CLAIMS

1. An antisense oligonucleotide conjugate comprising
   a. an antisense oligomer (A) of between 12 - 22 nucleotides in length, which comprises a contiguous sequence of 10 – 16 nucleotides which are complementary to a corresponding length of SEQ ID NO 30 or 31 or 32 or 33 or 34 or 45, and
   b. at least one ~~non-nucleotide or non-polynucleotide~~asialoglycoprotein receptor targeting conjugate moiety (C) covalently attached to said oligomer (A).
2. The oligonucleotide conjugate according to claim 1, wherein the antisense oligomer comprises a contiguous sequence selected from the group consisting of SEQ ID NO 25, 26, 27, 28, 29 and 44.
3. The oligonucleotide conjugate according any one of claims 1 or 2, wherein the antisense oligomer targets PCSK9.
4. The oligonucleotide conjugate according to any one of the claims 1 to 3, wherein the antisense oligomer comprises a contiguous sequence selected from the group consisting of SEQ ID NO 1, 2, 3, 4, 5, 6, 7, and 8.
5. The oligonucleotide conjugate according to any one of the claims 1 to 4, wherein the conjugate moiety (C) ~~is selected from the group consisting of or a carbohydrate, such as~~ comprises an N-acetylgalactosamine (GalNAc) ~~or a GalNAc cluster; a lipophilic group~~, such as a ~~lipid, a fatty acid; a sterol, such as cholesterol or tocopherol; or a statin~~ mono-valent, di-valent , tri-valent or tetra-valent GalNAc.
6. The antisense oligonucleotide conjugate according to any one of claims 1 to 5, wherein the conjugate moiety (C) enhances delivery and/or uptake to liver cells.
7. The antisense oligonucleotide conjugate according to ~~any one of~~ claims 1 to 6, wherein the conjugate moiety (C) comprises a ~~sterol such as tocophorol, cholesterol, such as those shown as Conj 5, Conj 5, Conj 6 or Conj 6a~~ trivalent GalNAc.
8. The antisense oligonucleotide conjugate according to claim ~~1 to 6~~7, wherein the ~~conjugate moiety (C) comprises a carbohydrate such as GalNAc or trivalent~~three GalNAc moieties are attached to a di-lysine branch point group via PEG spacers, such as those shown as Conj 1, 2, ~~3 or 4, or~~ 1a~~,~~ or 2a~~, 3a or 4a~~.
9. The antisense oligonucleotide conjugate according to claim 7 or 8, wherein the conjugate moiety (C) comprises Conj 2a.
10. The antisense oligonucleotide conjugate according to any one of claims 1 to 9, which is selected from the group consisting of SEQ ID NO ~~9, 10, 11, 12, 13, 14, 15, 16,~~ 17, 18, 19, 20, 21, 22, 23, and 24.

11. The antisense oligonucleotide conjugate according to any one of claims 1 to 10, wherein the antisense oligomer (A) is conjugated to the conjugate moiety (C) via a linker region positioned between the contiguous sequence of the oligomer and the conjugate moiety (B and/or Y).

12. The antisense oligonucleotide conjugate according to claim 11, wherein the linker is selected from a C6 to C12 amino alkyl groups or a biocleavable phosphate nucleotide linker comprising between 1 to 6 nucleotides.

~~13. The antisense oligonucleotide conjugate according to claim 12, wherein the linker is a biocleavable phosphate nucleotide linker comprising between 1 to 6 nucleotides.~~

~~14.~~13. A oligomer of between 12 - 22 nucleotides in length, which ~~either~~ comprises

~~a.~~ a contiguous sequence of 16 nucleotides which are complementary to a corresponding length of SEQ ID NO 31~~, or~~

~~b. a contiguous sequence of 10 – 16 nucleotides which are complementary to a corresponding length of SEQ ID NO 33 or 34 or 45~~.

~~15.~~14. The oligomer according to claim ~~14~~13, which comprises a ~~contiguous~~ sequence ~~selected from the group consisting~~ of 16 nucleotides corresponding to SEQ ID NO 26~~, 27, 28, 29 and 44~~.

~~16.~~15. The oligomer according any one of claims ~~14~~ 13 or ~~15~~14, wherein the oligomer targets PCSK9.

~~17.~~16. The oligomer according to any one of claims ~~14~~ 13 to ~~16~~ 15 wherein the contiguous sequence comprises affinity enhancing nucleotide analogues.

~~18.~~17. The oligomer according to any one of claims ~~14~~ 13 to ~~17~~16, which is a gapmer.

~~19. The oligomer according to any one of claims 14 to 18, wherein the oligomer comprises a contiguous sequence of 13, 14, 15 or 16 nucleotides.~~

~~20.~~18. The oligomer according to any one of claims ~~14~~ 13 to ~~19~~17, wherein the oligomer comprises one or more nucleoside linkages selected from the group consisting of phosphorothioate, phosphorodithioate and boranophosphate.

~~21.~~19. The~~n~~ oligomer according to any one of claims ~~14~~ 13 to ~~20~~18, which comprises a contiguous sequence ~~selected from the group consisting~~ of SEQ ID NO 2~~,~~ or 3~~, 4, 5, 6, 7, and 8~~.

~~22.~~20. A pharmaceutical composition comprising the oligomer or antisense oligonucleotide conjugate according to any one of claims 1 to ~~21~~ 19 and a pharmaceutically acceptable diluent, carrier, salt or adjuvant.

~~23.~~21. The oligomer or antisense oligonucleotide conjugate or pharmaceutical composition according to any one of claims 1 to ~~22~~20, for use as a medicament, such as for the treatment of hypercholesterolemia or related disorder, such as a disorder selected from the group consisting of atherosclerosis, hyperlipidemia, hypercholesterolemia, familiar

hypercholesterolemia *e.g.* gain of function mutations in PCSK9, HDL/LDL cholesterol imbalance, dyslipidemias, *e.g.,* familial hyperlipidemia (FCHL) or familial hypercholesterolemia (FHC), acquired hyperlipidemia, statin-resistant hypercholesterolemia, coronary artery disease (CAD), and coronary heart disease (CHD).

~~24.~~22. The use of an oligomer or antisense oligonucleotide conjugate or pharmaceutical composition according to any one of the claims 1 to ~~22~~20, for the manufacture of a medicament for the treatment of hypercholesterolemia or a related disorder, such as a disorder selected from the group consisting of atherosclerosis, hyperlipidemia, hypercholesterolemia, familiar hypercholesterolemia *e.g.* gain of function mutations in PCSK9, HDL/LDL cholesterol imbalance, dyslipidemias, *e.g.,* familial hyperlipidemia (FCHL) or familial hypercholesterolemia(FHC), acquired hyperlipidemia, statin-resistant hypercholesterolemia, coronary artery disease (CAD), and coronary heart disease (CHD).

~~25. A method of treating hypercholesterolemia or a related disorder, such as a disorder selected from the group consisting atherosclerosis, hyperlipidemia, hypercholesterolemia, familiar hypercholesterolemia *e.g.* gain of function mutations in PCSK9, HDL/LDL cholesterol imbalance, dyslipidemias, *e.g.,* familial hypercholesterolemia(FHC), acquired hyperlipidemia, statin-resistant hypercholesterolemia, coronary artery disease (CAD), and coronary heart disease (CHD), said method comprising administering an effective amount of an oligomer or antisense oligonucleotide conjugate or pharmaceutical composition according to any one of the claims 1 to 22, to a patient suffering from, or likely to suffer from hypercholesterolemia or a related disorder.~~

~~26.~~23. An ~~in vivo or~~ in vitro method for the inhibition of PCSK9 in a cell which is expressing PCSK9, said method comprising administering an oligomer or antisense oligonucleotide conjugate or pharmaceutical composition according to any one of the claims 1 to ~~22~~ 20 to said cell.