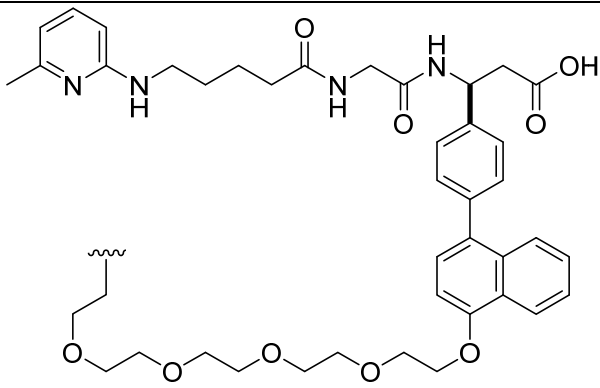
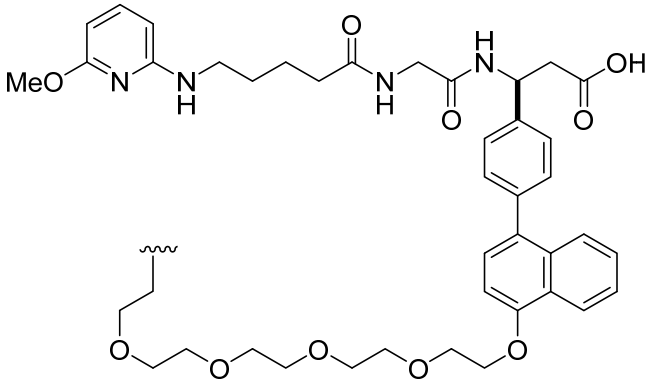
~~12. The RNAi agent of claim 11, wherein the targeting ligand is linked to the sense strand.~~

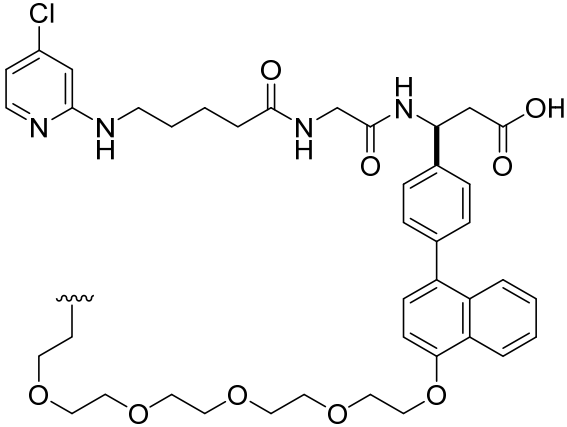
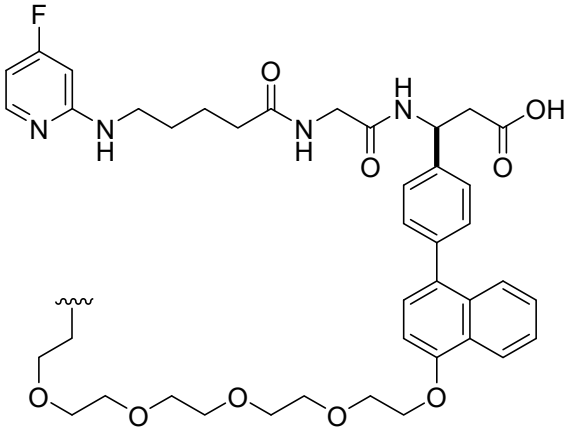
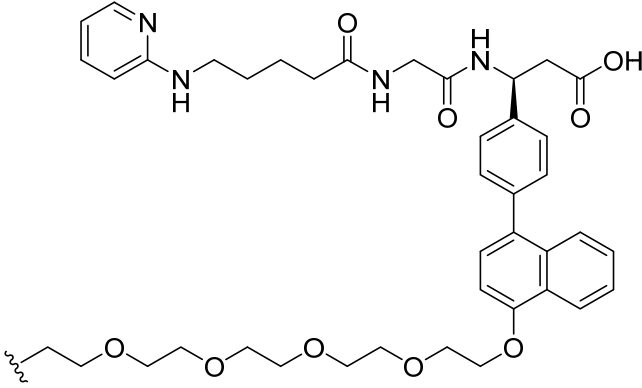
~~13. The RNAi agent of claim 12, wherein the targeting ligand is linked to the 5' terminal end of the sense strand.~~

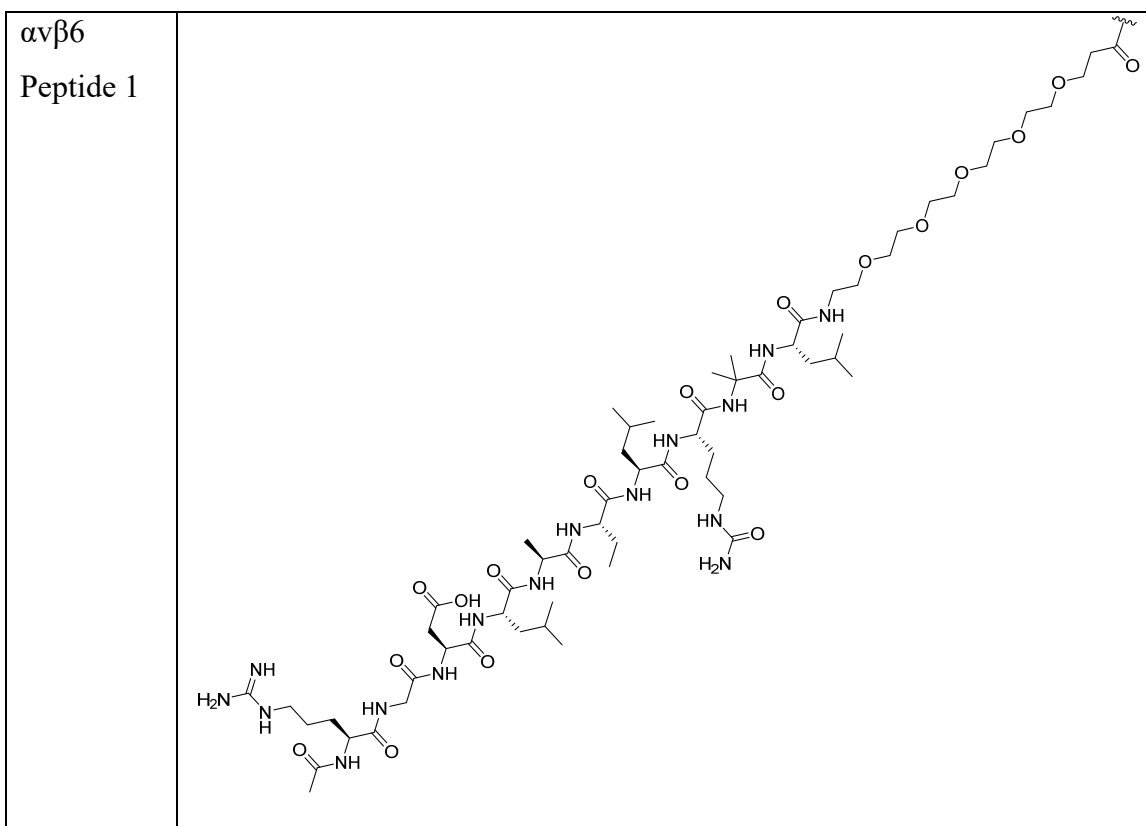
~~14. The RNAi agent of any one of claims 11-13, wherein the targeting ligand has affinity for a skeletal muscle cell and/or a cell receptor expressed on a skeletal muscle cell.~~

15.8. _____ The RNAi agent of ~~any of claims 711-14~~, wherein the targeting ligand is selected from the group consisting of:

Compound Number	Formula
40b	
41b	
42b	

55b	 <p>Chemical structure of compound 55b: A molecule featuring a 4-methylpyrimidin-2-yl group connected via an amide linkage to a 6-oxoheptanamide chain. This chain is further connected via an amide linkage to a 2-((4-(naphthalen-1-yl)phenyl)amino)propanoic acid moiety. The molecule is terminated by a poly(ethylene glycol) (PEG) chain, indicated by a wavy line at the end of the PEG segment.</p>
56b	 <p>Chemical structure of compound 56b: A molecule featuring a 4-methylpyridin-2-yl group connected via an amide linkage to a 6-oxoheptanamide chain. This chain is further connected via an amide linkage to a 2-((4-(naphthalen-1-yl)phenyl)amino)propanoic acid moiety. The molecule is terminated by a poly(ethylene glycol) (PEG) chain, indicated by a wavy line at the end of the PEG segment.</p>
57b	 <p>Chemical structure of compound 57b: A molecule featuring a 4-methoxy-2-pyridyl group connected via an amide linkage to a 6-oxoheptanamide chain. This chain is further connected via an amide linkage to a 2-((4-(naphthalen-1-yl)phenyl)amino)propanoic acid moiety. The molecule is terminated by a poly(ethylene glycol) (PEG) chain, indicated by a wavy line at the end of the PEG segment.</p>

58b	 <p>Chemical structure of compound 58b: A molecule featuring a 4-chlorophenyl group connected via an amide bond to a 6-oxoheptanamide chain. This chain is further connected via another amide bond to a 2-amino-3-((4-(naphthalen-1-yl)phenyl)propanoic acid) moiety. The molecule is terminated with a poly(ethylene glycol) (PEG) chain, indicated by a wavy line at the end of the PEG segment.</p>
59b	 <p>Chemical structure of compound 59b: A molecule featuring a 4-fluorophenyl group connected via an amide bond to a 6-oxoheptanamide chain. This chain is further connected via another amide bond to a 2-amino-3-((4-(naphthalen-1-yl)phenyl)propanoic acid) moiety. The molecule is terminated with a poly(ethylene glycol) (PEG) chain, indicated by a wavy line at the end of the PEG segment.</p>
60b	 <p>Chemical structure of compound 60b: A molecule featuring a pyridine ring connected via an amide bond to a 6-oxoheptanamide chain. This chain is further connected via another amide bond to a 2-amino-3-((4-(naphthalen-1-yl)phenyl)propanoic acid) moiety. The molecule is terminated with a poly(ethylene glycol) (PEG) chain, indicated by a wavy line at the end of the PEG segment.</p>



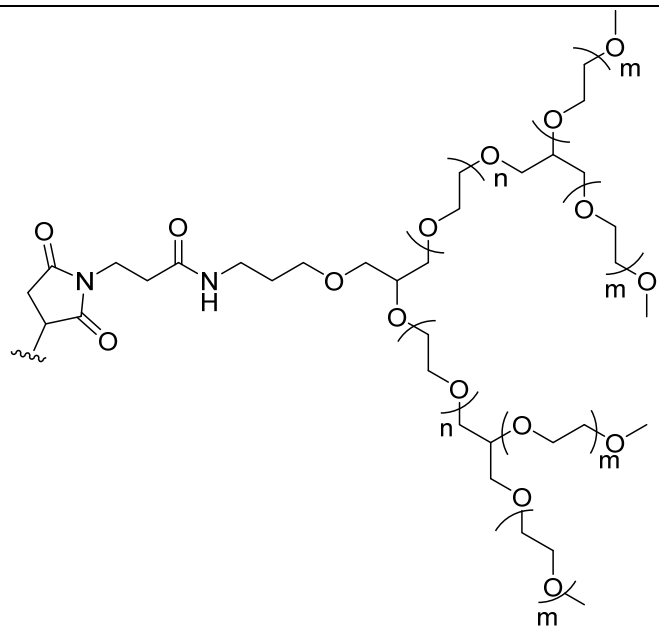
or a pharmaceutically acceptable salt thereof, wherein  indicates the point of connection to the RNAi agent.

~~16.9.~~ 16.9. The RNAi agent of any one of claims 1-~~8~~15, wherein the RNAi agent is further linked to a pharmacokinetic/pharmacodynamic (PK/PD) modulator.

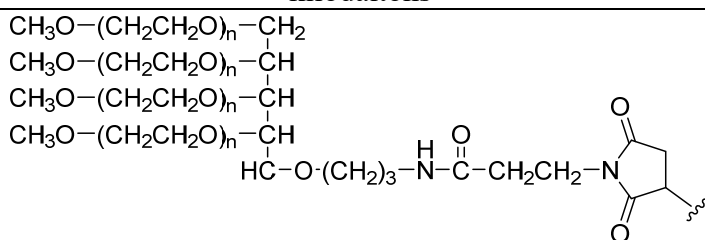
~~17.10.~~ 17.10. The RNAi agent of claim ~~9~~16, wherein the PK/PD modulator is linked to the sense strand.

~~18.11.~~ 18.11. The RNAi agent of claim ~~10~~7, wherein the PK/PD modulator is linked to the 3' terminal end of the sense strand.

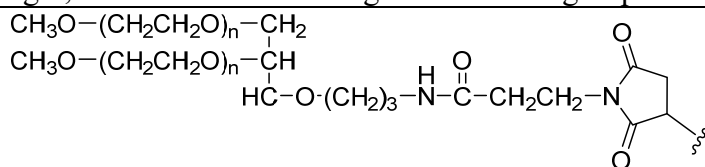
~~19.12.~~ 19.12. The RNAi agent of any one of claims ~~9-11~~16-18, wherein the PK/PD modulator is selected from the group consisting of:



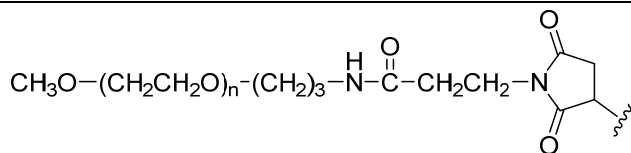
PEG40K (2x2-arm),
wherein n and m are integers, and the molecular weight of the PEG groups is about 40 kilodaltons



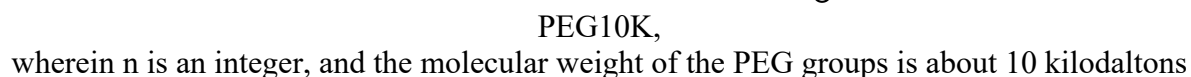
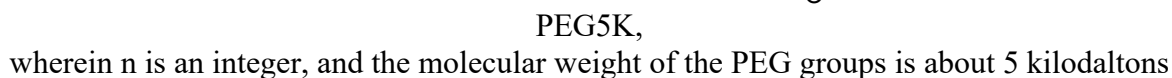
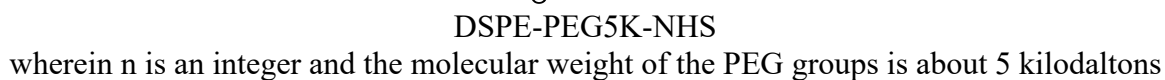
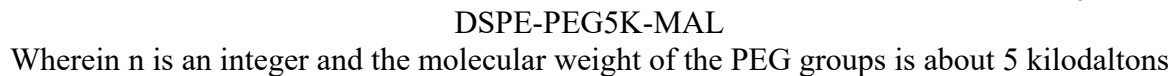
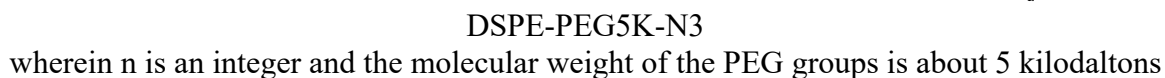
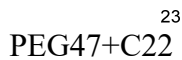
PEG40K (4-arm),
wherein n is an integer, and the molecular weight of the PEG groups is about 40 kilodaltons

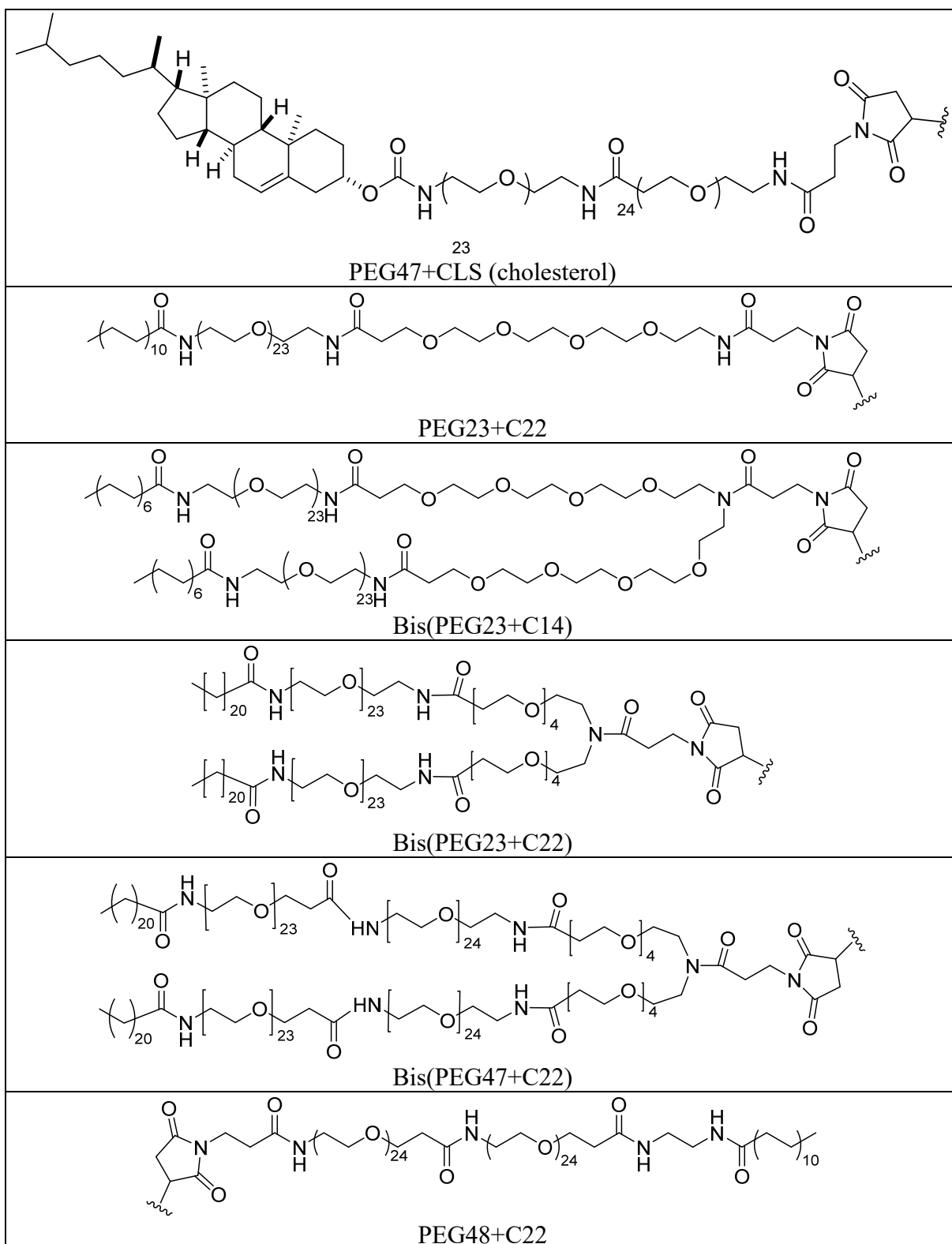


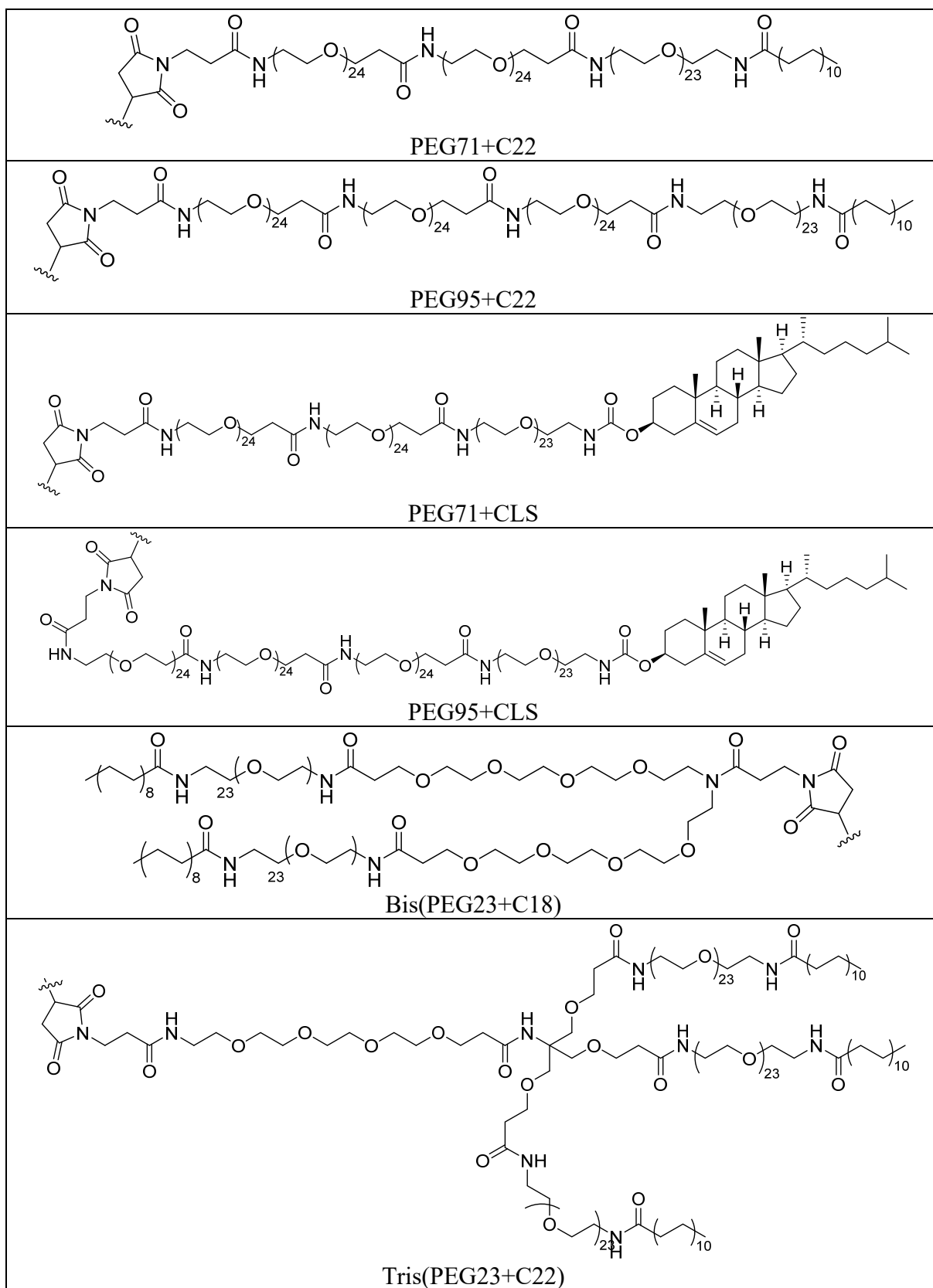
PEG40K (2-arm),
wherein n is an integer, and the molecular weight of the PEG groups is about 40 kilodaltons

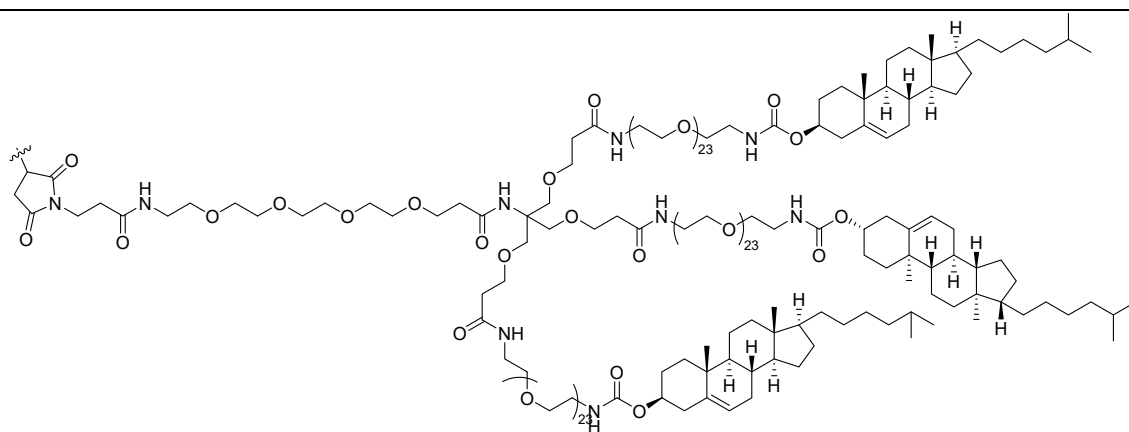


PEG40K,
wherein n is an integer, and the molecular weight of the PEG groups is about 40 kilodaltons

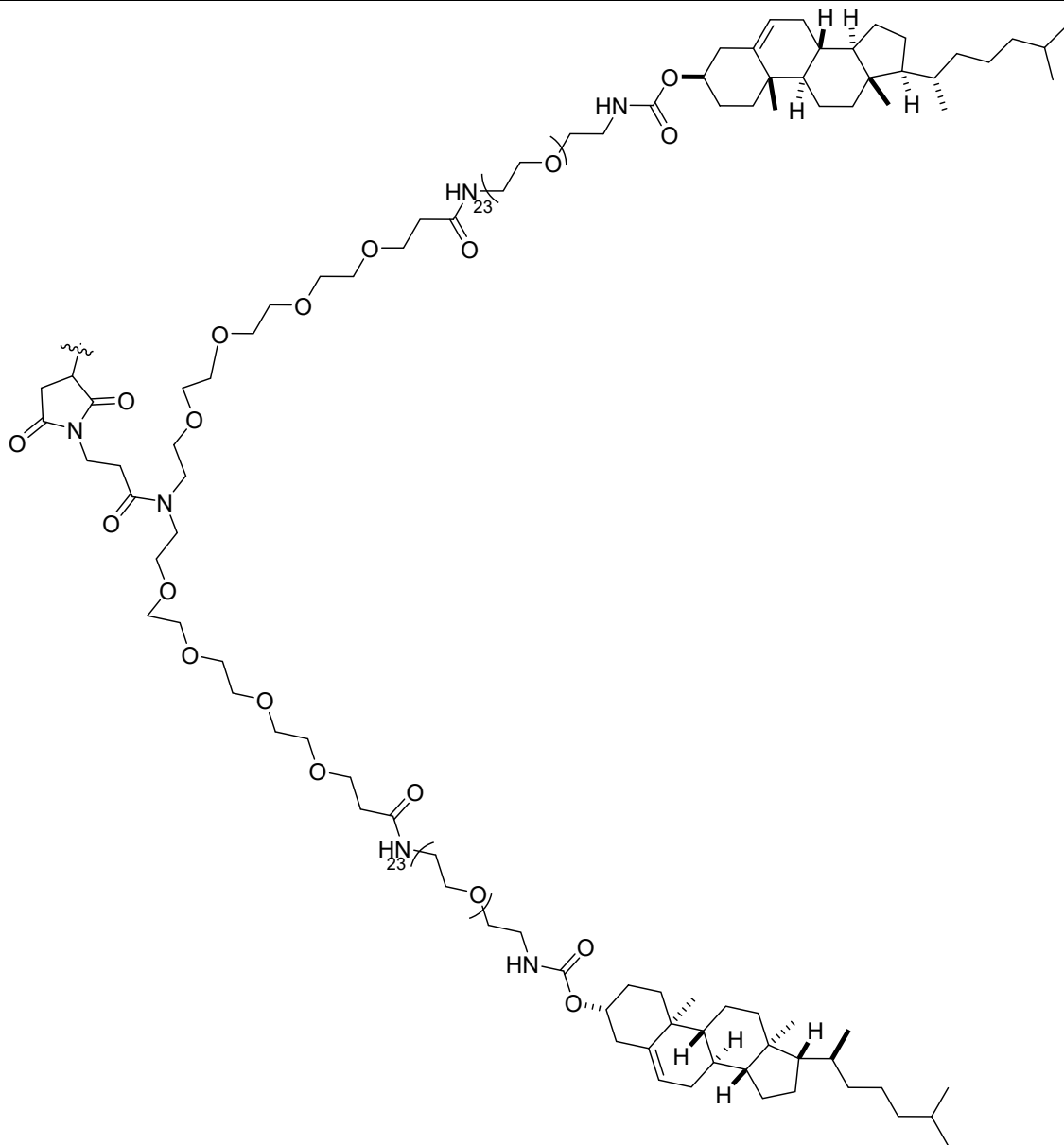




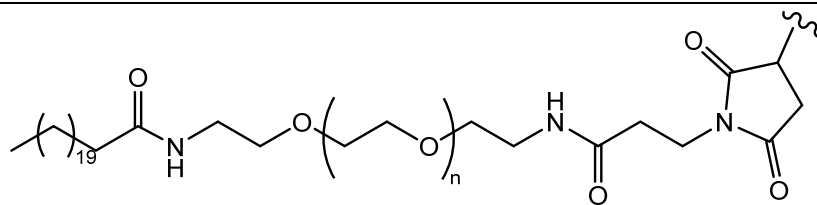




Tris(PEG23+CLS)

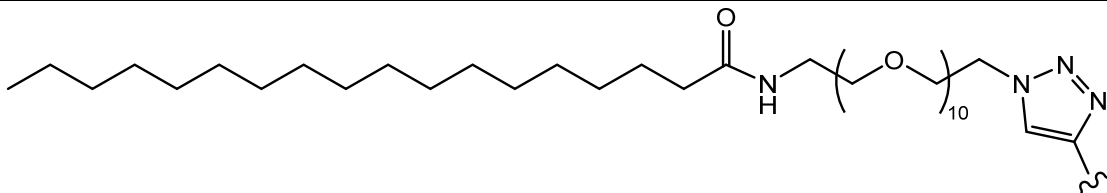


Bis(PEG23+CLS)

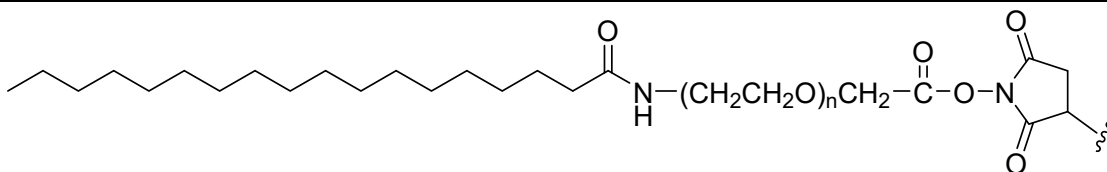


PEG5K+C22

wherein n is an integer and the molecular weight of the PEG units is about 5 kilodaltons

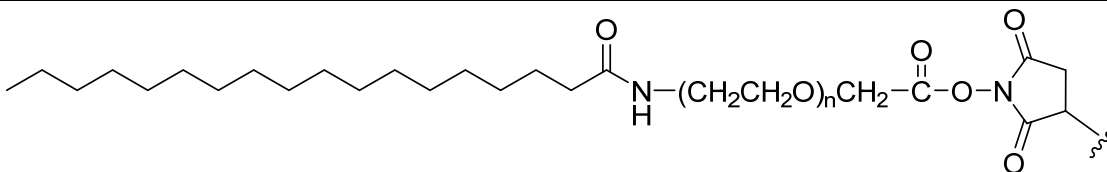


C18



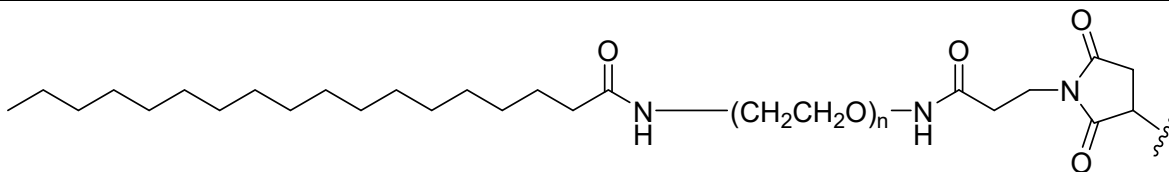
(NHS)-PEG1K+C18

wherein n is an integer and the molecular weight of the PEG units is about 1 kilodalton



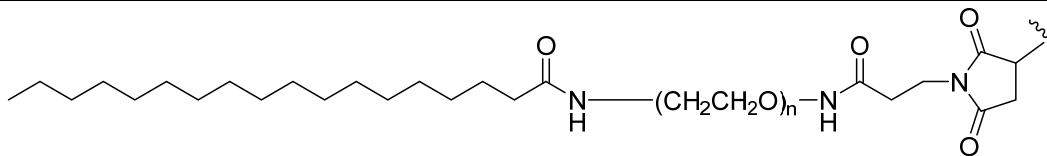
(NHS)-PEG2K+C18

wherein n is an integer and the molecular weight of the PEG units is about 2 kilodaltons



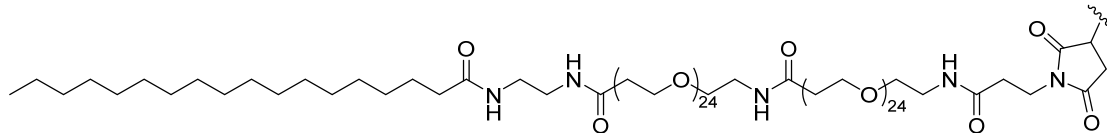
(NHS)-PEG5K+C18

wherein n is an integer and the molecular weight of the PEG units is about 5 kilodaltons



(MAL)-PEG5K+C18

wherein n is an integer and the molecular weight of the PEG units is about 5 kilodaltons

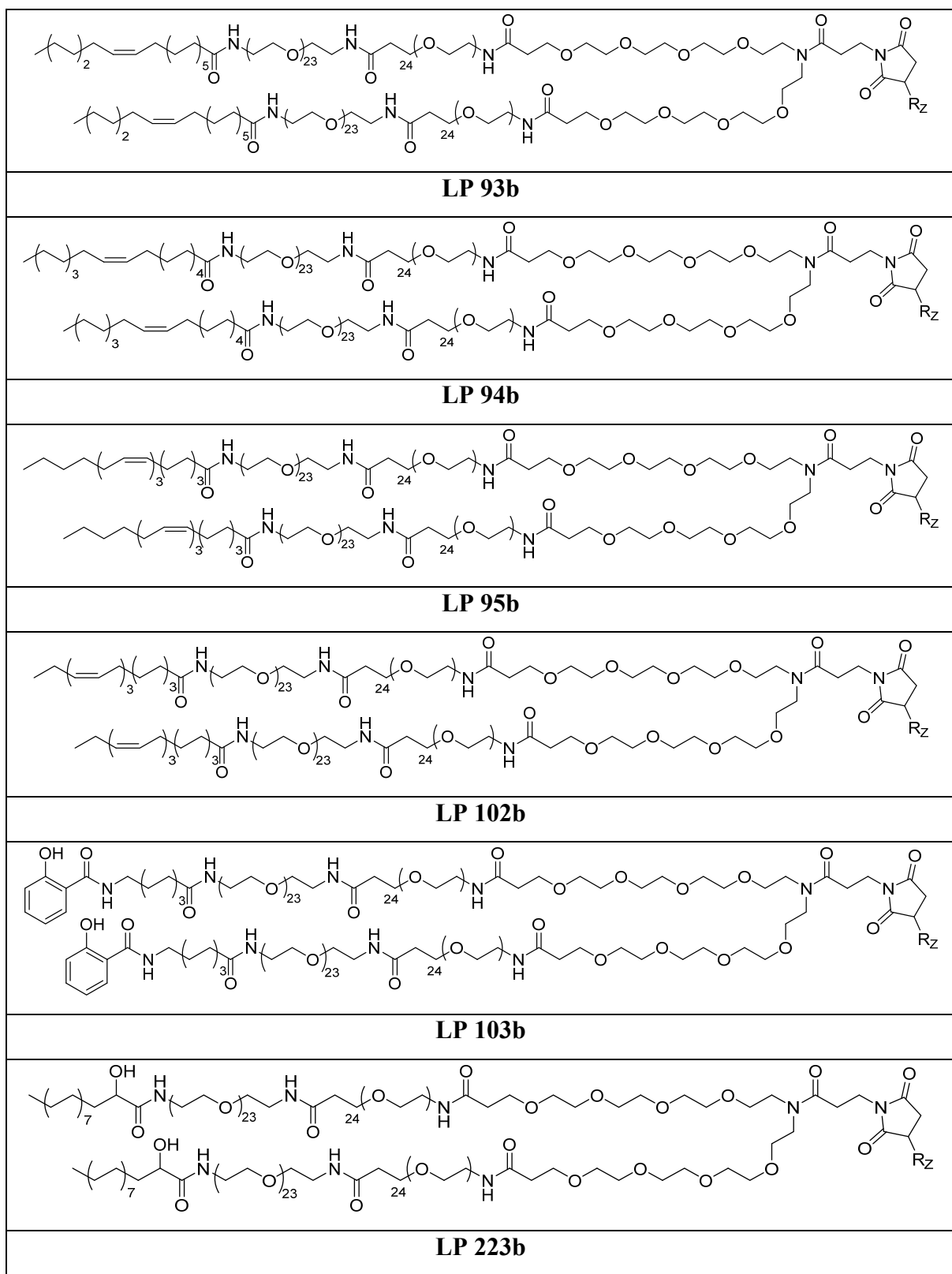


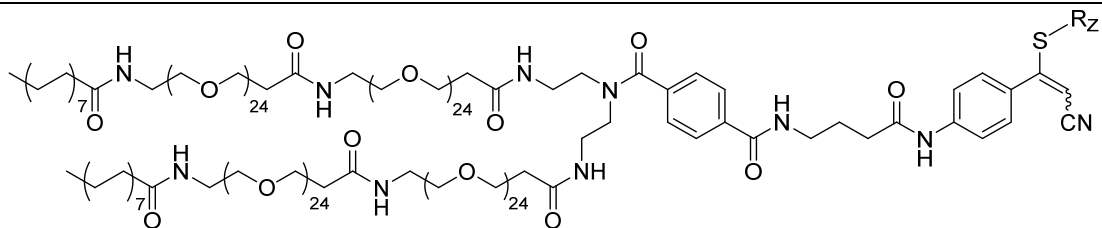
PEG48+C18

or a pharmaceutically acceptable salt thereof, wherein $\sim$ indicates the point of connection to the RNAi agent.

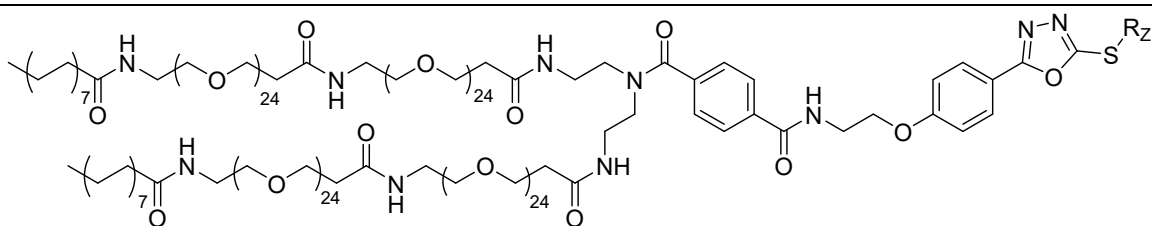
20.13. The RNAi agent of any one of claims 9-11, 17-19, wherein the PK/PD modulator is selected from the group consisting of:

LP 1b
LP 28b
LP 29b
LP 48b
LP 49b

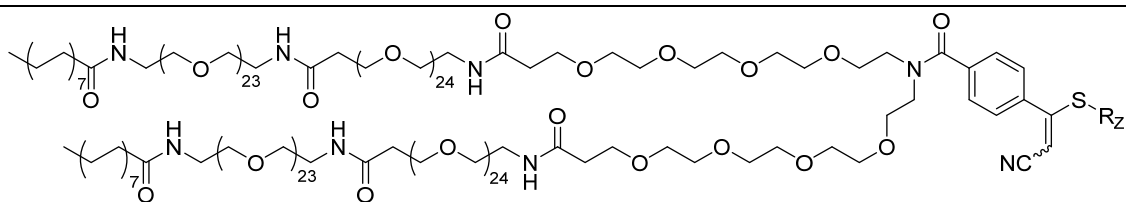




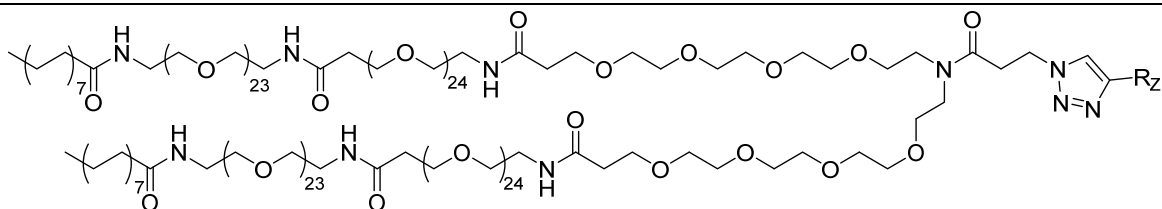
LP 224b



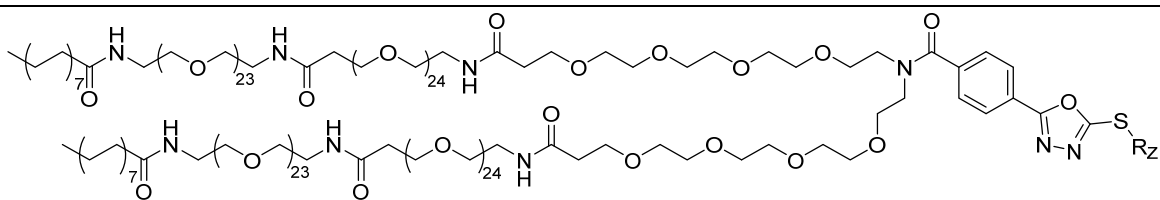
LP 225b



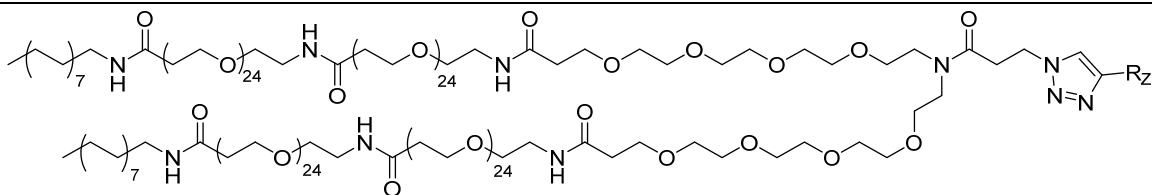
LP 226b



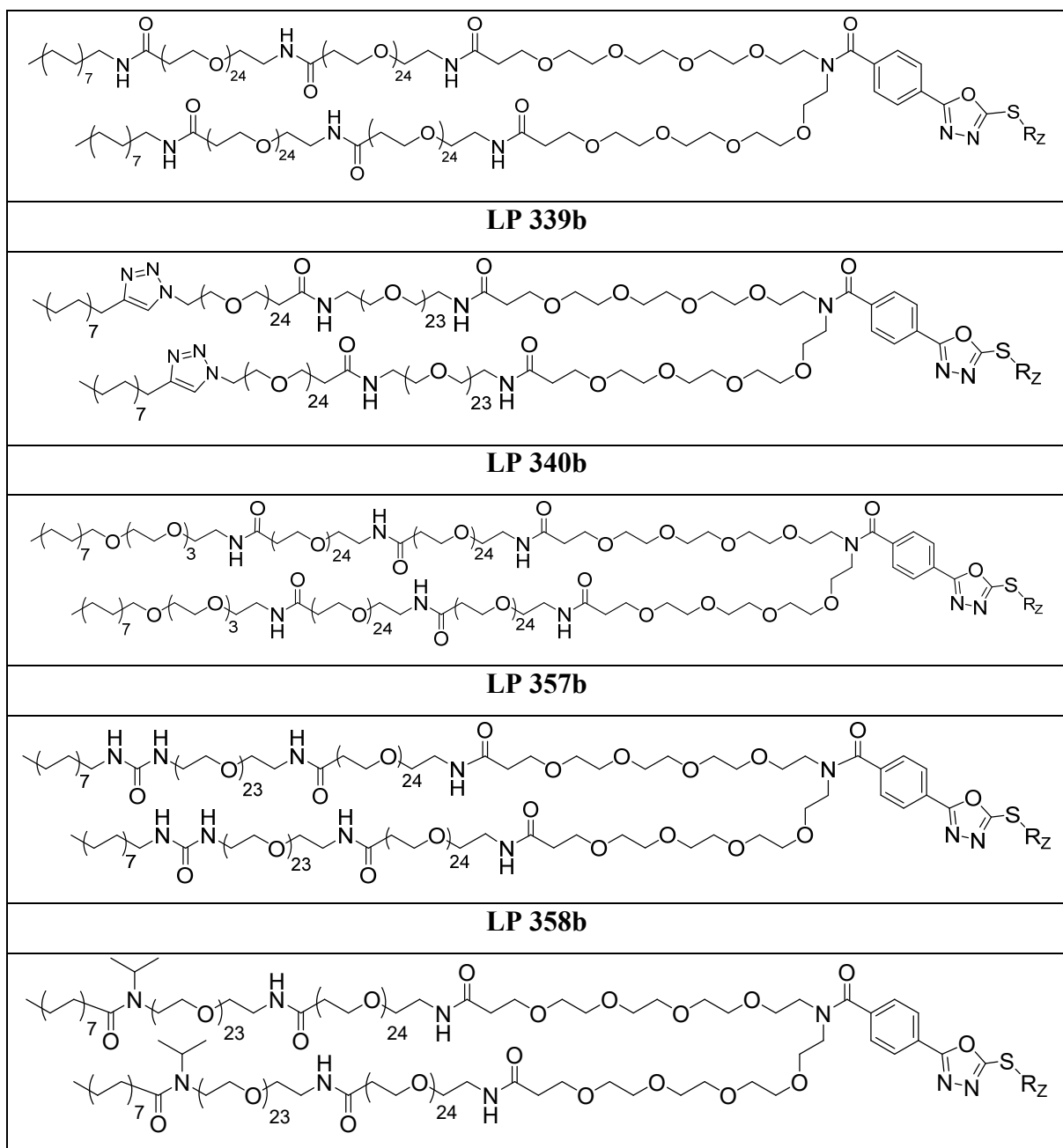
LP 238b



LP 246b



LP 247b



wherein R_z comprises the RNAi agent.

~~21. The RNAi agent of any one of claims 1-20, wherein the sense strand is between 15 and 49 nucleotides in length, and the antisense strand is between 17 and 30 nucleotides in length.~~

~~22. The RNAi agent of claim 21, wherein the sense strand and the antisense strand are each between 18 and 24 nucleotides in length.~~

~~23. The RNAi agent of claim 22, wherein the sense strand and the antisense strand are each 21 nucleotides in length.~~

~~24. The RNAi agent of claim 23, wherein the RNAi agent has two blunt ends.~~

~~25. The RNAi agent of any one of claims 1-24, wherein the sense strand comprises one or two terminal caps.~~

~~26. The RNAi agent of any one of claims 1-25, wherein the sense strand comprises one or two inverted abasic deoxyribose residues.~~

~~27.~~14. The RNAi agent of any one of claims 1-~~13~~26, comprising an antisense strand that consists of, consists essentially of, or comprises a nucleotide sequence that differs by 0 or 1 nucleotides from one of the following nucleotide sequences (5' → 3'):

UAGAAUUUCACGGAAGAAC (SEQ ID NO:22);

UGAAACCAGAUCUGAAUCC (SEQ ID NO:10);

UUGAAACCAGAUCUGAAUC (SEQ ID NO:14);

UAGAAUUUCACGGAAGAACAG (SEQ ID NO:164);

UGAAACCAGAUCUGAAUCCUG (SEQ ID NO:162);

UUGAAACCAGAUCUGAAUCCU (SEQ ID NO:163); and

UUGAAACCAGAUCUGAAUCCC (SEQ ID NO:169).

~~28.~~15. The RNAi agent of claim ~~14~~27, wherein all or substantially all of the nucleotides are modified nucleotides.

~~29~~.16. The RNAi agent of any one of claims 1-~~152~~8, comprising an antisense strand that comprises, consists of, or consists essentially of a modified nucleotide sequence that differs by 0 or 1 nucleotides from one of the following nucleotide sequences (5' → 3'):

usAfsGfsAfauuucacGfgAfaGfaacasg (SEQ ID NO:82);
cPrpusAfsGfsAfauuucacGfgAfaGfaacasg (SEQ ID NO:84);
cPrpusAfsGfsAfauuucacGfgAfaGfaacasg (SEQ ID NO:100);
cPrpusAfsGfsaauuucacGfgAfaGfaacasg (SEQ ID NO:101);
cPrpusGfsasaaccagauCfuGfaAfuccusg (SEQ ID NO:97);
cPrpusGfsasAfaccagauCfuGfaAfuccusg (SEQ ID NO:99);
cPrpusGfsasAfaCfcAfgAfuCfuGfaAfuCfcUfsg (SEQ ID NO:75);
usGfsasaaccagauCfuGfaAfuccusg (SEQ ID NO:96);
cPrpusUfsgsAfaAfcCfaGfaUfcUfgAfaUfcCfsu (SEQ ID NO:76);
cPrpusUfsgsaaccagaUfcUfgAfauccsc (SEQ ID NO:89); and
cPrpusUfsgsAfaAfcCfaGfaUfcUfgAfaUfcCfsc (SEQ ID NO:87);

wherein a, c, g, and u represent 2'-O-methyl adenosine, 2'-O-methyl cytidine, 2'-O-methyl guanosine, and 2'-O-methyl uridine, respectively; Af, Cf, Gf, and Uf represent 2'-fluoro adenosine, 2'-fluoro cytidine, 2'-fluoro guanosine, and 2'-fluoro uridine, respectively; cPrpu represents a 5'-cyclopropyl phosphonate-2'-O-methyl uridine; s represents a phosphorothioate linkage; and wherein all or substantially all of the nucleotides on the sense strand are modified nucleotides.

~~30~~.17. The RNAi agent of claim ~~16~~29, wherein the sense strand comprises, consists of, or consists essentially of a modified nucleotide sequence that differs by 0 or 1 nucleotides from one of the following nucleotide sequences (5' → 3'):

caggauucAfGfAfucugguuua (SEQ ID NO:147);
aggauucaGfAfUfcugguuucaa (SEQ ID NO:148)
cuguucuuCfCfGfugaaauucua (SEQ ID NO:149);
gggauucaGfAfUfcugguuucaa (SEQ ID NO:156); and
gggauucaGfaUfCfugguuucaa (SEQ ID NO:159);

wherein a, c, g, and u represent 2'-O-methyl adenosine, 2'-O-methyl cytidine, 2'-O-methyl guanosine, and 2'-O-methyl uridine, respectively; Af, Cf, Gf, and Uf represent 2'-fluoro adenosine, 2'-fluoro cytidine, 2'-fluoro guanosine, and 2'-fluoro uridine, respectively; and wherein all or substantially all of the nucleotides on the antisense strand are modified nucleotides.

~~31-18.~~ 18. An RNAi agent of any one of claims 1-~~1730~~, comprising:

- (i) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') usAfsGfsAfauuucacGfgAfaGfaacag (SEQ ID NO:82), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cuguucuuCfCfGfugaaaauucua (SEQ ID NO:149);
- (ii) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusAfsGfsAfauuucacGfgAfaGfaacag (SEQ ID NO:84), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cuguucuuCfCfGfugaaaauucua (SEQ ID NO:149);
- (iii) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusAfsGfsAfauuucacGfgAfaGfaacag (SEQ ID NO:100), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cuguucuuCfCfGfugaaaauucua (SEQ ID NO:149);
- (iv) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusAfsGfsaauuucacGfgAfaGfaacag (SEQ ID NO:101), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cuguucuuCfCfGfugaaaauucua (SEQ ID NO:149);
- (v) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusGfsasaaccagauCfuGfaAfuccug (SEQ ID NO:97), and a sense strand that consists of, consists essentially of, or

- comprises the modified nucleotide sequence (5' → 3') caggauucAfGfAfucugguuuc (SEQ ID NO:147);
- (vi) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusGfsasAfaccagauCfuGfaAfuccusg (SEQ ID NO:99), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') caggauucAfGfAfucugguuuc (SEQ ID NO:147);
 - (vii) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusGfsasAfaCfcAfgAfuCfuGfaAfuCfcUfsg (SEQ ID NO:75), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') caggauucAfGfAfucugguuuc (SEQ ID NO:147);
 - (viii) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') usGfsasaaccagauCfuGfaAfuccusg (SEQ ID NO:96), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') caggauucAfGfAfucugguuuc (SEQ ID NO:147);
 - (ix) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusUfsgsAfaAfcCfaGfaUfcUfgAfaUfcCfsu (SEQ ID NO:76), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') aggauucaGfAfUfcugguuuc (SEQ ID NO:148);
 - (x) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusUfsgsaaaccagaUfcUfgAfauccsc (SEQ ID NO:89), and a sense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') gggauucaGfAfUfcugguuuc (SEQ ID NO:156); or
 - (xi) an antisense strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') cPrpusUfsgsAfaAfcCfaGfaUfcUfgAfaUfcCfsc (SEQ ID NO:87), and a sense

strand that consists of, consists essentially of, or comprises the modified nucleotide sequence (5' → 3') gggauucaGfaUfCfugguuucaa (SEQ ID NO:159); wherein a, c, g, and u represent 2'-O-methyl adenosine, 2'-O-methyl cytidine, 2'-O-methyl guanosine, and 2'-O-methyl uridine, respectively; Af, Cf, Gf, and Uf represent 2'-fluoro adenosine, 2'-fluoro cytidine, 2'-fluoro guanosine, and 2'-fluoro uridine, respectively; cPrpu represents a 5'-cyclopropyl phosphonate-2'-O-methyl uridine; s represents a phosphorothioate linkage; and wherein the respective sense strand further optionally includes an inverted abasic residue at the 3' terminal end of the nucleotide sequence and at the 5' terminal end of the nucleotide sequence; and the sense strand also optionally includes a targeting ligand that is covalently linked to the inverted abasic residue at the 5' terminal end of the sense strand, wherein the targeting ligand has affinity for skeletal muscle cells and/or a receptor present on skeletal muscle cells, and wherein the sense strand further optionally includes a PK/PD modulator that is covalently linked to the inverted abasic residue at the 3' terminal end of the sense strand.

~~32.19.~~ The RNAi agent of claim 1, wherein the RNAi agent is comprised of a sense strand and an antisense strand that form a duplex having the structure of any one of the duplexes in Table 5.1, Table 5.2, Table 5.3, or Table 5.4.

~~33. The RNAi agent of claim 32, wherein the sense strand further includes inverted abasic deoxyribose residues at the 3' end and/or at the 5' end of the nucleotide sequence.~~

~~34. The RNAi agent of claim 33, wherein all or substantially all of the nucleotides are modified nucleotides.~~

~~35.20.~~ The RNAi agent of ~~any one of claims 19~~ 32-34, wherein the sense strand of the RNAi agent is linked to a targeting ligand.

~~36. The RNAi agent of claim 35, wherein the targeting ligand has affinity for a cell receptor expressed on a skeletal muscle cell.~~

~~37.~~21. The RNAi agent of ~~any one of claims 2035-36~~, wherein the targeting ligand comprises a compound having the structure set forth in Table 6.2 or Table 6.3.

~~38.~~22. The RNAi agent of any one of claims 1-~~21~~37, wherein the RNAi agent is a pharmaceutically acceptable salt.

~~39.~~23. The RNAi agent of claim ~~22~~38, wherein the RNAi agent is in the sodium salt form.

~~40.~~24. A pharmaceutical composition comprising the RNAi agent of any one of claims 1-~~23~~39, wherein the composition further comprises a pharmaceutically acceptable excipient.

~~41.~~25. A method for inhibiting expression of a *DUX4* gene in a cell *in vitro*, the method comprising introducing into a cell an effective amount of an RNAi agent of any one of claims 1-~~23~~39 or the composition of claim ~~24~~40.

~~42. The method of claim 41, wherein the cell is within a subject.~~

~~43. The method of claim 42, wherein the subject is a human subject.~~

~~44. The method of any one of claims 41-43, wherein the DUX4 gene expression is inhibited by at least about 40%.~~

~~45. The method of any one of claims 41-44, wherein the DUX4 protein levels are reduced by at least about 40%.~~

46. ~~26.~~ A method of A composition comprising the RNAi agent of any one of claims 1-23, for use in treating one or more symptoms or diseases that can be ameliorated at least in part by a reduction in DUX4 protein levels, or a reduction in DUX4 mRNA levels, ~~the method comprising administering to a human subject in need thereof a therapeutically effective amount of the pharmaceutical composition of claim 40.~~

47. ~~27.~~ The method pharmaceutical composition of claim ~~26~~46, wherein the disease is FSHD.

48. ~~28.~~ The method pharmaceutical composition of any one of claims ~~25-27~~41-47, wherein the DUX4 gene expression is reduced in one or more of paraspinal, facial, torso, abdominal, and limb muscle tissues of ~~a~~the subject.

49. ~~29.~~ The method pharmaceutical composition of any one of claims ~~25-28~~41-48, wherein the DUX4 gene expression is reduced in one or more of the triceps, biceps, quadriceps, gastrocnemius, soleus, EDL (extensor digitorum longus), TA (Tibialis anterior), or diaphragm of ~~a~~the subject.

50. ~~30.~~ The method pharmaceutical composition of any one of claims ~~25-29~~41-49, wherein the RNAi agent is administered at a dose of about 0.5 mg/kg to about 10.0 mg/kg of body weight.

51. ~~31.~~ The method pharmaceutical composition of claim ~~30~~50, wherein the RNAi agent is administered by subcutaneous (SQ) injection.

52. ~~Use of the RNAi agent of any one of claims 1-39 or the composition according to claim 40, for the treatment of a disease, disorder, or symptom that is mediated at least in part by a reduction in DUX4 protein levels or a reduction in DUX4 mRNA levels, or both.~~

~~53.~~32. Use of the pharmaceutical composition according to claim ~~2440~~, for the manufacture of a medicament for treatment of a disease, disorder, or symptom that is mediated at least in part by a reduction in DUX4 protein levels or a reduction in DUX4 mRNA levels, or both.

~~54.~~33. A composition for inhibiting expression of a double homeobox 4 (*DUX4*) gene, the composition comprising:

- i. an RNAi agent comprising an antisense strand 18 to 49 nucleotides in length that is at least partially complementary to a portion of SEQ ID NO:1 or SEQ ID NO:2;
- ii. a targeting ligand linked to the RNAi agent, wherein the targeting ligand has affinity for skeletal muscle cells; and
- iii. a PK/PD modulator linked to the RNAi agent.

~~55.~~34. An RNAi agent for inhibiting expression of a double homeobox 4 (*DUX4*) gene, comprising:

- i. a sense strand comprising a nucleotide sequence that comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from a stretch of 15 contiguous nucleotides of SEQ ID NO:1; and
- ii. an antisense strand comprising a nucleotide sequence that is at least partially complementary to the sense strand.

~~56.~~35. An RNAi agent for inhibiting expression of a double homeobox 4 (*DUX4*) gene, comprising:

- i. an antisense strand comprising a nucleotide sequence that comprises at least 15 contiguous nucleotides that are at least partially complementary to a stretch of 15 contiguous nucleotides of SEQ ID NO:1; and
- ii. a sense strand comprising a nucleotide sequence that is at least partially complementary to the antisense strand.