Modification Motif iv:

XmsXfsXmXmXmXmXmXmXmXmXmXmXfXmXfXmXmXmXmXmsXmsXm;

wherein, for each Modification Motif, individual “X’s” represent ribonucleotides from the 5’ end to the 3’ end of the sense strand or the antisense strand in sequence, “Xm” represents a ribonucleotide comprising a 2’-O-methyl modification, “Xf” represents a ribonucleotide comprising a 2’-fluoro modification, and “s” represents a phosphorothioate backbone linkage between two flanking ribonucleotides.

In some embodiments, the sense strand of the dsRNA molecule has a structure as set forth in (B1), (B2), or (B3), and the antisense strand of the dsRNA molecule has a structure as set forth in (B4), (B5), (B6), (B7), (B8), or (B9).

(B1), (B2) or (B3) are (A1), (A2) or (A3) comprising the modifications as defined in Modification Motif i:

(B1): SEQ ID NO: 5 comprising the modifications as defined in Modification Motif i,

(B2): SEQ ID NO: 17comprising the modifications as defined in Modification Motif i, and

(B3): SEQ ID NO: 85 comprising the modifications as defined in Modification Motif i.

(B4), (B5), or (B6) are (A4), (A5) or (A6) comprising the modifications as defined in Modification Motif iii, and (B7), (B8), or (B9) are (A4), (A5) or (A6) comprising the modifications as defined in Modification Motif iv:

(B4): SEQ ID NO: 105 comprising the modifications as defined in Modification Motif iii,

(B5): SEQ ID NO: 117 comprising the modifications as defined in Modification Motif iii,

(B6): SEQ ID NO: 185 comprising the modifications as defined in Modification Motif iii,

(B7): SEQ ID NO: 105 comprising the modifications as defined in Modification Motif iv,

(B8): SEQ ID NO: 117comprising the modifications as defined in Modification Motif iv, and

(B9): SEQ ID NO: 185 comprising the modifications as defined in Modification Motif iv.

For (B1) to (B9):

Modification Motif i:

XmsXmsXmXmXmXmXfXmXfXfXfXmXmXmXmXmXmXmXmXmXm;

Modification Motif iii:

XmsXfsXmXmXmXfXmXmXmXmXmXmXmXfXmXfXmXmXmXmXmsXmsXm;

and

Modification Motif iv:

XmsXfsXmXmXmXmXmXmXmXmXmXmXmXfXmXfXmXmXmXmXmsXmsXm;

wherein, for each Modification Motif, individual “X’s” represent ribonucleotides from the 5’ end to the 3’ end of the sense strand or the antisense strand in sequence, “Xm” represents a ribonucleotide comprising a 2’-O-methyl modification, “Xf” represents a ribonucleotide comprising a 2’-fluoro modification, and “s” represents a phosphorothioate backbone linkage between two flanking ribonucleotides.

In some preferred embodiments, the dsRNA molecule is selected from the group consisting of:

5-E04, comprising a sense strand of SEQ ID NO: 5 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 105 comprising the modifications as defined in Modification Motif iii;

5-E05, comprising a sense strand of SEQ ID NO: 5 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 105 comprising the modifications as defined in Modification Motif iv;

7-E04, comprising a sense strand of SEQ ID NO: 7 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 107 comprising the modifications as defined in Modification Motif iii;

7-E05, comprising a sense strand of SEQ ID NO: 7 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 107 comprising the modifications as defined in Modification Motif iv;

17-E04, comprising a sense strand of SEQ ID NO: 17 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 117 comprising the modifications as defined in Modification Motif iii;

17-E05, comprising a sense strand of SEQ ID NO: 17 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 117 comprising the modifications as defined in Modification Motif iv;

32-E04, comprising a sense strand of SEQ ID NO: 32 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 132 comprising the modifications as defined in Modification Motif iii;

32-E05, comprising a sense strand of SEQ ID NO: 32 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 132 comprising the modifications as defined in Modification Motif iv;

85-E04, comprising a sense strand of SEQ ID NO: 85 comprising the modifications as defined in Modification Motif i, and an antisense strand of SEQ ID NO: 185 comprising the modifications as defined in Modification Motif iii; and

WHAT IS CLAIMED IS:

1. A dsRNA molecule for inhibiting the gene expression of complement component 5 (C5), comprising a sense strand and an antisense strand that are complementary to form a double-stranded region, wherein the sense strand and/or the antisense strand comprises or consists of 15 to 25 nucleotides, the antisense strand comprises contiguous bases that are complementary to at least 15, 16, 17, 18, 19, 20, or 21 contiguous bases in the sequence as set forth in any one of SEQ ID NOs: 1 to 98, the double-stranded region has a length of 15 to 25 nt, and at least one nucleotide in the dsRNA molecule comprises a modification.

2. The dsRNA molecule according to claim 1, wherein:

the base sequence of the sense strand is as set forth in SEQ ID NO: 85 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 185; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 5 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 105; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 17 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 117; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 1 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 101; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 2 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 102; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 3 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 103; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 4 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 104; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 6 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 106; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 7 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 107; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 8 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 108; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 9 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 109; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 10 and the base

sequence of the antisense strand is as set forth in SEQ ID NO: 110; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 11 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 111; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 12 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 112; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 13 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 113; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 14 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 114; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 15 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 115; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 16 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 116; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 18 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 118; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 19 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 119; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 20 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 120; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 21 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 121; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 22 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 122; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 23 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 123; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 24 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 124; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 25 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 125; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 26 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 126; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 27 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 127; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 28 and the base

sequence of the antisense strand is as set forth in SEQ ID NO: 128; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 29 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 129; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 30 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 130; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 31 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 131; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 32 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 132; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 33 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 133; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 34 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 134; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 35 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 135; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 36 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 136; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 37 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 137; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 38 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 138; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 39 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 139; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 40 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 140; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 41 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 141; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 42 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 142; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 43 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 143; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 44 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 144; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 45 and the base

sequence of the antisense strand is as set forth in SEQ ID NO: 145; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 46 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 146; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 47 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 147; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 48 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 148; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 49 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 149; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 50 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 150; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 51 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 151; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 52 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 152; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 53 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 153; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 54 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 154; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 55 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 155; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 56 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 156; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 57 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 157; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 58 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 158; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 59 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 159; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 60 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 160; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 61 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 161; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 62 and the base

sequence of the antisense strand is as set forth in SEQ ID NO: 162; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 63 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 163; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 64 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 164; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 65 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 165; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 66 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 166; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 67 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 167; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 68 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 168; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 69 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 169; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 70 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 170; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 71 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 171; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 72 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 172; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 73 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 173; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 74 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 174; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 75 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 175; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 76 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 176; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 77 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 177; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 78 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 178; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 79 and the base

sequence of the antisense strand is as set forth in SEQ ID NO: 179; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 80 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 180; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 81 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 181; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 82 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 182; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 83 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 183; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 84 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 184; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 86 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 186; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 87 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 187; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 88 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 188; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 89 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 189; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 90 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 190; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 91 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 191; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 92 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 192; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 93 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 193; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 94 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 194; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 95 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 195; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 96 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 196; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 97 and the base

sequence of the antisense strand is as set forth in SEQ ID NO: 197; or

the base sequence of the sense strand is as set forth in SEQ ID NO: 98 and the base sequence of the antisense strand is as set forth in SEQ ID NO: 198.

3. The dsRNA molecule according to claim 1 or 2, wherein the modification is one or more selected from the group consisting of a locked nucleic acid modification, an open or unlocked nucleic acid modification, a 2'-methoxyethyl modification, a 2'-O-methyl modification, a 2'-O-allyl modification, a 2'-C-allyl modification, a 2'-fluoro modification, a 2'-deoxy modification, a phosphorothioate backbone modification, a DNA modification, a fluorescent probe modification, and a ligand modification.

4. The dsRNA molecule according to any one of claims 1 to 3, wherein the dsRNA molecule comprises modifications, wherein:

(i) the sense strand has a length of 21 nt, has 2'-fluoro modifications at positions 7 and 9 to 11 from the 5' end and 2'-O-methyl modifications at the remaining positions, and has phosphorothioate backbone linkages among the contiguous nucleotides at positions 1 to 3 from the 5' end; and

(ii) the antisense strand has a length of 23 nt, has 2'-fluoro modifications at positions 2, 14, and 16 and optional position 6 from the 5' end and 2'-O-methyl modifications at the remaining positions, and has phosphorothioate backbone linkages among the contiguous nucleotides at positions 1 to 3 from the 5' end and among the contiguous nucleotides at positions 1 to 3 from the 3' end.

5. The dsRNA molecule according to any one of claims 1 to 4, wherein:

the base sequence of the sense strand of the dsRNA molecule is set forth in SEQ ID NO: 85, and the base sequence of the antisense strand of the dsRNA molecule is set forth in SEQ ID NO: 185; or

the base sequence of the sense strand of the dsRNA molecule is set forth in SEQ ID NO: 5, and the base sequence of the antisense strand of the dsRNA molecule is set forth in SEQ ID NO: 105; or

the base sequence of the sense strand of the dsRNA molecule is set forth in SEQ ID NO: 17, and the base sequence of the antisense strand of the dsRNA molecule is set forth in SEQ ID NO: 117.

6. The dsRNA molecule according to any one of claims 1 to 5, wherein:

the sense strand of the dsRNA molecule comprises the modifications as defined in Modification Motif i:

Modification Motif i:

XmsXmsXmXmXmXmXfXmXfXfXfXmXmXmXmXmXmXmXmXmXm; and

the antisense strand of the dsRNA molecule comprises the modifications as defined in Modification Motif iii or Modification Motif iv:

Modification Motif iii:

XmsXfsXmXmXmXfXmXmXmXmXmXmXmXfXmXfXmXmXmXmXmsXmsXm, or

Modification Motif iv:

XmsXfsXmXmXmXmXmXmXmXmXmXmXmXmXfXmXfXmXmXmXmXmsXmsXm;

wherein, for each Modification Motif, individual "X's" represent ribonucleotides from the 5' end to the 3' end of the sense strand or the antisense strand in sequence, "Xm" represents a ribonucleotide comprising a 2'-O-methyl modification, "Xf" represents a ribonucleotide comprising a 2'-fluoro modification, and "s" represents a phosphorothioate backbone linkage between two flanking ribonucleotides.

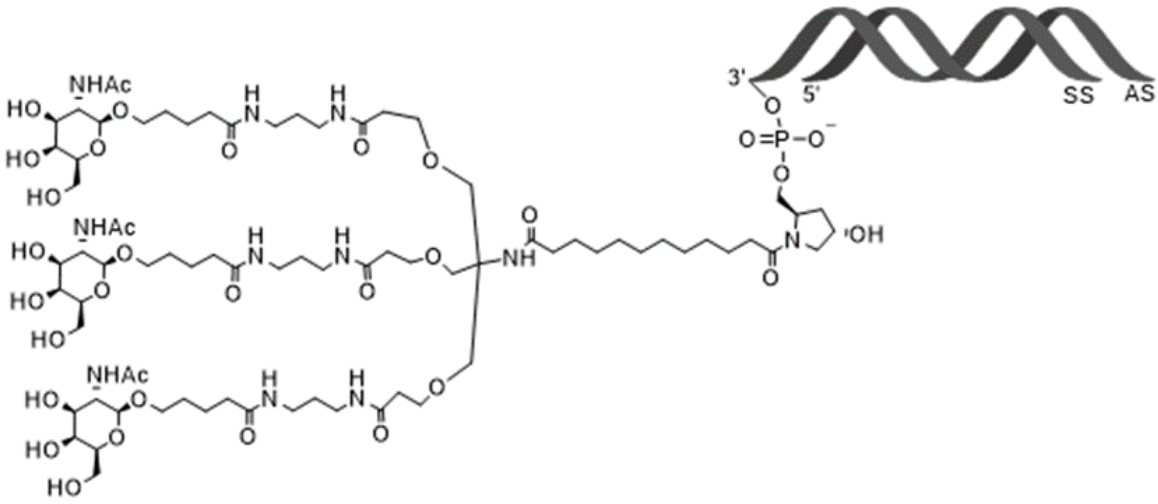
7. The dsRNA molecule according to claim any one of claims 1 to 6, wherein the dsRNA molecule further comprises a ligand that targets a liver.

8. The dsRNA molecule according to claim 7, wherein the ligand targets parenchymal cells of a liver.

9. The dsRNA molecule according to claim 7, wherein the ligand is conjugated to the 3' end of the sense strand.

10. The dsRNA molecule according to claim 7, wherein the ligand is an N-acetylgalactosamine (GalNAc) derivative or analog.

11. The dsRNA molecule according to any one of claims 1 to 10, wherein the dsRNA molecule further comprises a ligand conjugated to the 3' end of the sense strand, the ligand is L96, and the dsRNA molecule has the structure of Formula I:



Formula I,

wherein "SS" represents the sense strand, and "AS" represents the antisense strand.

12. The dsRNA molecule according to claim 6, wherein the sense strand comprises the modifications as defined in Modification Motif i, and the antisense strand comprises the modifications as defined in Modification Motif iv.

13. A pharmaceutical composition comprising the dsRNA molecule according to any one of claims 1 to 12, and a pharmaceutically acceptable excipient.

14. The pharmaceutical composition according to claim 13, wherein the pharmaceutical composition further comprises an additional compound that inhibits complement proteins or complement protein expressions.

15. Use of the pharmaceutical composition according to claim 13 in the manufacture of a medicament for inhibiting the gene expression of complement C5, or reducing C5 protein in a serum, or preventing and/or treating a disease mediated by complement C5 gene, or alleviating symptoms of a disease mediated by complement C5 gene in a subject.

16. The use according to claim 15, wherein the disease mediated by complement C5 gene is one or more selected from the group consisting of ophthalmic diseases, including dry/wet age-related macular degeneration (AMD), and geographic atrophy (GA); hematologic diseases, including paroxysmal nocturnal hemoglobinuria (PNH), and thrombotic microangiopathies (TMAs); cardiovascular diseases; autoimmune diseases, including rheumatoid arthritis, and lupus erythematosus; renal diseases, including atypical hemolytic uremic syndrome (aHUS), C3 glomerulopathy (C3G), IgA nephropathy and lupus nephritis; neurological diseases, including Alzheimer's disease (AD), and myasthenia gravis (gMG); neoplastic diseases,

including complement-associated liver cancer or lung cancer; surgery-related diseases, including hepatic ischemia-reperfusion injury, burn rehabilitation, and post-transplant rejection; and respiratory diseases, including asthma, idiopathic pulmonary fibrosis, and chronic obstructive pulmonary disease (COPD).

17. A double-stranded nucleic acid for inhibiting the gene expression of C5, or a pharmaceutically acceptable salt thereof, wherein the double-stranded nucleic acid comprises a first strand and a second strand, wherein:

the base sequence of the first strand is AUCGUAACAACAUUUCUUCACUA (SEQ ID NO: 185), and the base sequence of the second strand is GUGAAGAAAUGUUGUUACGAU (SEQ ID NO: 85); or

the base sequence of the first strand is GUAUCCAUAAACUUGAAUCACAA (SEQ ID NO: 105), and the base sequence of the second strand is GUGAUUCAAGUUUAUGGAUAC (SEQ ID NO: 5); and

the first strand has the modifications as defined in Modification Motif iv:

Modification Motif iv:

XmsXfsXmXmXmXmXmXmXmXmXmXmXfXmXfXmXmXmXmXmsXmsXm; and

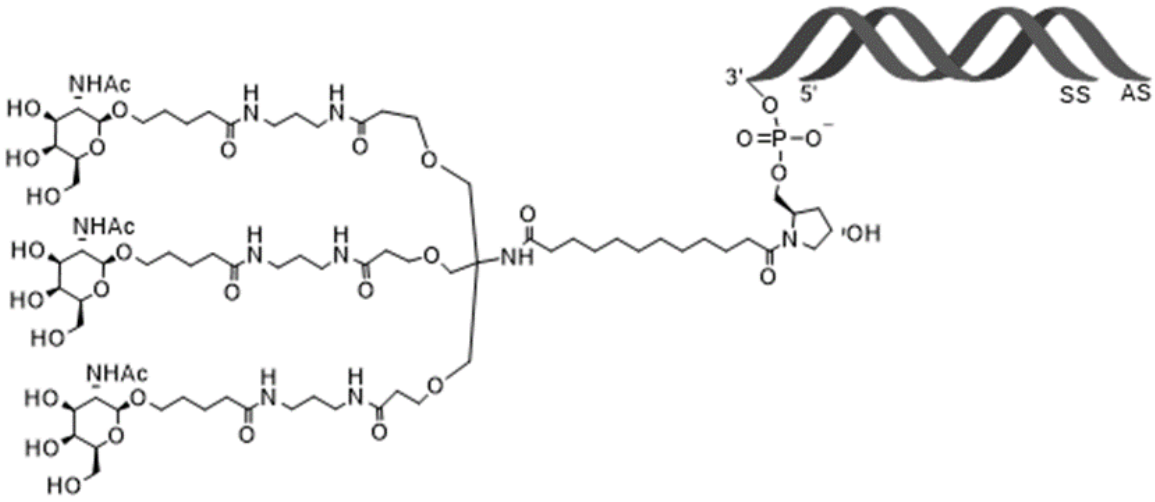
the second strand is conjugated to an L96 ligand at the 3’ end and has the modifications as defined in Modification Motif i:

Modification Motif i:

XmsXmsXmXmXmXmXfXmXfXfXfXmXmXmXmXmXmXmXmXmXm;

wherein individual “X’s” represent ribonucleotides from the 5’ end to the 3’ end of the first strand or the second strand in sequence, “Xm” represents a 2’-O-methyl modified ribonucleotide A, U, C or G, “Xf” represents a 2’-fluoro modified ribonucleotide A, U, C or G, and “s” represents a phosphorothioate backbone linkage between two flanking ribonucleotides, and

the double-stranded nucleic acid has the below structure:



wherein "SS" represents the second strand, and "AS" represents the first strand.

18. A pharmaceutical composition comprising the double-stranded nucleic acid or a pharmaceutically acceptable salt thereof according to claim 17, and a pharmaceutically acceptable carrier.

19. Use of the pharmaceutical composition of claim 18 in the manufacture of a medicament for inhibiting the gene expression of complement C5, or reducing C5 protein in a serum, or preventing and/or treating a disease mediated by complement C5 gene, or alleviating symptoms of a disease mediated by complement C5 gene in a subject.

20. The use according to claim 19, wherein the disease mediated by complement C5 gene is one or more selected from the group consisting of ophthalmic diseases, including dry/wet age-related macular degeneration (AMD), and geographic atrophy (GA); hematologic diseases, including paroxysmal nocturnal hemoglobinuria (PNH), and thrombotic microangiopathies (TMAs); cardiovascular diseases; autoimmune diseases, including rheumatoid arthritis, and lupus erythematosus; renal diseases, including atypical hemolytic uremic syndrome (aHUS), C3 glomerulopathy (C3G), IgA nephropathy and lupus nephritis; neurological diseases, including Alzheimer's disease (AD), and myasthenia gravis (gMG); neoplastic diseases, including complement-associated liver cancer or lung cancer; surgery-related diseases, including hepatic ischemia-reperfusion injury, burn rehabilitation, and post-transplant rejection; and respiratory diseases, including asthma, idiopathic pulmonary fibrosis, and chronic obstructive pulmonary disease (COPD).

21. A pharmaceutical composition according to claims 13 or 18 for use in therapy.