CLAIMS:

1. An RNAi agent for inhibiting expression of an HSD17B13 gene, comprising:

an antisense strand containing at least 19 contiguous nucleotides differing by 0 or 1 nucleotide from the sequence described in SEQ. NO. 3; and

a sense strand that is at least partially complementary to the antisense strand and contains at least 19 contiguous nucleotides.

2. The RNAi agent according to claim 1, wherein the RNAi agent is linked to a targeting ligand.

3. The RNAi agent according to claim 2, wherein the targeting ligand includes N-acetyl-galactosamine.

4. The RNAi agent according to claim 3, wherein the targeting ligand has a structure selected from the group consisting of: (NAG13), (NAG13)s, (NAG18), (NAG18)s, (NAG24), (NAG24)s, (NAG25), (NAG25)s, (NAG26), (NAG26)s, (NAG27), (NAG27)s, (NAG28), (NAG28)s, (NAG29), (NAG29)s, (NAG30), (NAG30)s, (NAG31), (NAG31)s, (NAG32), (NAG32)s, (NAG33), (NAG33)s, (NAG34), (NAG34)s, (NAG35), (NAG35)s, (NAG36), (NAG36)s, (NAG37), (NAG37)s, (NAG38), (NAG38)s, (NAG39), (NAG39)s.

5. The RNAi agent according to claim 4, wherein the targeting ligand contains a structure of (NAG37) or (NAG37)s.

6. The RNAi agent according to any one of claims 1 to 5, wherein the antisense strand comprises, consists of, or essentially consists of the following nucleotide sequences (5′ → 3′):
usCfsasUfcUfaUfcAfgAfcUfuCfuUfaCfsg (SEQ ID NO:2); or
usCfsasUfcUfaucagAfcUfuCfuUfaCfsg (SEQ ID NO:4);

including modified nucleotide sequences that differ by 0 or 1 nucleotide from one of the aforementioned sequences,
where in the above sequences, a, c, g, and u represent 2′-O-methyladenosine, 2′-O-methylcytidine, 2′-O-methylguanosine, and 2′-O-methyluridine, respectively; Af, Cf, and Uf represent 2′-fluoroadenosine, 2′-fluorocytidine, and 2′-fluorouridine, respectively; s is a phosphorothioate bond; and all or substantially all of the nucleotides on the sense strand are modified nucleotides.

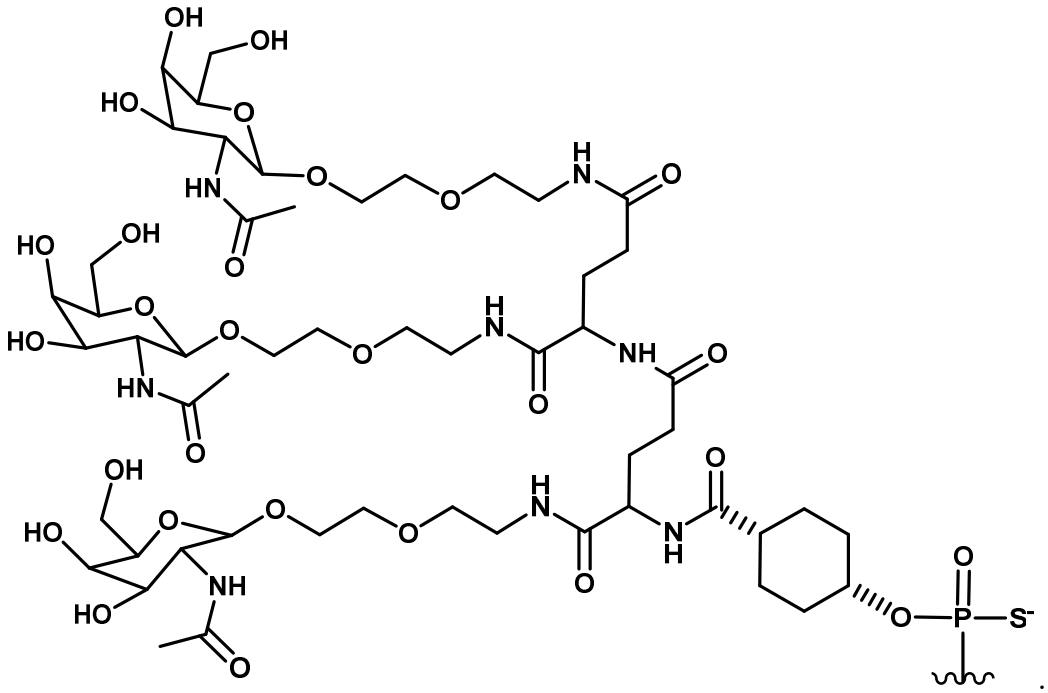
7. The RNAi agent according to any one of claims 1 to 6, wherein the sense strand comprises, consists of, or essentially consists of the following nucleotide sequences (5′ → 3′):
scguaagaaGfUfCfugauagaugas (SEQ ID NO: 14); or
scguaagaaGfuCfuGfauagaugas (SEQ ID NO: 15);
including modified nucleotide sequences that differ by 0 or 1 nucleotide from one of the aforementioned sequences,
where in the above sequences, a, c, g, and u represent 2′-O-methyladenosine, 2′-O-methylcytidine, 2′-O-methylguanosine, and 2′-O-methyluridine, respectively; Cf, Gf, and Uf represent 2′-fluorocytidine, 2′-fluoroguanosine, and 2′-fluorouridine, respectively; s is a phosphorothioate bond; and all or substantially all of the nucleotides on the antisense strand are modified nucleotides.

8. The RNAi agent according to any one of claims 1 to 7, wherein the RNAi agent includes a double-stranded structure of: AD06214 (SEQ ID NO: 2 and 14) or AD06280 (SEQ ID NO: 4 and 15).

9. The RNAi agent according to claim 1, wherein the antisense strand contains a modified nucleotide sequence of (5′ → 3′) usCfsasUfcUfaUfcAfgAfcUfuCfuUfaCfsg (SEQ ID NO:2), and the sense strand contains a modified nucleotide sequence of (5′ → 3′) (NAG37)s(invAb)scguaagaaGfUfCfugauagaugas(invAb) (SEQ ID NO:14); and
in the sequences, a, c, g, and u represent 2′-O-methyladenosine, 2′-O-methylcytidine, 2′-O-methylguanosine, and 2′-O-methyluridine, respectively; Af, Cf, Gf, and Uf represent 2′-

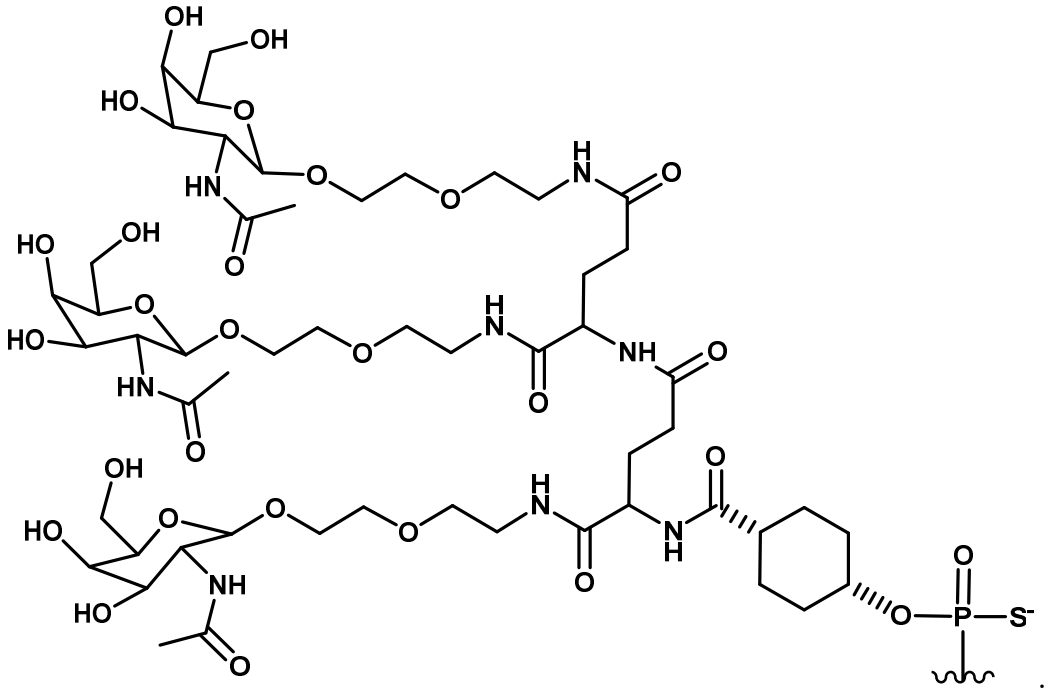
fluoroadenosine, 2′-fluorocytidine, 2′-fluoroguanosine, or 2′-fluorouridine; s is a phosphorothioate bond; (invAb) is an inverse abasic deoxyribose residual group; and (NAG37)s contains the following chemical structure:

[Chem. Fig. 1]



10. The RNAi agent according to claim 1, wherein the antisense strand contains a modified nucleotide sequence of (5′ → 3′) usCfsasUfcUfaucagAfcUfuCfuUfaCfsg (SEQ ID NO:4), and the sense strand contains a modified nucleotide sequence of (5′ → 3′) (NAG37)s(invAb)scguaagaaGfuCfuGfauagaugas(invAb) (SEQ ID NO:15); and
in the sequences, a, c, g, and u represent 2′-O-methyladenosine, 2′-O-methylcytidine, 2′-O-methylguanosine, and 2′-O-methyluridine, respectively; Af, Cf, Gf, and Uf represent 2′-fluoroadenosine, 2′-fluorocytidine, 2′-fluoroguanosine, and 2′-fluorouridine; s is a phosphorothioate bond; (invAb) is an inverse abasic deoxyribose residual group; and (NAG37)s contains the following chemical structure:

[Chem. Fig. 2]



11. The RNAi agent according to claim 1, wherein
the RNAi agent includes: the chemical structures of FIG. 1A to 1D;
[Chem. Fig. 3-1]

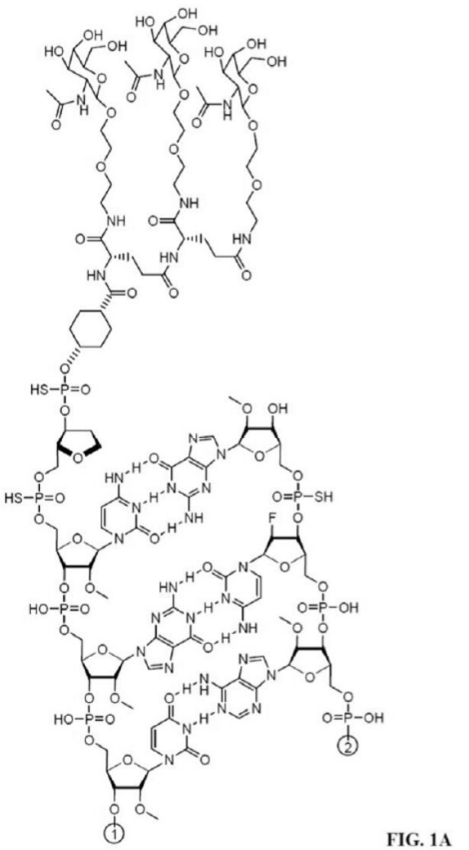


FIG. 1A

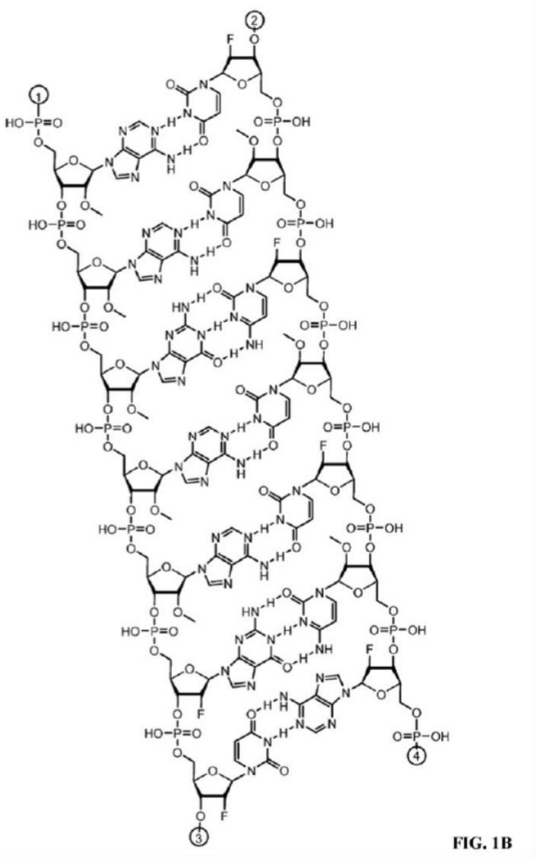


FIG. 1B

[Chem. Fig. 3-2]

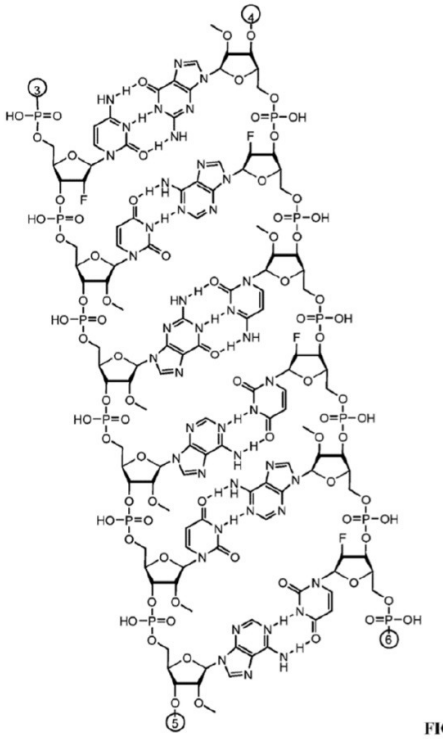


FIG. 1C

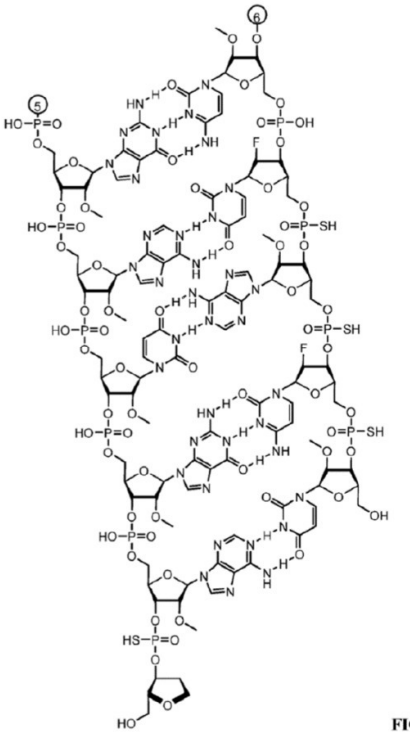


FIG. 1D

the chemical structures of FIG. 2A to 2D;

[Chem. Fig. 4-1]

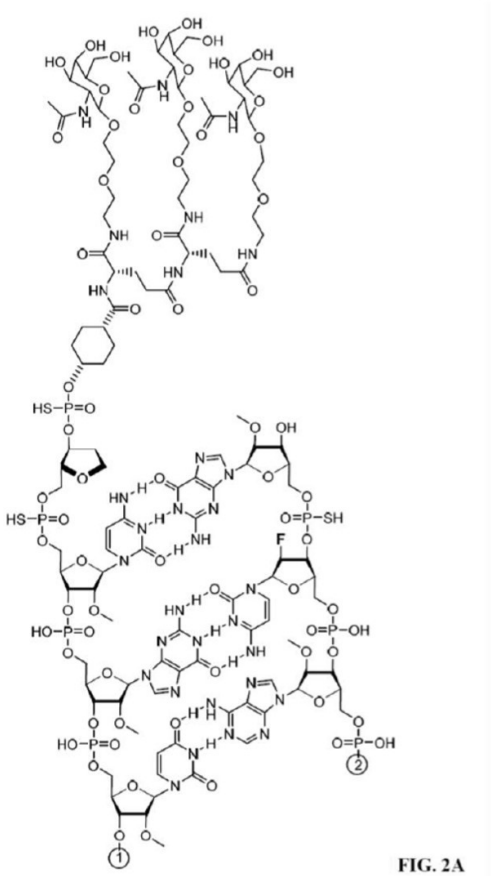


FIG. 2A

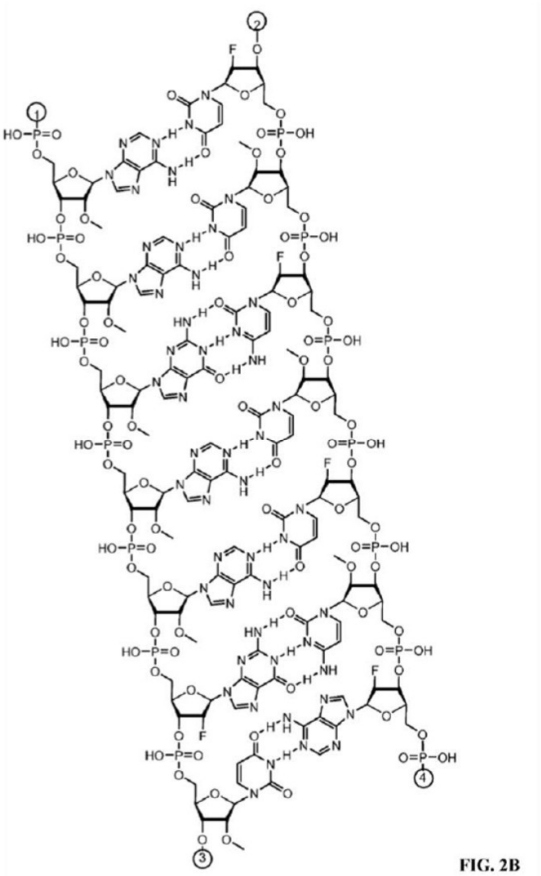


FIG. 2B

[Chem. Fig. 4-2]

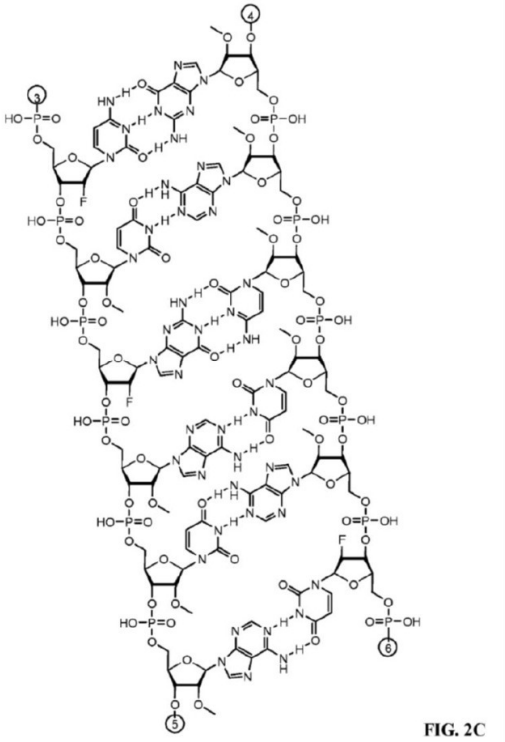


FIG. 2C

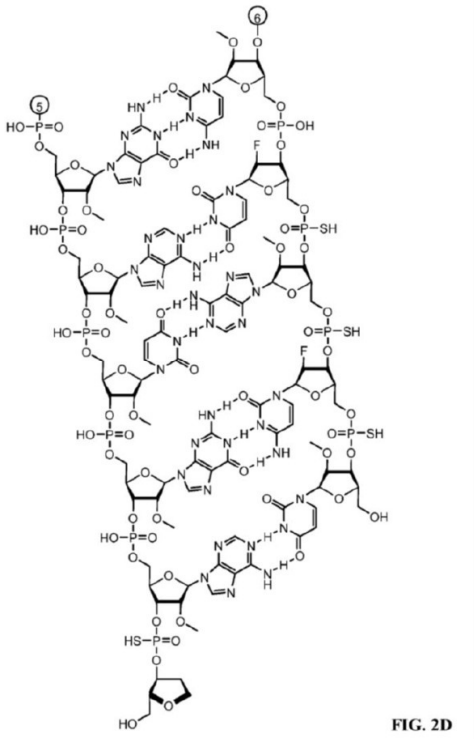


FIG. 2D

the chemical structures of FIG. 6A to 6D;

[Chem. Fig. 5-1]

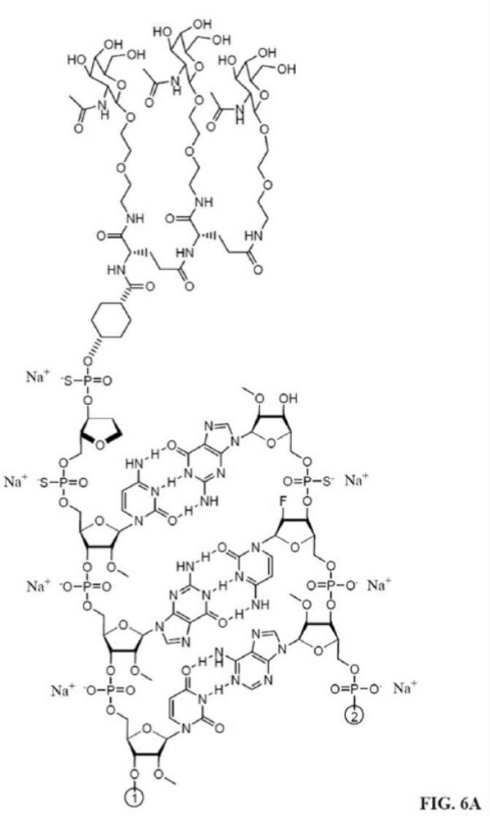


FIG. 6A

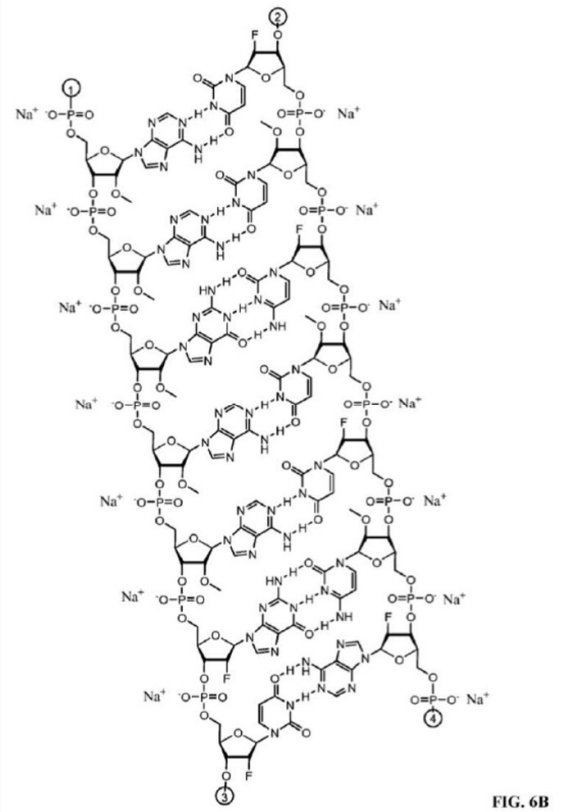


FIG. 6B

[Chem. Fig. 5-2]

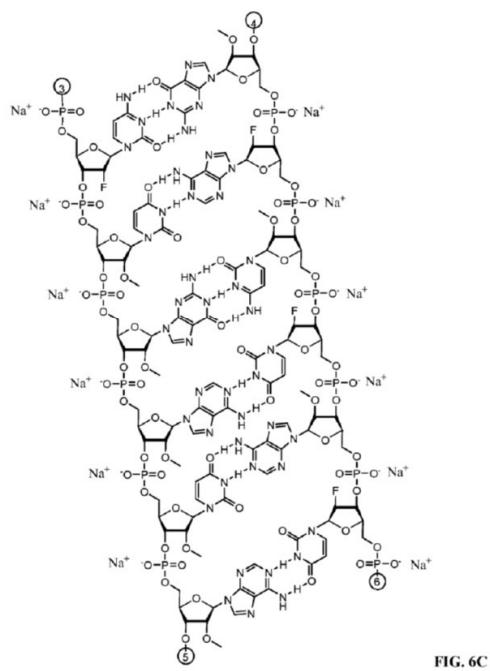


FIG. 6C

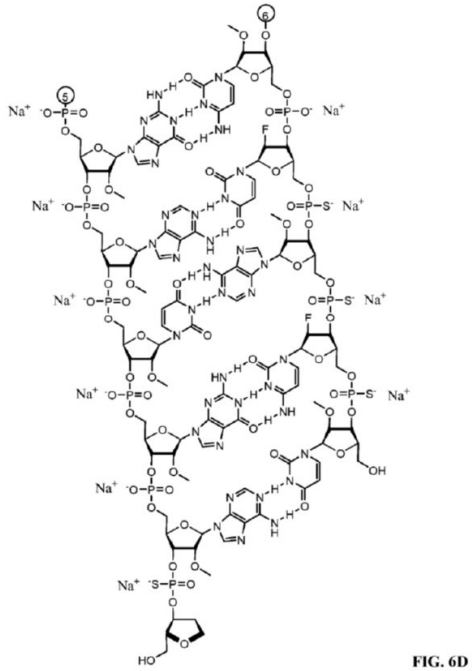


FIG. 6D

and the chemical structures of FIG. 7A to 7D;

[Chem. Fig. 6-1]

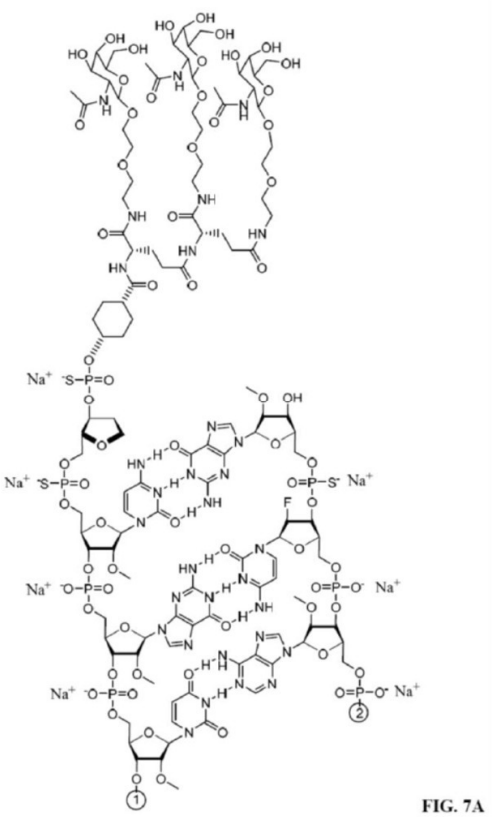


FIG. 7A

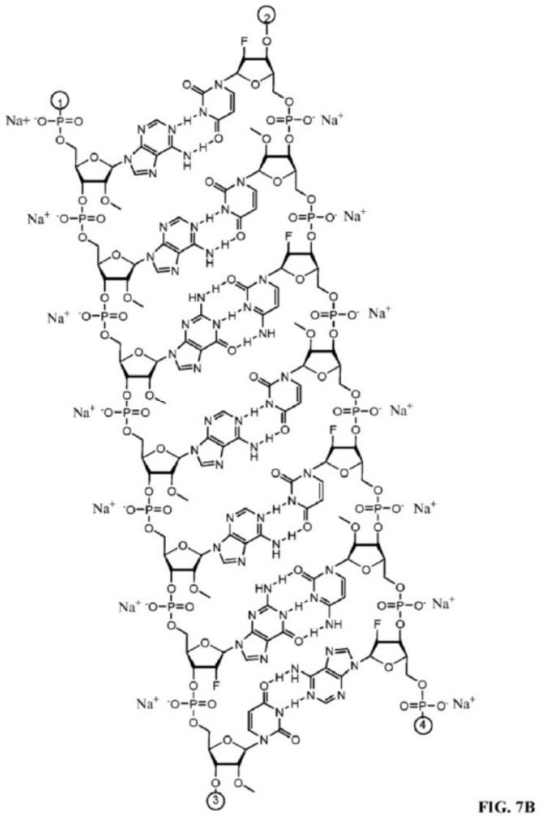


FIG. 7B

[Chem. Fig. 6-2]

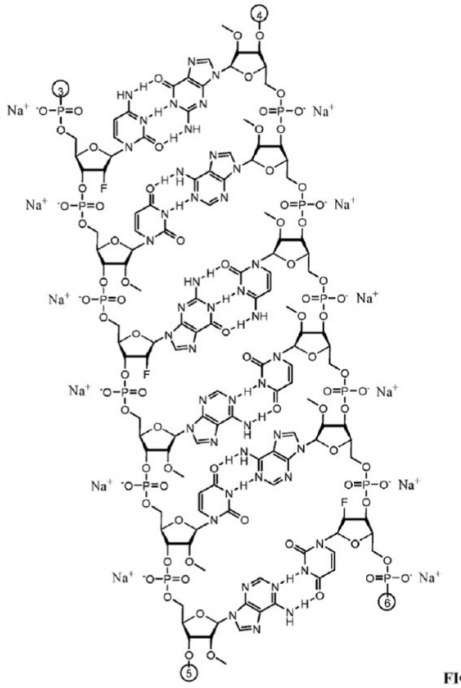


FIG. 7C

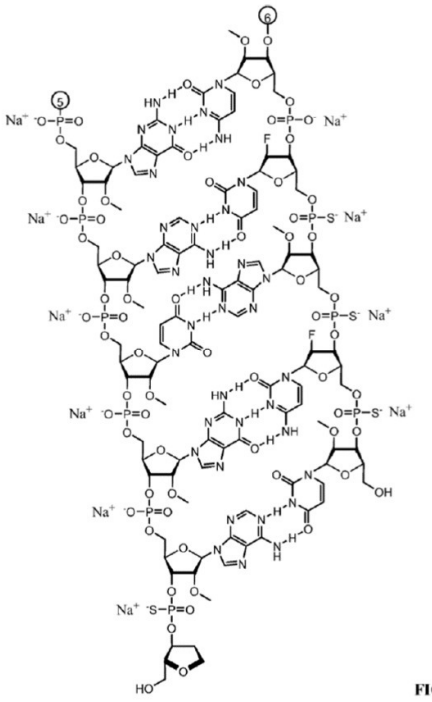


FIG. 7D

12. The RNAi agent according to claim 1, wherein

the RNAi agent includes: the chemical structures of FIG. 2A to 2D;

[Chem. Fig. 7-1]

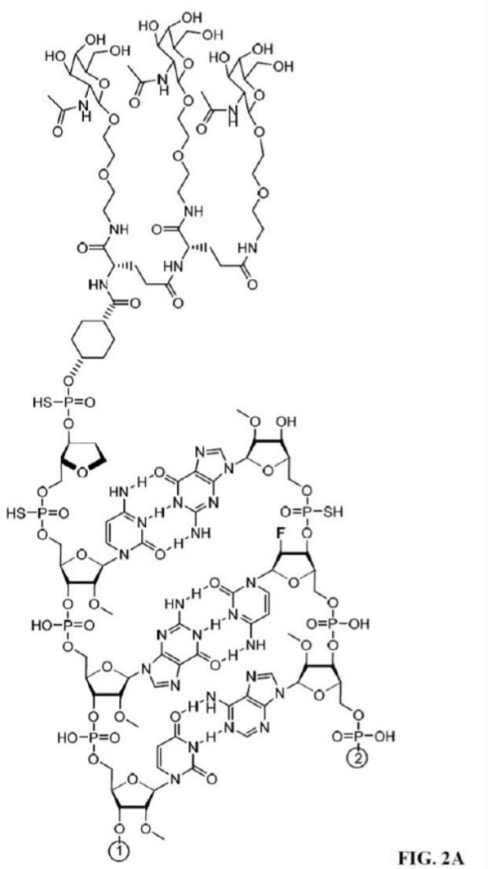


FIG. 2A

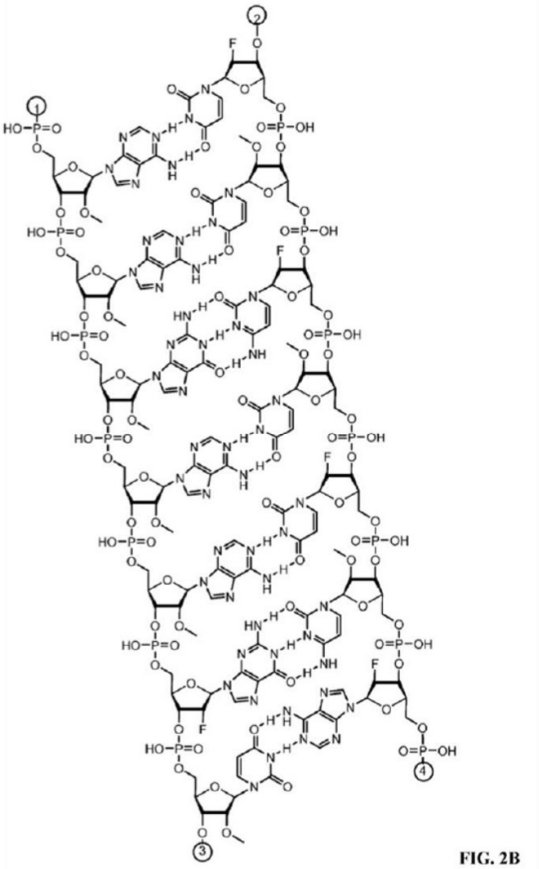


FIG. 2B

[Chem. Fig. 7-2]

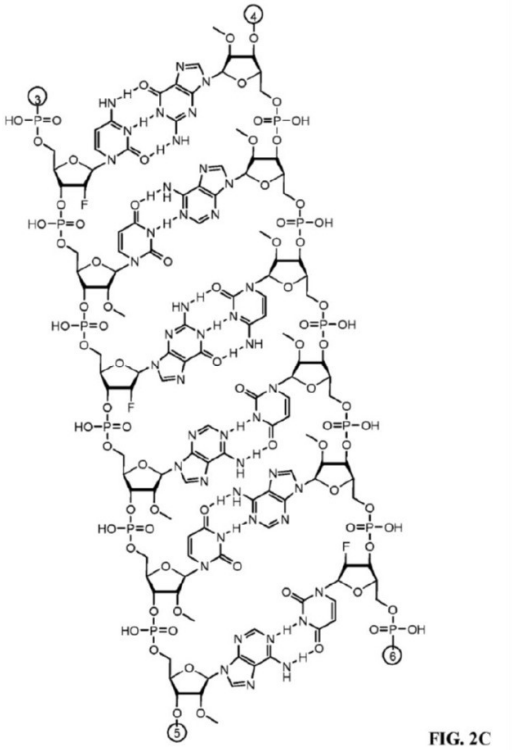


FIG. 2C

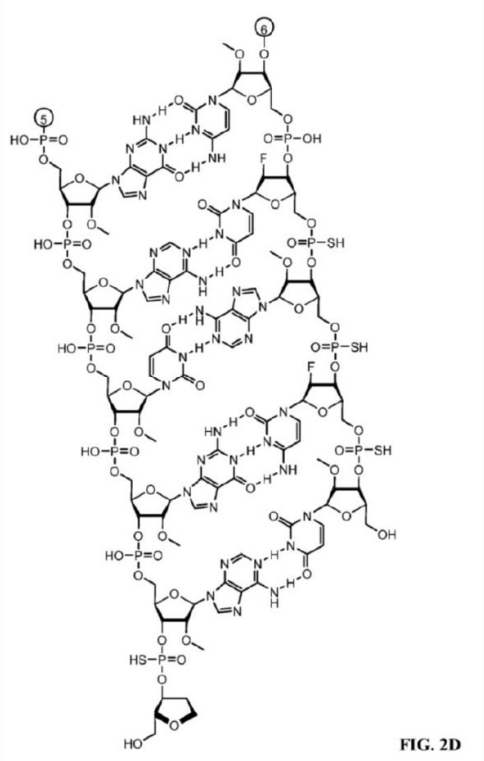


FIG. 2D

13. The RNAi agent according to claim 1, wherein

the RNAi agent includes: the chemical structures of FIG. 7A to 7D;

[Chem. Fig. 8-1]

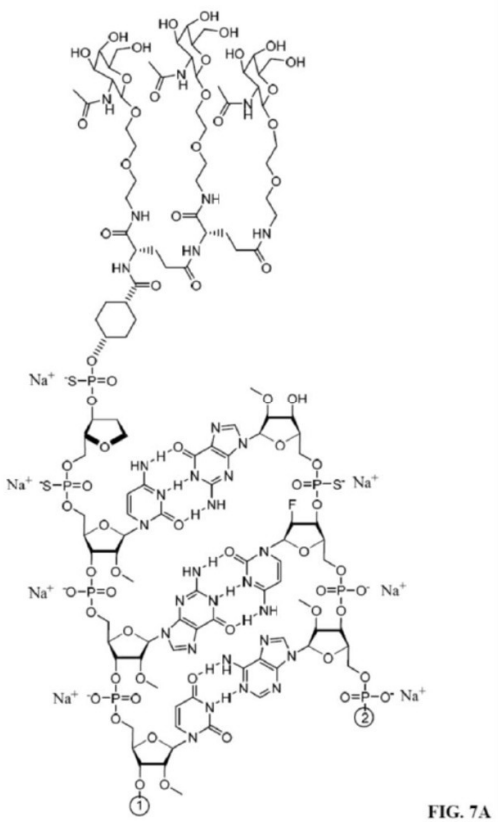


FIG. 7A

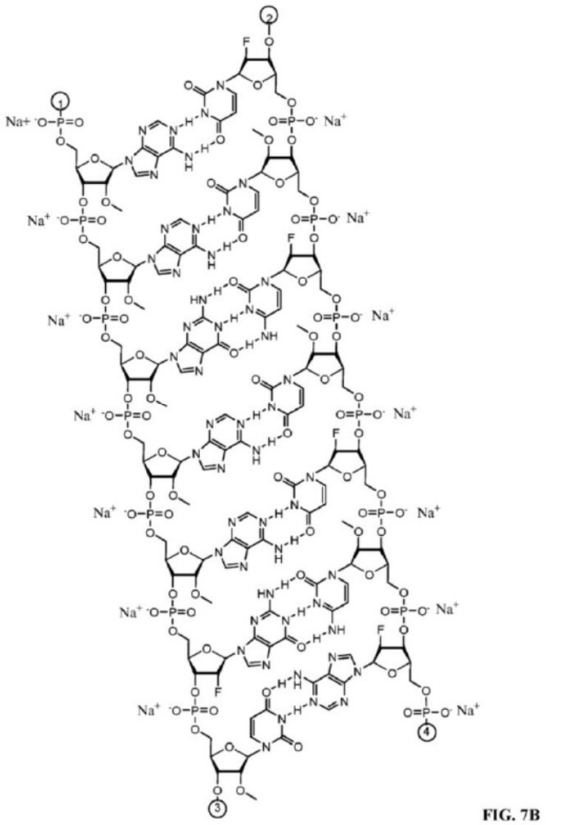


FIG. 7B

[Chem. Fig. 8-2]

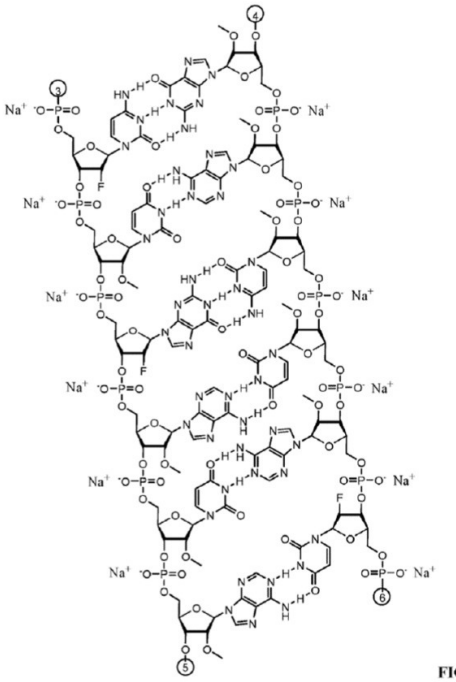


FIG. 7C

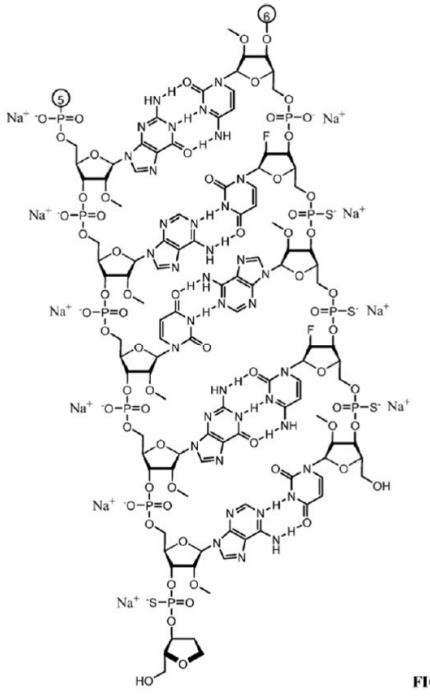


FIG. 7D

14. A composition, comprising the RNAi agent according to any one of claims 1-13, and further comprising a pharmaceutically acceptable excipient.

15. The composition according to claim 14, wherein the composition further comprises a second RNAi agent to inhibit expression of HSD17B13.

16. The composition according to claim 14 or 15, wherein the composition further comprises one or more additional therapeutic agents.

17. The composition according to any one of claims 14 to 16 that is a pharmaceutical composition.

18. The pharmaceutical composition according to claim 17, for use in the treatment of a disease, disorder, or condition mediated at least in part by HSD17B13 gene expression.

19. The pharmaceutical composition according to claim 18, wherein the disease is an alcohol-related liver disease.

20. The pharmaceutical composition according to claim 18, wherein the disease is a non-alcoholic fatty liver disease (NAFLD).

21. The pharmaceutical composition according to claim 20, wherein the disease is non-alcoholic steatohepatitis (NASH).

22. A method of inhibiting the expression of the HSD17B13 gene in cells in vitro, the method comprising introducing into the cells an effective amount of the RNAi agent according to any one of claims 1 to 13 or a composition according to any one of claims 14 to 16.

23. The method of claim 22, wherein the cells are derived from a human subject.

24. Use of an RNAi agent according to any one of claims 1-13 or a composition according to any one of claims 14-16, for the manufacture of a medicament for the treatment of a disease, disorder, or symptom mediated at least in part by HSD17B13 gene expression.

25. The use according to claim 24, wherein the disease is alcohol-related liver disease.

26. The use according to claim 24, wherein the disease is a non-alcoholic fatty liver disease (NAFLD).

27. The use according to claim 26, wherein the disease is non-alcoholic steatohepatitis (NASH).