CLAIMS

1. An oligomeric compound comprising a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide consists of 10 to 300 linked nucleosides, and the conjugate group comprises a bicycle ligand and a conjugate linker, wherein
   the bicycle ligand comprises a polypeptide consisting of 13-22 linked amino acids or amino acid mimetics and a molecular scaffold, wherein
      each of a first, a second, and a third amino acid of the polypeptide comprises a reactive group, each of which separately forms a bond with the molecular scaffold, thereby forming two polypeptide loops attached to the molecular scaffold; and
   wherein a portion of the bicycle ligand binds to a type 1 transferrin receptor; and
   wherein the modified oligonucleotide is covalently linked to the bicycle ligand through the conjugate linker.
2. The oligomeric compound of claim 1, wherein the conjugate group consists of the bicycle ligand and a conjugate linker; and/or
   wherein the oligomeric compound consists of the modified oligonucleotide and the conjugate group.
3. The oligomeric compound of either one of claims 1 or 2, wherein the three reactive groups are each the thiol of a cysteine.
4. The oligomeric compound of any one of claims 1-3, wherein the polypeptide has the following formula, from N-terminal to C-terminal:
      $[B]_n$-$[Z_i]$-$[J]_m$-$[Z_{ii}]$-$[O]_o$-$[Z_{iii}]$-$[U]_p$, wherein:
      Z_i, Z_{ii}, and Z_{iii} are the first, second, and third amino acids comprising a reactive group;
      each B, J, O, and U is independently selected amino acids or amino acid mimetics;
      n is from 0 to 5;
      m is from 3 to 7;
      o is from 3 to 7;
      p is from 0 to 5;
      wherein the sum of m+o is less than 12;
   optionally wherein:
      (i) m is 7 and o is 3; or
      (ii) m is 2 and o is 9; or
      (iii) m and o are both 6; or
      (iv) m is 3 and o is 8;
   and/or

(a) n is 0; or

(b) n is 3 or 4;

and/or

(I) p is 0; or

(II) p is 3 or 4.

5. The oligomeric compound of any one of claims 1-4, wherein the polypeptide has an N-terminal modification; optionally wherein:

(i) the N-terminal modification is an acetyl group; or

(ii) the N-terminal modification is an azidopropyl group;

or wherein the polypeptide has a C-terminal modification; optionally wherein the C-terminal modification is an amide group.

6. The oligomeric compound of any one of claims 1-5, wherein the conjugate linker is attached to the N-terminal amino acid of the bicycle ligand;

and/or the conjugate linker is attached to the C-terminal amino acid of the bicycle ligand;

and/or the conjugate linker is attached to a side chain of an amino acid within one of the polypeptide loops of the bicycle ligand;

and/or the bicycle ligand comprises a C-terminal extension, optionally wherein the C-terminal extension is selected from PEG10 or PEG24;

and/or the bicycle ligand comprises an N-terminal extension, optionally wherein the N-terminal extension is selected from PEG10 or PEG24.

7. The oligomeric compound of any one of claims 1-6, wherein the conjugate group is attached:

(i) to the 5'-terminal nucleoside of the modified oligonucleotide; optionally wherein the conjugate group is attached to the 5'-position of the 5'-terminal nucleoside of the modified oligonucleotide; or

(ii) to the 3'-terminal nucleoside of the modified oligonucleotide; optionally wherein the conjugate group is attached to the 3'-position of the 3'-terminal nucleoside of the modified oligonucleotide; or

(iii) to an internal nucleoside of the modified oligonucleotide; or

(iv) through a modified internucleoside linkage,

wherein optionally for any one of (i)-(iv) the conjugate group is attached through a 2'-modified furanosyl sugar moiety.

8. The oligomeric compound of any one of claims 1-7, wherein the bicycle ligand has an amino acid sequence with at least 80% identity to any one of SEQ ID NOs: 26-27, 36-56, 58-65, 67-76, 79-88, 90-152, or 192-246; optionally wherein the bicycle ligand has an amino acid sequence with at least 85%, at least 90%, at least 95%, or 100% identity to any one of SEQ ID NOs: 26-27, 36-56, 58-65, 67-76, 79-88, 90-152, or 192-246.

9. The oligomeric compound of any one of claims 4-8, wherein $[Z_i]$-$[J]_m$-$[Z_{ii}]$-$[O]_o$-$[Z_{iii}]$ has an amino acid sequence with at least 85%, at least 90%, at least 95%, or 100% identity to any of SEQ ID NOs: 26-27, 35-56, 58-65, 67-76, 79-88, 90-152, or 192-246; and/or wherein $[Z_i]$-$[J]_m$-$[Z_{ii}]$-$[O]_o$-$[Z_{iii}]$ has an amino acid sequence of CXXDXXXGCISYC (SEQ ID NO: 35), wherein each "X" is an independently selected amino acid.
10. The oligomeric compound of any one of claims 1-9, wherein the bicycle ligand comprises at least one, at least two, or at least three non-natural amino acids; optionally wherein at least one non-natural amino acid is selected from a $_D$-amino acid, allo-isoleucine, 2-amino-3-ethyl-pentanoic acid, aminoisobutyric acid, aminobutyric acid, azetidine, 7-azatryptophan, 6-azidolysine, β-cyclobutylalanine, β-methyl isoleucine, 4, 4-biphenylalanine, cis-hydroxyproline, cyclobutyl glycine, cyclohexyl glycine, cyclopentyl alanine, cyclopentyl glycine, 2,6-dimethyl tyrosine, 3,3-diphenyl alanine, 4-trans-hydroxy-L-proline, 1-napthaylalanine, 2-napthylalanine, N-methyl alanine, 1-methyl histidine, 3-methyl histidine, N-methyl-tryptophan, pipecolic acid,4-pyridylalanine, sarcosine, t-butyl alanine, or 3-t-butyl tyrosine; optionally wherein at least one non-natural amino acid is selected from 4-trans-hydroxy-L-proline, 6-azidolysine, and t-butyl glycine;
and/or wherein the molecular scaffold is:
    (i) 1,1',1"-(1,3,5-triazinane-1,3,5-triyl)triprop-2-en-1-one (TATA); or
    (ii) 1,1',1"-(1,3,5-triazinane-1,3, 5-triyl)tris(2-bromoethanone) (TATB);
and/or wherein the bicycle ligand does not inhibit the binding of transferrin to the transferrin receptor.
11. The oligomeric compound of any one of claims 1-10, wherein at least one nucleoside of the modified oligonucleotide comprises a modified sugar moiety; optionally wherein at least one modified sugar moiety comprises a bicyclic sugar moiety; optionally wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from –O-CH2-; and –O-CH(CH3)-;
and/or wherein at least one modified sugar moiety comprises a non-bicyclic modified sugar moiety; optionally wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety or 2'-OMe sugar moiety;
and/or at least one nucleoside of the modified oligonucleotide compound comprises a sugar surrogate.
12. The oligomeric compound of any one of claims 1-11, wherein:
(a) the modified oligonucleotide comprises at least one modified internucleoside linkage; optionally:
    (i) wherein at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage; or each internucleoside linkage is a modified internucleoside linkage; optionally wherein each internucleoside linkage is a phosphorothioate internucleoside linkage; or

(ii) wherein at least one modified internucleoside linkage is a mesyl phosphoramidate internucleoside linkage; or

(b) the modified oligonucleotide comprises at least one phosphodiester internucleoside linkage; and/or each internucleoside linkage of the modified oligonucleotide is independently selected from a phosphodiester or a phosphorothioate internucleoside linkage; and/or the modified oligonucleotide comprises at least one modified internucleoside linkage, optionally wherein at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.

13. The oligomeric compound of claim 12, wherein each internucleoside linkage is independently selected from a phosphodiester, a phosphorothioate internucleoside, or a mesyl phosphoramidate internucleoside linkage; or
wherein each internucleoside linkage is independently selected from a phosphorothioate internucleoside or a mesyl phosphoramidate internucleoside linkage.
14. The oligomeric compound of any one of claims 1-13, wherein the modified oligonucleotide comprises at least one modified nucleobase; optionally wherein the modified nucleobase is 5-methylcytosine.
15. The oligomeric compound of any one of claims 1-14, wherein the modified oligonucleotide comprises a deoxy region consisting of 5-12 contiguous 2'-deoxynucleosides; optionally wherein each nucleoside of the deoxy region is a 2'-β-D-deoxynucleoside;
and/or wherein the deoxy region consists of 7, 8, 9, 10, or 7-10 linked nucleosides;
and/or wherein each nucleoside immediately adjacent to the deoxy region comprises a modified sugar moiety;
and/or wherein the deoxy region is flanked on the 5'-side by a 5'-region consisting of 1-6 linked 5'-region nucleosides and on the 3'-side by a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein the 3'-most nucleoside of the 5'-region comprises a modified sugar moiety; and the 5'-most nucleoside of the 3'-region comprises a modified sugar moiety; optionally wherein each nucleoside of the 3'-region comprises a modified sugar moiety and/or wherein each nucleoside of the 5'-region comprises a modified sugar moiety.
16. The oligomeric compound of any one of claims 1-15, wherein the modified oligonucleotide has a sugar motif comprising:
a 5'-region consisting of 1-6 linked 5'-region nucleosides;
an internal region consisting of 6-10 linked internal region nucleosides; and
a 3'-region consisting of 1-6 linked 3'-region nucleosides;
wherein each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety; and each of the internal region nucleosides is selected from a 2'-deoxynucleoside and a 2'-substituted nucleoside; optionally

wherein the modified oligonucleotide has a sugar motif comprising:

a 5'-region consisting of 1-6 linked 5'-region nucleosides;

an internal region consisting of 6-10 linked internal region nucleosides; and

a 3'-region consisting of 1-6 linked 3'-region nucleosides;

wherein each of the 5'-region nucleosides and each of the 3'-region nucleosides is a cEt nucleoside or a 2'-MOE nucleoside; and each of the internal region nucleosides is a 2'-β-D-deoxynucleoside.

17. The oligomeric compound of any one of claims 1-14, wherein each nucleoside of the modified oligonucleotide comprises a 2'-sugar moiety; optionally wherein each 2'-sugar moiety is selected from 2'-OMe, 2'-MOE, or 2'-NMA;

and/or wherein each nucleoside of the modified oligonucleotide comprises the same 2'-sugar moiety.

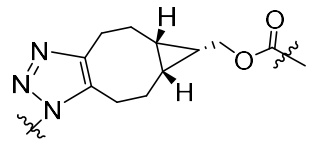
18. The oligomeric compound of any one of claims 1-17, wherein the conjugate linker is cleavable; and/or

(i) the conjugate linker comprises 1-3 linker nucleosides; or

(ii) the conjugate linker does not comprise any linker nucleosides;

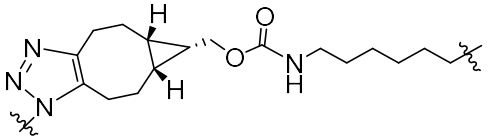
and/or wherein the conjugate group comprises:

(a)



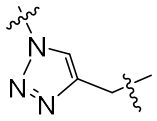
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(b)



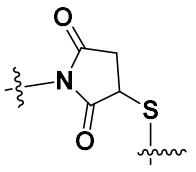
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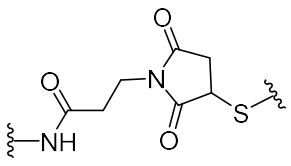
(c)



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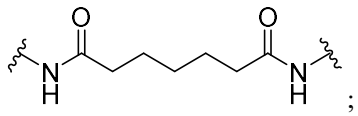
(d)



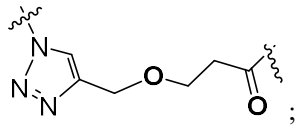
, optionally 

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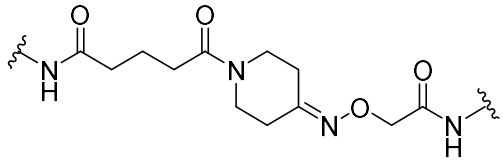
(e)


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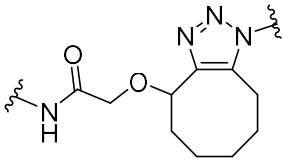
(f)


;

(g)


; or

(h)


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19. The oligomeric compound of any one of claims 1-18, wherein the modified oligonucleotide is complementary to a target nucleic acid expressed in muscle.

20. The oligomeric compound of any one of claims 1-19, wherein the modified oligonucleotide is capable of reducing the amount of a target nucleic acid through the activation of Rnase H;
or wherein the modified oligonucleotide is capable of reducing the amount of a target nucleic acid through the activation of RISC/Ago2;
or wherein the modified oligonucleotide is capable of modulating the splicing of a target nucleic acid.

21. The oligomeric compound of any one of claims 1-19, wherein the modified oligonucleotide is a guide RNA, a tracrRNA, or a scout RNA.

22. The oligomeric compound of any one of claims 1-21, wherein the modified oligonucleotide is complementary to the complement of a target nucleic acid expressed in muscle.

23. The oligomeric compound of any one of claims 19-22, wherein the target nucleic acid is associated with a muscle disease;

and/or the target nucleic acid is selected from CaMK2d, NLRP3, PLN, DMD, DMPK, DNM2, DUX4, or HPRT;

and/or wherein the muscle target nucleic acid has a sequence selected from any of SEQ ID NOs: 1-15;

and/or wherein the target nucleic acid is expressed in at least one of the following tissues: skeletal muscle (including but not limited to quadriceps, gastrocnemius, tibialis anterior,

triceps, masseter, extensor digitorum longus (EDL), soleus, diaphragm), heart, sciatic nerve, aorta, or liver.

24. The oligomeric compound of any one of claims 1-23, wherein the nucleobase sequence of the modified oligonucleotide comprises at least 12, at least 13, at least 14, at least 15, or at least 16 contiguous nucleobases of any of the nucleobase sequences of any of SEQ ID NOs: 167-191; and/or the modified oligonucleotide consists of 10 to 25, 10 to 30, 12 to 20, 12 to 25, 12 to 30, 13 to 20, 13 to 25, 13 to 30, 14 to 20, 14 to 25, 14 to 30, 15 to 20, 15 to 25, 15 to 30, 16 to 18, 16 to 20, 16 to 25, 16 to 30, 17 to 20, 17 to 25, 17 to 30, 18 to 20, 18 to 25, 18 to 30, 19 to 20, 19 to 25, 19 to 30, 20 to 25, 20 to 30, 21 to 25, 21 to 30, 21 to 50, 22 to 25, 22 to 30, 23 to 25, 23 to 30, 20 to 100, 40 to 100, 50 to 100, 50 to 200, 100 to 300, 150-300, or 200-300 linked nucleosides.
25. An oligomeric duplex, comprising a first oligomeric compound comprising a first modified oligonucleotide and a second compound oligomeric comprising a second modified oligonucleotide consisting of 16 to 30 linked nucleosides, wherein the nucleobase sequence of the second modified oligonucleotide comprises a complementary region of at least 12 nucleobases that is at least 90% complementary to an equal length portion of the first modified oligonucleotide, and wherein the second oligomeric compounds is an oligomeric compound of any of claims 1-20 or 24.
26. The oligomeric duplex of claim 25:

    (i) wherein the first modified oligonucleotide is complementary to a muscle target nucleic acid; optionally wherein the duplex is capable of reducing the amount of a target nucleic acid through the activation of RISC/Ago2; and/or

    (ii) wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety; optionally wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety; optionally wherein the bicyclic sugar moiety of the second modified oligonucleotide comprises a 2'-4' bridge selected from –O-CH_2-; and –O-CH(CH_3)-; optionally wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety; optionally wherein the non-bicyclic modified sugar moiety of the second modified oligonucleotide is a 2'-MOE sugar moiety, a 2'-F sugar moiety, or 2'-OMe sugar moiety;

    and/or:

    (a) at least one nucleoside of the second modified oligonucleotide comprises a sugar surrogate; or

    (b) wherein at least one internucleoside linkage of the second modified oligonucleotide is a modified internucleoside linkage; optionally wherein at least one modified internucleoside linkage of the second modified oligonucleotide is a phosphorothioate internucleoside linkage.

27. The oligomeric duplex of either one of claims 25-26, wherein at least one internucleoside linkage of the second modified oligonucleotide is a phosphodiester internucleoside linkage; and/or wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester or a phosphorothioate internucleoside linkage; and/or wherein the second modified oligonucleotide comprises at least one modified nucleobase; optionally wherein the modified nucleobase of the second modified oligonucleotide is 5-methylcytosine;
and/or:
(a) the first oligomeric compound comprises a 5'-stabilized phosphate group; optionally wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate; or
(b) wherein the second oligomeric compound comprises a 5'-stabilized phosphate group; optionally wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate; and/or
(i) the first modified oligonucleotide comprises a glycol nucleic acid (GNA) sugar surrogate;
(ii) first modified oligonucleotide comprises a 2'-NMA sugar moiety;
(iii) the second modified oligonucleotide comprises a glycol nucleic acid (GNA) sugar surrogate; and/or
(iv) the second modified oligonucleotide compound comprises a 2'-NMA sugar moiety.
28. Use of an oligomeric compound according to any one of claims 1-24 or an oligomeric duplex of any one of claims 25-27 in the manufacture of a medicament for the treatment of a disease or condition capable of being treated by modulating a nucleic acid target in a subject.
29. The use according to claim 28, wherein the nucleic acid target is expressed in at least one of skeletal muscle (including but not limited to quadriceps, gastrocnemius, tibialis anterior, triceps, masseter, extensor digitorum longus (EDL), soleus, diaphragm), heart, sciatic nerve, aorta, or liver; and/or:
    (i) wherein the medicament is formulated to result in reduction of the nucleic acid target; or
    (ii) wherein the medicament is formulated to result in a change in the splicing of the nucleic acid target;
and/or:
    (a) wherein the medicament is formulated for administration via intravenous or subcutaneous dosing; or
    (b) wherein the medicament is formulated for administration at a dose of 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, 60 mg, 65 mg, 70 mg, 75 mg, 80 mg, 85 mg, 90 mg, 95 mg, 100 mg, 105 mg, 110 mg, 115 mg, 120 mg, 125 mg, 130 mg, 135 mg, 140 mg, 145 mg, 150 mg, 155 mg, 160 mg, 165

mg, 170 mg, 175 mg, 180 mg, 185 mg, 190 mg, 195 mg, 200 mg, 205 mg, 210 mg, 215 mg, 220 mg, 225 mg, 230 mg, 235 mg, 240 mg, 245 mg, 250 mg, 255 mg, 260 mg, 265 mg, 270 mg, 275 mg, 280 mg, 285 mg, 290 mg, 295 mg, 300 mg, 305 mg, 310 mg, 315 mg, 320 mg, 325 mg, 330 mg, 335 mg, 340 mg, 345 mg, or 350 mg;

and/or wherein the medicament is formulated for administration once every 4 weeks, once every 6 weeks, once every 8 weeks, once every 12 weeks, once every 16 weeks, once every 20 weeks, once every 24 weeks, once every 6 months, or once a year.

30. A bicycle ligand specific for transferrin receptor 1 (TfR1) which comprises an amino acid sequence selected from: CP[HyP]DAYLGC[tBuGly]SYCEPWK (SEQ ID NO: 245, herein referred to as BCY21757) and CP[HyP]DAYLGC[tBuGly]SYCEPWC (SEQ ID NO: 246, herein referred to as BCY21758), wherein HyP represents trans-4-hydroxy-L-proline and tBuGly represents t-butyl-glycine.

31. The bicycle ligand of claim 30:

(i) which comprises an N-terminal acetyl group and a C-terminal $CONH_2$ group;
and/or which is a pharmaceutically acceptable salt; optionally wherein the pharmaceutically acceptable salt is selected from the sodium, potassium, calcium or ammonium salt; or
(ii) wherein the first, second and third cysteine residues within said peptide ligands are covalently bonded to a molecular scaffold such that two polypeptide loops are formed on said molecular scaffold; optionally wherein the molecular scaffold is 1,1',1"-(1,3,5-triazinane-1,3,5-triyl)triprop-2-en-1-one (TATA).