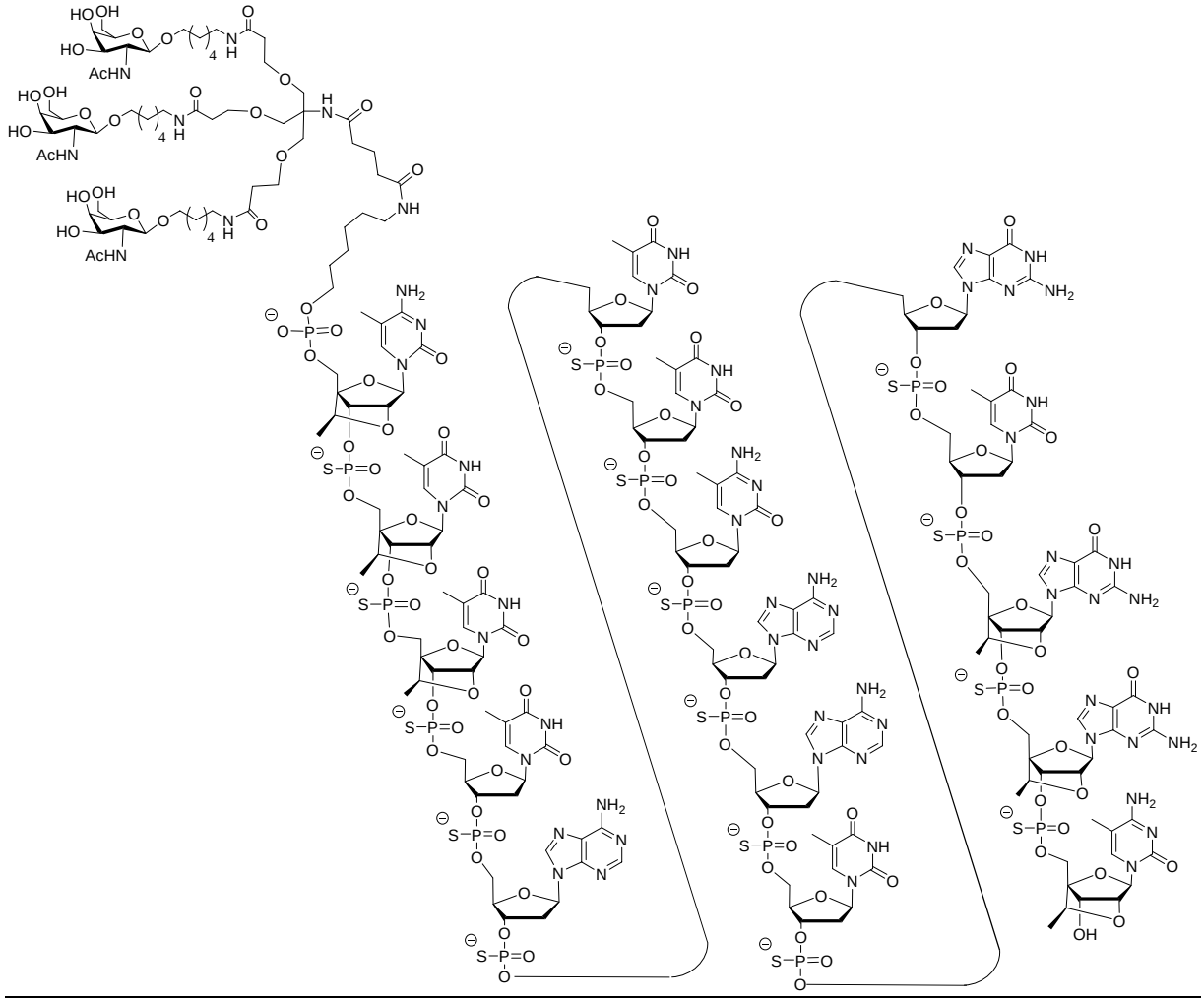
WHAT IS CLAIMED:

1. A compound, wherein the anionic form of the compound has the following formula (SEQ ID NO: 1089):



or a pharmaceutically acceptable salt thereof ~~comprising a modified oligonucleotide 8 to 80 linked nucleosides in length having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, or at least 12 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 17-2169~~.

~~2. A compound comprising a modified oligonucleotide 8 to 80 nucleosides in length and having a nucleobase sequence comprising the nucleobase sequence of any one of SEQ ID NOs: 17-2169.~~

~~3. A compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NOs: 17-2169.~~

4. A compound comprising a modified oligonucleotide 8 to 80 linked nucleosides in length, wherein the modified oligonucleotide has a nucleobase sequence comprising a portion of at least 8 contiguous nucleobases 100% complementary to an equal length portion of nucleobases 5567-5642, 5644-5731, 5567-5731, 5567-5620, 13697-13733, 20553-20676, 20664-20824, 20553-20824, and 25844-25912 of SEQ ID NO: 2, and wherein the nucleobase sequence of the modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to SEQ ID NO: 2.

5. A compound comprising a modified oligonucleotide 8 to 80 linked nucleosides in length, wherein the modified oligonucleotide has a nucleobase sequence complementary within nucleobases 5567-5642, 5644-5731, 5567-5731, 5567-5620, 13697-13733, 20553-20676, 20664-20824, 20553-20824, and 25844-25912 of SEQ ID NO: 2, and wherein said modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to SEQ ID NO: 2.

6. A compound comprising a modified oligonucleotide 8 to 80 linked nucleosides in length, wherein the modified oligonucleotide has a nucleobase sequence comprising a portion of at least 8 contiguous nucleobases complementary to an equal length portion of nucleobases 5567-5642, 5644-5731, 5567-5731, 5567-5620, 13697-13733, 20553-20676, 20664-20824, 20553-20824, and 25844-25912 of a PNPLA3 nucleic acid having the nucleobase sequence of SEQ ID NO: 2, wherein the nucleobase sequence of the modified oligonucleotide is complementary to SEQ ID NO: 2.

7. A compound comprising a modified oligonucleotide 8 to 80 linked nucleosides in length, wherein the modified oligonucleotide has a nucleobase sequence comprising a 16 nucleobase portion complementary to an equal length portion of nucleobases 5567-5642, 5644-5731, 5567-5731, 5567-5620, 13697-13733, 20553-20676, 20664-20824, 20553-20824, and 25844-25912 of SEQ ID NO: 2.

8. A compound comprising a modified oligonucleotide 8 to 80 linked nucleosides in length, wherein the modified oligonucleotide has a nucleobase sequence comprising any one of SEQ ID NOs: 1089, 1757, 141, 1982, 330, 1665, 408, 830, and 899.

9. A compound comprising a modified oligonucleotide having a nucleobase sequence consisting of any one of SEQ ID NO: 1089, 1757, 141, 1982, 330, 1665, 408, 830, and 899.

10. The compound of any one of claims 1-9, wherein the oligonucleotide is at least 80%, at least 85%, at least 90%, at least 95% or 100% complementary to SEQ ID NO: 2 over the entire length of the oligonucleotide.

11. The compound of any one of claims 1-10, wherein the modified oligonucleotide comprises at least one modification selected from at least one modified internucleoside linkage, at least one modified sugar, and at least one modified nucleobase.

12. The compound of claim 11, wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

13. The compound of claim 11 or 12, wherein the modified sugar is a bicyclic sugar.

14. The compound of claim 13, wherein the bicyclic sugar is selected from the group consisting of: 4'-(CH_2)-O-2' (LNA); 4'-(CH_2)$_2$-O-2' (ENA); and 4'-CH(CH_3)-O-2' (cEt).

15. The compound of claim 11 or claim 12, wherein the modified sugar is 2'-O-methoxyethyl.

16. The compound of any one of claims 11-15, wherein the modified nucleobase is a 5-methylcytosine.

17. The compound of any one of claims 1-16, wherein the modified oligonucleotide comprises:

a gap segment consisting of linked deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned immediately adjacent to and between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

18. The compound of any one of claims 1-17, wherein the compound is single-stranded.

19. The compound of any one of claims 1-17, wherein the compound is double-stranded.

20. The compound of any one of claims 1-19, wherein the compound comprises ribonucleotides.

21. The compound of any one of claims 1-19, wherein the compound comprises deoxyribonucleotides.

22. The compound of any one of claims 1-21, wherein the modified oligonucleotide consists of 10 to 30 linked nucleosides.

23. The compound of any one of claims 1-21, wherein the modified oligonucleotide consists of 12 to 30 linked nucleosides.

24. The compound of any one of claims 1-21, wherein the modified oligonucleotide consists of 15 to 30 linked nucleosides.

25. A compound comprising a modified oligonucleotide 16 linked nucleosides in length, wherein the modified oligonucleotide has a nucleobase sequence comprising any one of SEQ ID NOs: 1089, 1757, 141, 1982, 330, 1665, 408, 830, and 899, wherein the modified oligonucleotide comprises:

a gap segment consisting of linked deoxynucleosides;

a 5' wing segment consisting of linked nucleosides; and

a 3’ wing segment consisting of linked nucleosides;

wherein the gap segment is positioned between the 5’ wing segment and the 3’ wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

26. A compound comprising a modified oligonucleotide 16 linked nucleosides in length having a nucleobase sequence consisting of any one of SEQ ID NOs: 1089, 1757, 141, 1982, 330, 1665, 408, 830, and 899, wherein the modified oligonucleotide comprises

a gap segment consisting of ten linked deoxynucleosides;

a 5’ wing segment consisting of three linked nucleosides; and

a 3’ wing segment consisting of three linked nucleosides;

wherein the gap segment is positioned between the 5’ wing segment and the 3’ wing segment; wherein the 5’ wing segment and the 3’ wing segment comprise cEt sugars; wherein each internucleoside linkage is a phosphorothioate linkage; and wherein each cytosine is a 5-methylcytosine.

27. The compound of any preceding claim, comprising a conjugated moiety and a conjugate linker.

28. The compound of claim 27, wherein the conjugate group comprises a GalNAc cluster comprising 1-3 GalNAc ligands.

29. The compound of claim 27 or claim 28, wherein the conjugate linker consists of a single bond.

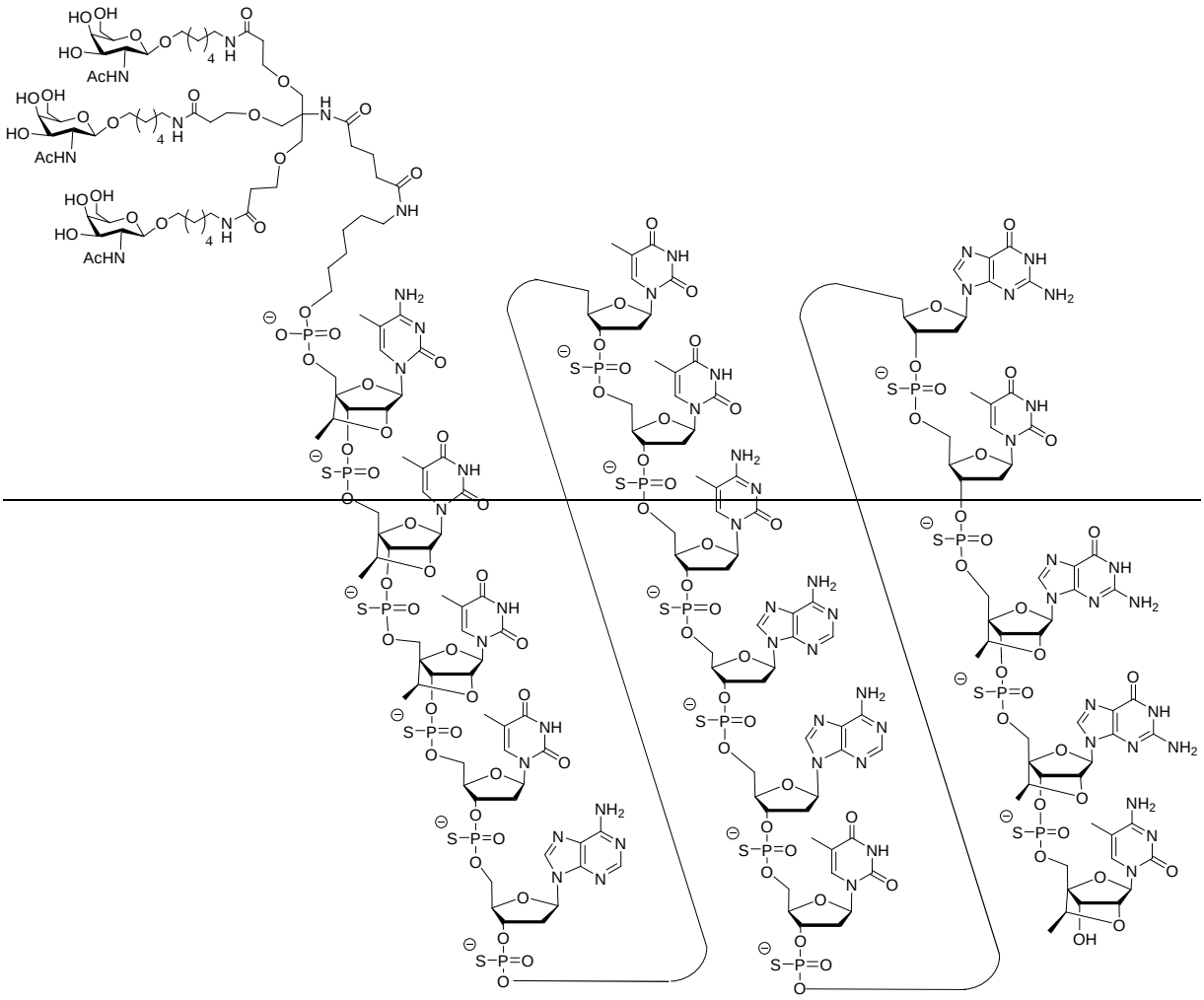
30. The compound of claim 29, wherein the conjugate linker is cleavable.

31. The compound of claim 29, wherein the conjugate linker comprises 1-3 linker-nucleosides.

32. The compound of any one of claims 27-31, wherein the wherein the conjugate group is attached to the modified oligonucleotide at the 5’-end of the modified oligonucleotide.

33. The compound of any one of claims 27-31, wherein the conjugate group is attached to the modified oligonucleotide at the 3’-end of the modified oligonucleotide.

34. A compound having the following formula or salt thereof:



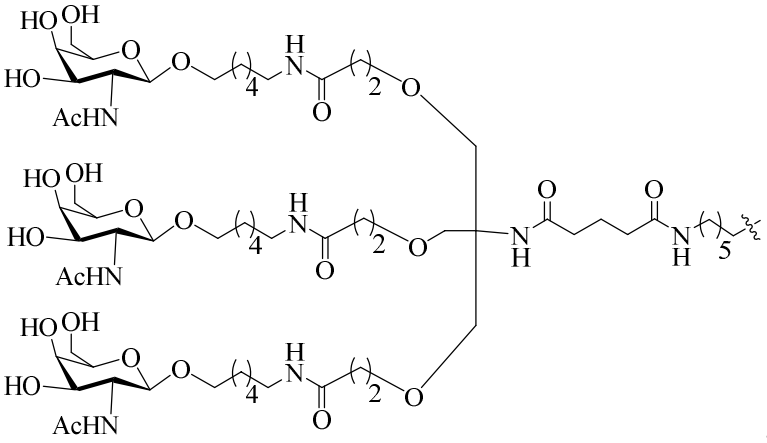
~~35~~2. A modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide is 16 linked nucleosides in length and ~~consists of~~has the nucleobase sequence of SEQ ID NO: 1089, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked deoxynucleosides;

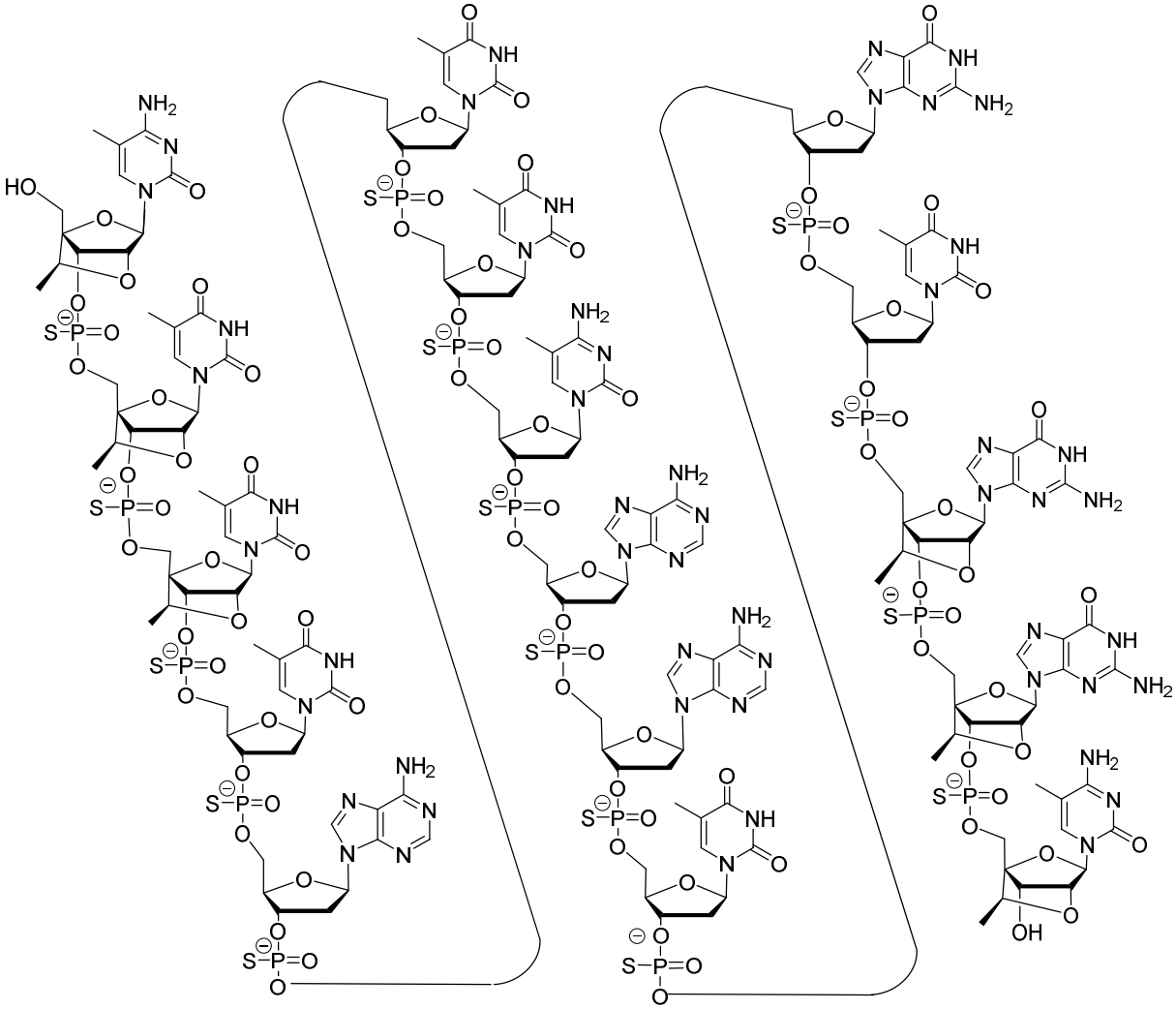
a 5’ wing segment consisting of three linked nucleosides; and

a 3’ wing segment consisting of three linked nucleosides;

wherein the gap segment is positioned between the 5’ wing segment and the 3’ wing segment, wherein each nucleoside of each wing segment comprises a cEt sugar; wherein each internucleoside linkage is a phosphorothioate linkage; wherein each cytosine is a 5-methylcytosine; and wherein the conjugate group is positioned at the 5’end of the modified oligonucleotide and is



~~363~~. A compound, wherein the anionic form of the compound has the following formula (SEQ ID NO: 1089) ~~having the following formula or salt thereof~~:



or a pharmaceutically acceptable salt thereof.

~~37. A compound or modified oligonucleotide of any of claims 1-36, wherein the compound of modified oligonucleotide is in a pharmaceutically acceptable salt form.~~

~~38. The compound or modified oligonucleotide of claim 37, wherein the pharmaceutically acceptable salt is a sodium salt.~~

~~39. The compound or modified oligonucleotide of claim 37, wherein the pharmaceutically acceptable salt is a potassium salt.~~

~~40. A composition comprising the compound or modified oligonucleotide of any one of claims 1-39 and a pharmaceutically acceptable carrier.~~

~~41. A composition comprising a compound or modified oligonucleotide of any preceding claim, for use in therapy.~~

~~42. A method of treating, preventing, or ameliorating a disease associated with PNPLA3 in an individual comprising administering to the individual a compound targeted to PNPLA3, thereby treating, preventing, or ameliorating the disease.~~

~~43 A method of administering the compound of claims 1-39 or composition of claim 40 or claim 41 to an individual.~~

~~44. The method of claim 42, wherein the compound is an antisense compound targeted to PNPLA3.~~

~~45. The method of claim 42 or 43, wherein the disease is liver disease, NAFLD, hepatic steatosis, non-alcoholic steatohepatitis (NASH), liver cirrhosis, hepatocellular carcinoma, alcoholic liver disease, alcoholic steatohepatitis (ASH), HCV hepatitis, chronic hepatitis, hereditary hemochromatosis, or primary sclerosing cholangitis.~~

~~46. The method of any of claims 42-45, wherein administering the compound inhibits or reduces or improves liver damage, steatosis, liver fibrosis, liver inflammation, liver scarring or cirrhosis, liver failure, liver enlargement, elevated transaminases, or hepatic fat accumulation in the individual.~~

~~47. A method of inhibiting expression of PNPLA3 in a cell comprising contacting the cell with a compound targeted to PNPLA3, thereby inhibiting expression of PNPLA3 in the cell.~~

~~48. The method of claim 47, wherein the cell is in the liver of an individual.~~

~~49. The method of claim 48, wherein the individual has, or is at risk of having, liver disease, NAFLD, hepatic steatosis, non-alcoholic steatohepatitis (NASH), liver cirrhosis, hepatocellular carcinoma, alcoholic liver disease, alcoholic steatohepatitis (ASH), HCV hepatitis, chronic hepatitis, hereditary hemochromatosis, or primary sclerosing cholangitis.~~

~~50. A method of reducing or inhibiting liver damage, steatosis, liver fibrosis, liver inflammation, liver scarring or cirrhosis, liver failure, liver enlargement, elevated transaminases, or hepatic~~

~~fat accumulation in an individual, comprising administering a compound targeted to PNPLA3 to the individual, thereby reducing or inhibiting liver damage, steatosis, liver fibrosis, liver inflammation, liver scarring or cirrhosis, liver failure, liver enlargement, elevated transaminases, or hepatic fat accumulation in the individual.~~

~~51. The method of claim 50, wherein the individual has, or is at risk of having, liver disease, NAFLD, hepatic steatosis, non-alcoholic steatohepatitis (NASH), liver cirrhosis, hepatocellular carcinoma, alcoholic liver disease, alcoholic steatohepatitis (ASH), HCV hepatitis, chronic hepatitis, hereditary hemochromatosis, or primary sclerosing cholangitis.~~

~~52. The method of any one of claims 47-51, wherein the compound is an antisense compound targeted to PNPLA3.~~

~~53. The method of any one of claims 47-51, wherein the compound is the compound of any one of claims 1-39 or composition of claim 40 or claim 41.~~

~~54. The method of claim 50 or 51, wherein the compound or composition is administered parenterally.~~

~~55. Use of a compound targeted to PNPLA3 for treating, preventing, or ameliorating a disease associated with PNPLA3.~~

~~56. The use of claim 55, wherein the disease liver disease, NAFLD, hepatic steatosis, non-alcoholic steatohepatitis (NASH), liver cirrhosis, hepatocellular carcinoma, alcoholic liver disease, alcoholic steatohepatitis (ASH), HCV hepatitis, chronic hepatitis, hereditary hemochromatosis, or primary sclerosing cholangitis.~~

~~57. The use of claim 55 or 56, wherein the compound is an antisense compound targeted to PNPLA3.~~

~~58. The use of any one of claims 55-57, wherein the compound is the compound of any one of claims 1-39 or composition of claim 40 or claim 41.~~

~~59. Use of a compound targeted to PNPLA3 in the manufacture of a medicament for treating, preventing, or ameliorating a disease associated with PNPLA3.~~

~~60. The use of claim 59, wherein the disease liver disease, NAFLD, hepatic steatosis, non-alcoholic steatohepatitis (NASH), liver cirrhosis, hepatocellular carcinoma, alcoholic liver disease, alcoholic steatohepatitis (ASH), HCV hepatitis, chronic hepatitis, hereditary hemochromatosis, or primary sclerosing cholangitis.~~

~~61. The use of claim 59 or 60, wherein the compound is an antisense compound targeted to PNPLA3.~~

~~62. The use of any one of claims 59-61, wherein the compound is the compound of any one of claims 1-39 or composition of claim 40 or claim 41.~~

4. A modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide is 16 linked nucleosides in length and has the nucleobase sequence of SEQ ID NO: 1089, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked deoxynucleosides;

a 5’ wing segment consisting of three linked nucleosides; and

a 3’ wing segment consisting of three linked nucleosides;

wherein the gap segment is positioned between the 5’ wing segment and the 3’ wing segment, wherein each nucleoside of each wing segment comprises a cEt sugar; wherein at least one internucleoside linkage is a phosphorothioate linkage; wherein each cytosine is a 5-methylcytosine.

5. A compound comprising a modified oligonucleotide and a conjugate group, wherein the modified oligonucleotide is 16 linked nucleosides in length and has the nucleobase sequence of SEQ ID NO: 1089, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked deoxynucleosides;

a 5’ wing segment consisting of three linked nucleosides; and

a 3’ wing segment consisting of three linked nucleosides;

wherein the gap segment is positioned between the 5’ wing segment and the 3’ wing segment, wherein each nucleoside of each wing segment comprises a cEt sugar; wherein each internucleoside linkage is a phosphorothioate linkage; wherein each cytosine is a 5-methylcytosine.

6. A modified oligonucleotide, wherein the modified oligonucleotide consists of 16 linked nucleosides and has the nucleobase sequence consisting of SEQ ID NO: 1089, wherein the modified oligonucleotide comprises:

a gap segment consisting of ten linked deoxynucleosides;

a 5’ wing segment consisting of three linked nucleosides; and

a 3’ wing segment consisting of three linked nucleosides;

wherein the gap segment is positioned between the 5’ wing segment and the 3’ wing segment, wherein each nucleoside of each wing segment comprises a cEt sugar; wherein each internucleoside linkage is a phosphorothioate linkage; wherein each cytosine is a 5-methylcytosine.

7. The compound or modified oligonucleotide of claims 1-3, wherein the pharmaceutically acceptable salt is a sodium salt.

8. The compound or modified oligonucleotide of claims 1-3, wherein the pharmaceutically acceptable salt is a potassium salt.

9. A composition comprising the compound or modified oligonucleotide of 1-6 and a pharmaceutically acceptable carrier.