We claim:

1. A double stranded RNAi agent for inhibiting expression of hepatitis B virus (HBV) in a cell, wherein the double stranded RNAi agent comprises a sense strand and an antisense strand forming a double-stranded region, wherein the sense strand comprises 5'- GGUGGACUUCUCUCAAUUUUA -3' (SEQ ID NO: 11), and the antisense strand comprises 5'- UAAAAUUGAGAGAAGUCCACCAC -3' (SEQ ID NO: 12),

wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand are modified nucleotides,

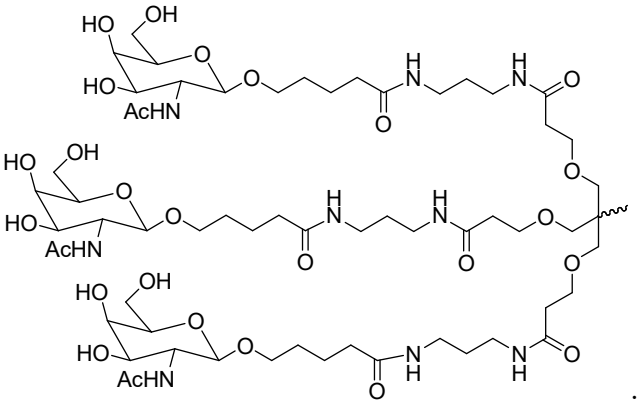
wherein the sense strand is conjugated to a ligand attached at the 3'-terminus, and

wherein the ligand is one or more GalNAc derivatives attached through a bivalent or trivalent branched linker.

2. The double stranded RNAi agent of claim 1, wherein at least one of the modified nucleotides is selected from the group consisting of a deoxy-nucleotide, a 3'-terminal deoxy-thymine (dT) nucleotide, a 2'-O-methyl modified nucleotide, a 2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked nucleotide, an unlocked nucleotide, a conformationally restricted nucleotide, a constrained ethyl nucleotide, an abasic nucleotide, a 2'-amino-modified nucleotide, a 2'-O-allyl-modified nucleotide, 2'-C-alkyl-modified nucleotide, , a 2'-methoxyethyl modified nucleotide, a 2'-O-alkyl-modified nucleotide, a morpholino nucleotide, a phosphoramidate, a non-natural base comprising nucleotide, a tetrahydropyran modified nucleotide, a 1,5-anhydrohexitol modified nucleotide, a cyclohexenyl modified nucleotide, a nucleotide comprising a phosphorothioate group, a nucleotide comprising a methylphosphonate group, a nucleotide comprising a 5'-phosphate, and a nucleotide comprising a 5'-phosphate mimic.

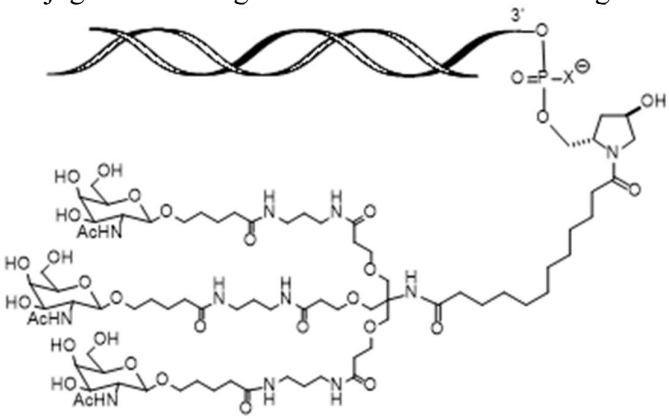
3. The double stranded RNAi agent of claim 1, wherein the sense strand comprises 5'- gsgsuggaCfuUfCfUfcucaAfUfuuua -3' (SEQ ID NO:25) and the antisense strand comprises
5'- usAfsaaaUfuGfAfgagaAfgUfccaccsasc -3' (SEQ ID NO:26), wherein
A, C, G, and U are ribose A, C, G and U, respectively;
a, c, g and u are 2′-O-methyl (2′-OMe) A, C, G and U, respectively;
Af, Cf, Gf and Uf are 2′-fluoro A, C, G and U, respectively;
and s is a phosphorothioate linkage.

4. The double stranded RNAi agent of any one of claims 1 to 3, wherein the ligand is



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5. The double stranded RNAi agent of claim 4, wherein the RNAi agent is conjugated to the ligand as shown in the following schematic



wherein X is O or S.

6. The double stranded RNAi agent of claim 1, wherein the sense strand comprises 5'- gsgsuggaCfuUfCfUfcucaAfUfuuuaL96 -3' (SEQ ID NO: 994) and the antisense strand comprises 5'- usAfsaaaUfuGfAfgagaAfgUfccaccsasc -3' (SEQ ID NO: 1023), wherein a, c, g, and u are 2'-O-methyl (2'-OMe) A, 2'-OMe C, 2'-OMe G, and 2'-OMe U, respectively; Af, Cf, Gf, and Uf are 2'-fluoro A, 2'-fluoro C, 2'-fluoro G, and 2'-fluoro U, respectively; s is a phosphorothioate linkage; and L96 is N-[tris(GalNAc-alkyl)-amidodecanoyl)]-4-hydroxyprolinol.

7. A composition for inhibiting expression of hepatitis B virus (HBV) in a cell, comprising:

(a) a first double-stranded RNAi agent comprising a first sense strand and a first antisense strand forming a first double-stranded region,

wherein the first sense strand comprises 5'- GGUGGACUUCUCUCAAUUUUA -3' (SEQ ID NO: 11), and the first antisense strand comprises 5'-UAAAAUUGAGAGAAGUCCACCAC -3' (SEQ ID NO: 12),

wherein all of the nucleotides of the first sense strand and all of the nucleotides of the first antisense strand are modified nucleotides,

wherein the first sense strand is conjugated to a ligand attached at the 3'-terminus, and

wherein the ligand is one or more GalNAc derivatives attached through a bivalent or trivalent branched linker; and

(b) a second double-stranded RNAi agent comprising a second sense strand and a second antisense strand forming a second double-stranded region,

wherein the second sense strand comprises 5'- GUGUGCACUUCGCUUCACA -3' (SEQ ID NO: 39), and the second antisense strand comprises 5'-UGUGAAGCGAAGUGCACACUU -3' (SEQ ID NO: 40),

wherein all of the nucleotides of the second sense strand and all of the nucleotides of the second antisense strand are modified nucleotides,

wherein the second sense strand is conjugated to a ligand attached at the 3'-terminus, and

wherein the ligand is one or more GalNAc derivatives attached through a bivalent or trivalent branched linker.

8. The composition of claim 7, wherein at least one of the modified nucleotides is a deoxy-nucleotide, a 3'-terminal deoxy-thymine (dT) nucleotide, a 2'-O-methyl modified nucleotide, a 2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked nucleotide, an unlocked nucleotide, a conformationally restricted nucleotide, a constrained ethyl nucleotide, an abasic nucleotide, a 2'-amino-modified nucleotide, a 2'-O-allyl-modified nucleotide, 2'-C-alkyl-modified nucleotide, a 2'-methoxyethyl modified nucleotide, a 2'-O-alkyl-modified nucleotide, a morpholino nucleotide, a phosphoramidate, a non-natural base comprising nucleotide, a tetrahydropyran modified nucleotide, a 1,5-anhydrohexitol modified nucleotide, a cyclohexenyl modified nucleotide, a nucleotide comprising a phosphorothioate group, a nucleotide comprising a methylphosphonate group, a nucleotide comprising a 5'-phosphate, or a nucleotide comprising a 5'-phosphate mimic.

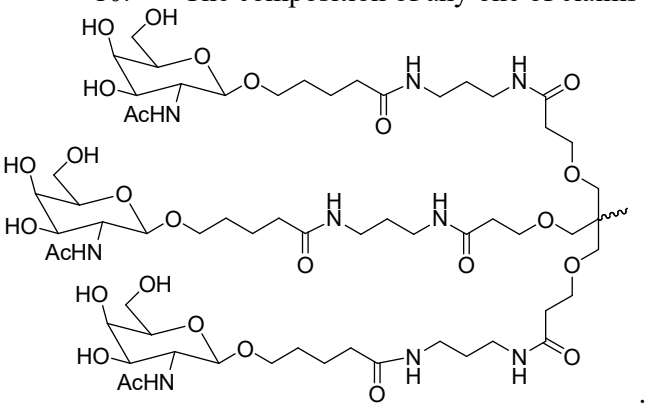
9. The composition of claim 7, wherein

(a) the first sense strand comprises 5'-gsgsuggaCfuUfCfUfcucaAfUfuuua – 3' (SEQ ID NO:25) and the first antisense strand comprises 5'-usAfsaaaUfuGfAfgagaAfgUfccaccsasc – 3' (SEQ ID NO:26); and(b) the second sense

strand comprises 5’- gsusguGfcAfCfUfucgcuucaca -3’ (SEQ ID NO:41) and the second antisense strand comprises 5’- usGfsugaAfgCfGfaaguGfcAfcacsusu -3’ (SEQ ID NO:42);

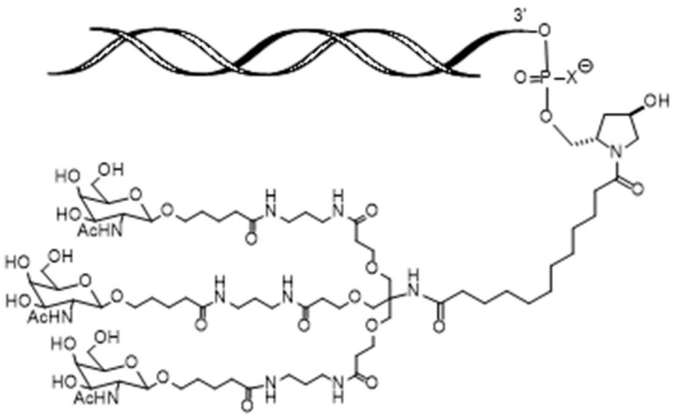
wherein a, c, g, and u are 2'-O-methyl (2'-OMe) A, 2'-OMe C, 2'-OMe G, and 2'-OMe U, respectively; Af, Cf, Gf, and Uf are 2'-fluoro A, 2'-fluoro C, 2'-fluoro G, and 2'-fluoro U, respectively; and s is a phosphorothioate linkage.

10. The composition of any one of claims 7 to 9, wherein the ligand is



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11. The composition of claim 10, wherein the RNAi agent is conjugated to the ligand as shown in the following schematic



wherein X is O or S.

12. The composition of claim 7, wherein

(a) the first sense strand comprises 5'- gsgsuggaCfuUfCfUfcucaAfUfuuuaL96 -3' (SEQ ID NO: 994) and the first antisense strand comprises 5'- usAfsaaaUfuGfAfgagaAfgUfccaccsasc -3' (SEQ ID NO: 1023); and

(b) the second sense strand comprises 5'- gsusguGfcAfCfUfucgcuucacaL96 -3' (SEQ ID NO: 1275) and the second antisense strand comprises 5'- usGfsugaAfgCfGfaaguGfcAfcacsusu -3' (SEQ ID NO: 1285);

wherein a, c, g, and u are 2'-O-methyl (2'-OMe) A, 2'-OMe C, 2'-OMe G, and 2'-OMe U, respectively; Af, Cf, Gf, and Uf are 2'-fluoro A, 2'-fluoro C, 2'-fluoro G, and 2'-fluoro U, respectively; s is a phosphorothioate linkage; and L96 is N-[tris(GalNAc-alkyl)-amidodecanoyl)]-4-hydroxyprolinol.

13. A cell containing the double stranded RNAi agent of any one of claims 1 to 6.

14. A pharmaceutical composition comprising:

(a) (i) the double stranded RNAi agent of any one of claims 1 to 6, or

(ii) the composition of any one of claims 7 to 12; and

(b) an unbuffered solution or a buffer solution.

15. The use of the double stranded RNAi agent of any one of claims 1 to 6, the composition of any one of claims 7 to 12, or the pharmaceutical composition of claim 14 in the manufacture of a medicament for reducing the viral load of Hepatitis B virus (HBV) in a subject infected with HBV.

16. The use of the double stranded RNAi agent of any one of claims 1 to 6, the composition of any one of claims 7 to 12, or the pharmaceutical composition of claim 14 in the manufacture of a medicament for treating Hepatitis B virus (HBV) infection in a subject.

17. The use of the double stranded RNAi agent of any one of claims 1 to 6, the composition of any one of claims 7 to 12, or the pharmaceutical composition of claim 14 in the manufacture of a medicament for treating Hepatitis B virus (HBV)-associated disorder in a subject, wherein the HBV-associated disorder is: hepatitis D virus (HDV) infection, delta hepatitis, acute hepatitis B; acute fulminant hepatitis B; chronic hepatitis B; liver fibrosis; end-stage liver disease; or hepatocellular carcinoma.

18. The use of claim 17, wherein the HBV-associated disorder is hepatitis D virus (HDV) infection.

19. The use of any one of claims 15 to 18, wherein the double stranded RNAi agent is to be administered to the subject at a weight-based dose of 0.01 mg/kg to 10 mg/kg

or 0.5 mg/kg to 50 mg/kg; a weight-based dose of 10 mg/kg to 30 mg/kg; a weight-based dose of 3 mg/kg; a weight-based dose of 10 mg/kg; or a fixed dose of about 50 mg to 200 mg.

20. The use of any one of claims 15 to 19, wherein the double stranded RNAi agent is to be administered subcutaneously or intravenously.

21. The use of any one of claims 15 to 20, wherein the double stranded RNAi agent is to be administered with an additional therapeutic agent.

22. The use of claim 21, wherein the additional therapeutic agent is an antiviral agent, a reverse transcriptase inhibitor, an immune stimulator, a therapeutic vaccine, a viral entry inhibitor, an oligonucleotide that inhibits the secretion or release of HbsAg, a capsid inhibitor, a covalently closed circular (ccc) HBV DNA inhibitor, or a combination of any of the foregoing.