

CLAIMS

1. An antisense oligonucleotide conjugate comprising:
 - a. an oligonucleotide (Region A) comprising a contiguous nucleotide sequence of 10 to 30 nucleotides in length with at least 90% complementarity to a PD-L1 target nucleic acid; and
 - b. at least one asialoglycoprotein receptor targeting conjugate moiety (Region C) covalently attached to the oligonucleotide in a).
2. The oligonucleotide conjugate of claim 1, wherein the contiguous nucleotide sequence is complementary to a target nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2 and/or SEQ ID NO: 3.
3. The oligonucleotide conjugate of claim 1 or 2, wherein the contiguous nucleotide sequence is complementary to a sub-sequence of the target nucleic acid, wherein the subsequence is selected from the group consisting of position 371-3068, 5467-12107 and 15317-19511 on SEQ ID NO: 1.
4. The oligonucleotide conjugate of claim 1 to 3, wherein the contiguous nucleotide sequence is complementary to a sub-sequence of the target nucleic acid, wherein the subsequence is selected from the group consisting of A221, A360, A180, A160 and A269.
5. The oligonucleotide conjugate of claim 1-4, wherein the oligonucleotide comprises a sequence selected from SEQ ID NO: 466, 640, 342, 287 and 566.
6. The oligonucleotide conjugate of claim 1-5, wherein the contiguous nucleotide sequence comprises one or more modified nucleosides, such as one or more 2' sugar modified nucleosides.
7. The oligonucleotide conjugate of claim 6, wherein the one or more 2' sugar modified nucleoside is independently selected from the group consisting of 2'-O-alkyl-RNA, 2'-O-methyl-RNA, 2'-alkoxy-RNA, 2'-O-methoxyethyl-RNA, 2'-amino-DNA, 2'-fluoro-DNA, arabino nucleic acid (ANA), 2'-fluoro-ANA and LNA nucleosides.
8. The oligonucleotide conjugate of any one of claims 6 or 7, wherein the all the modified nucleosides are LNA nucleosides.
9. The oligonucleotide conjugate of any one of claims 1-8, wherein the contiguous nucleotide sequence comprises at least one modified internucleoside linkage, such as at least one phosphorothioate internucleoside linkage.
10. The oligonucleotide conjugate of any one of claims 1-9, wherein the oligonucleotide is a gapmer.
11. The oligonucleotide conjugate of claim 10, wherein the gapmer has formula 5'-D'-F-G-F'-3' or 5'-F-G-F'-D''-3', where region F and F' independently comprise 1 - 7 modified

nucleosides, G is a region between 6 and 16 nucleosides which are capable of recruiting RNaseH and region D' or D'' is optional and comprise 0 - 5 phosphodiester linked nucleosides.

12. The oligonucleotide conjugate of any one of claims 1-11, wherein the asialoglycoprotein receptor targeting conjugate moiety comprises at least one carbohydrate moiety selected from group consisting of galactose, galactosamine, N-formyl-galactosamine, N-acetylgalactosamine, N-propionyl-galactosamine, N-n-butanoyl-galactosamine and N-isobutanoylgalactosamine.
13. The oligonucleotide conjugate of any one of claims 1-12, wherein the asialoglycoprotein receptor targeting conjugate moiety is mono-valent, di-valent, tri-valent or tetra-valent.
14. The oligonucleotide conjugate of any one of claims 1-13, wherein the asialoglycoprotein receptor targeting conjugate moiety is a tri-valent N-acetylgalactosamine (GalNAc) moiety.
15. The oligonucleotide conjugate of any one of claims 1-14, wherein the the asialoglycoprotein receptor targeting conjugate moiety is the trivalent GalNAc moiety in figure 3.
16. The oligonucleotide conjugate of any one of claims 1-15, wherein the oligonucleotide conjugate is selected from CMP ID NO: 766_2, 767_2, 768_2, 769_2 and 770_2.
17. An antisense oligonucleotide comprising an oligonucleotide or a contiguous nucleotide sequence according to any one of claims 1 to 11.
18. A pharmaceutical composition comprising the oligonucleotide conjugate of claims 1-16 or the oligonucleotides of claim 17 and a pharmaceutically acceptable diluent, solvent, carrier, salt and/or adjuvant.
19. An *in vivo* or *in vitro* method for modulating PD-L1 expression in a target cell which is expressing PD-L1, said method comprising administering an oligonucleotide conjugate of claims 1-16 or the oligonucleotides of claim 17 in an effective amount to said cell.
20. The oligonucleotide conjugate of claims 1-16 or the oligonucleotides of claim 17 or the pharmaceutical composition of claim 18 for use in restoration of immune response against a virus or parasite.
21. The use of claim 20, wherein the restoration of the immune response is an increase in the liver of CD8+ T cells specific to one or more HBV antigens when compared to a control.
22. The oligonucleotide conjugate of claims 1-16 or the oligonucleotides of claim 17 or the pharmaceutical composition of claim 18 for use as a medicament.
23. The oligonucleotide conjugate of claims 1-16 or the oligonucleotides of claim 17 or the pharmaceutical composition of claim 18 for use in the treatment or prevention of viral liver infections such as HBV, HCV and HDV; a parasite infections such as malaria,

toxoplasmosis, leishmaniasis and trypanosomiasis; or liver cancer or metastases in the liver.

24. Use of the oligonucleotide conjugate of claims 1-16 or the oligonucleotides of claim 17 or the pharmaceutical composition of claim 18, for the preparation of a medicament for treatment or prevention of viral liver infections such as HBV, HCV and HDV; parasite infections such as malaria, toxoplasmosis, leishmaniasis and trypanosomiasis; or liver cancer or metastases in the liver.