We claim:

1. A double stranded RNAi agent for inhibiting expression of hepatitis D virus (HDV) in a cell, wherein said double stranded RNAi agent comprises a sense strand and an antisense strand forming a double-stranded region selected from the group consisting of

(a) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:29, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:30;

(b) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:31, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:32;

(c) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:33, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:34;

(d) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:35, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:36;

(e) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:37, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:38;

(f) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:39, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:40;

(g) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:41, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:42;

(h) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:43, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:44; and

(i) a sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:2551, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:2552;

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

wherein said 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. A double stranded RNAi agent for inhibiting expression of hepatitis D virus (HDV) in a cell, wherein said double stranded RNAi agent comprises a sense strand and an antisense strand forming a double-stranded region,

wherein said sense strand comprises any one of the sense sequences provided in any one of Table 11, 12, 31, and 32, and said antisense strand comprises any one of the antisense sequences provided in any one of Table 11, 12, 31, and 32,

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

wherein said 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.

3. The double stranded RNAi agent of claim 1 or 2, wherein all of the nucleotides of said sense strand and all of the nucleotides of said antisense strand are modified nucleotides.

4. The double stranded RNAi agent of claim 1, wherein said sense strand and said antisense strand comprise a region of complementarity which comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from any one of the sequences listed in any one of Table 11, 12, 31, and 32.

5. The double stranded RNAi agent of claim 1 or 2, wherein said sense strand and said antisense strand comprise a region of complementarity which comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from any one of the sense and antisense strands of AD-70260.1, AD-70232.1, AD-70249.1, AD-70244.1, AD-70272.1, AD-70228.1, AD-70255.1, AD-70278.1, AD-70295.1, AD-67200.1, AD-67211.1, AD-67199.1, AD-67202.1, AD-67208.1, AD-67210.1, AD-70259.1, AD-70267.1, AD-70272.1, AD-

70271.1, AD-70268.1, AD-70269.1, AD-70232.1, AD-70256.1, AD-70257.1, and AD-70275.1.

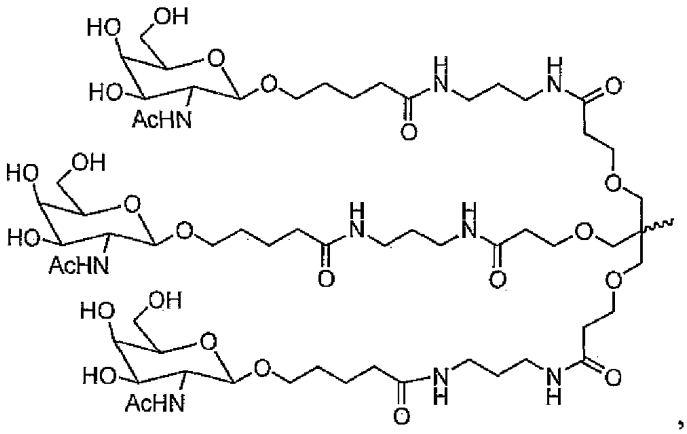
6. The double stranded RNAi agent of any one of claims 1-5, wherein at least one of said modified nucleotides is selected from the group consisting of a 3'-terminal deoxy-thymine (dT) nucleotide, a 2'-O-methyl modified nucleotide, a 2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked 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, 2'-hydroxly-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.

7. The double stranded RNAi agent of any claim 1, wherein at least one strand comprises a 3' overhang of at least 1 nucleotide or at least one strand comprises a 3' overhang of at least 2 nucleotides.

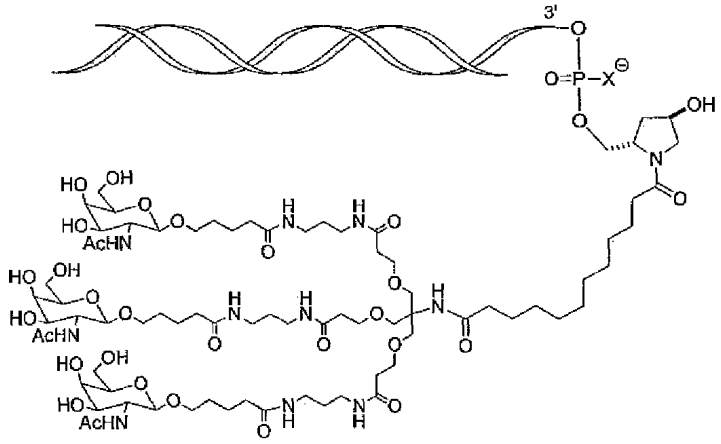
8. The double stranded RNAi agent of claim 1, wherein the double-stranded region is 15-30 nucleotide pairs in length; 17-23 nucleotide pairs in length; 17-25 nucleotide pairs in length; 23-27 nucleotide pairs in length; 19-21 nucleotide pairs in length; 21-23 nucleotide pairs in length.

9. The double stranded RNAi agent of claim 1, wherein each strand has 15-30 nucleotides.

10. The double stranded RNAi agent of claim 1 or 2, wherein the ligand is



, optionally, wherein the RNAi agent is conjugated to the ligand as shown in the following schematic



wherein X is O or S.

11. The double stranded RNAi agent of claim 1, wherein said RNAi agent is selected from the group of RNAi agents listed in any one of Table 11, 12, 31, and 32, optionally, wherein said RNAi agent is selected from AD-70260.1, AD-70232.1, AD-70249.1, AD-70244.1, AD-70272.1, AD-70228.1, AD-70255.1, AD-70278.1, AD-70295.1, AD-67200.1, AD-67211.1, AD-67199.1, AD-67202.1, AD-67208.1, AD-67210.1, AD-70259.1, AD-70267.1, AD-70272.1, AD-70271.1, AD-70268.1, AD-70269.1, AD-70232.1, AD-70256.1, AD-70257.1, or AD-70275.1.

12. A composition comprising two or more double stranded RNAi agents of any one of claims 1-11 for inhibiting expression of hepatitis D virus (HDV) in a cell.

13. A composition for inhibiting expression of hepatitis D virus (HDV) in a cell, said composition comprising:

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

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

wherein said 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 double-stranded region,

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

wherein said 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;

wherein the first and second sense strands each independently comprise a sequence selected from the group consisting of any one of the sense sequences provided in any one of Table 11, 12, 31, and 32, and

wherein the first and second antisense strands each independently comprise a sequence selected from the group consisting of any one of the antisense sequences provided in any one of Table 11, 12, 31, and 32 optionally, wherein said first and second sense strands each independently comprise a sequence selected from the group consisting of any one of the sense sequences AD-70260.1, AD-70232.1, AD-70249.1, AD-70244.1, AD-70272.1, AD-70228.1, AD-70255.1, AD-70278.1, AD-70295.1, AD-67200.1, AD-67211.1, AD-67199.1, AD-67202.1, AD-67208.1, AD-67210.1, AD-70259.1, AD-70267.1, AD-70272.1, AD-70271.1, AD-70268.1, AD-70269.1, AD-70232.1, AD-70256.1, AD-70257.1, or AD-70275.1 and optionally said first and second antisense strands each independently comprise a sequence selected from the group consisting of any one of the antisense sequences AD-70260.1, AD-70232.1, AD-70249.1, AD-70244.1, AD-70272.1, AD-70228.1, AD-70255.1, AD-70278.1, AD-70295.1, AD-67200.1, AD-67211.1, AD-67199.1, AD-67202.1, AD-67208.1, AD-67210.1, AD-70259.1, AD-70267.1, AD-70272.1, AD-70271.1, AD-70268.1, AD-70269.1, AD-70232.1, AD-70256.1, AD-70257.1, or AD-70275.1.

14. A double stranded RNAi agent comprising the RNAi agents provided in any one of Table 11, 12, 31, and 32.

15. A pharmaceutical composition comprising the double stranded RNAi agent claims 1 and 11, or the composition of claim12 or 13.

16. A method of inhibiting Hepatitis D virus (HDV) gene expression or replication in a cell, the method comprising:

(a) contacting the cell with the double stranded RNAi agent of claim 1 or 11, the composition of claim 12 or 13, or the pharmaceutical composition of claim 15; and

(b) maintaining the cell produced in step (a) for a time sufficient to obtain degradation of the mRNA transcript of an HDV gene, thereby inhibiting expression or replication of the HDV gene in the cell.

17. Use of the double stranded RNAi agent of claim 1 or 11, or the composition of claim 12 or 13, or the pharmaceutical composition of claim 15 in the manufacture of a medicament for treating a subject having a Hepatitis D virus (HDV) infection.

18. The use of claim 17, wherein the double stranded RNAi agent is to be administered at a dose of 0.01 mg/kg to 10 mg/kg; 0.5 mg/kg to 50 mg/kg; 10 mg/kg to 30 mg/kg; 3 mg/kg; 10 mg/kg; or at a fixed dose of 50 mg to 200 mg.

19. The use of claim 17, wherein the double stranded RNAi agent is to be administered subcutaneously or intravenously.

20. The use of claim 17, further comprising an additional therapeutic agent, optionally an antiviral agent, a reverse transcriptase inhibitor (e.g., Tenofovir disoproxil fumarate (TDF), Tenofovir alafenamide, Lamivudine, Adefovir dipivoxil, Entecavir (ETV), Telbivudine, or AGX-1009), an immune stimulator (e.g., pegylated interferon alfa 2a (PEG-IFN-□2a), Interferon alfa-2b, a recombinant human interleukin-7, or a Toll-like receptor 7 (TLR7) agonist), 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, a double-stranded iRNA agent targeting HBV e.g., a double-stranded iRNA agent targeting HBV is any one of the agents provided in any one of Tables 3, 4, 6, 14, 15, 24, 25, 27, and 28, e.g., AD-65403, AD-66810, or a combination thereof), and a combination of any of the foregoing.