Claims

1. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule in a phosphate buffered saline (PBS),

wherein the PBS is at a concentration of 5 mM,

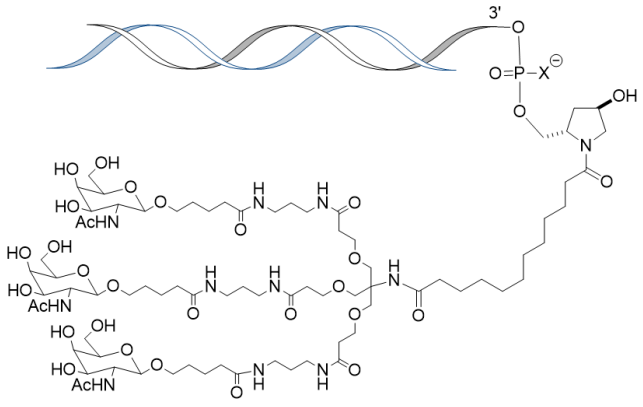
wherein the pH of the pharmaceutical composition is 6.8 to 7.2,

wherein the osmolality of the pharmaceutical composition is 300 mOsm/kg,

wherein the dsRNA molecule has a sense strand and an antisense strand, wherein the nucleotide sequence of the sense strand consists of 5'-GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:13) and the nucleotide sequence of the antisense strand consists of 5'- usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:14),

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

wherein a ligand is conjugated to the 3' end of the sense strand as shown in the following structure:




, wherein the X is O, and wherein the dsRNA molecule is at a free acid form concentration of 100 mg/mL.

2. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule in a phosphate buffered saline (PBS),

wherein the PBS is at a concentration of 5 mM,

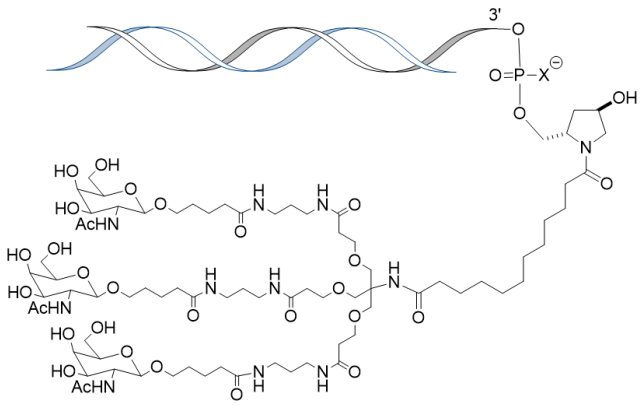
wherein the pH of the pharmaceutical composition is 6.8 to 7.2,

wherein the osmolality of the pharmaceutical composition is 300 mOsm/kg,

wherein the dsRNA molecule has a sense strand and an antisense strand, wherein the nucleotide sequence of the sense strand consists of 5'-GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:13) and the nucleotide sequence of the antisense strand consists of 5'- usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:14),

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

wherein a ligand is conjugated to the 3' end of the sense strand as shown in the following structure:




, wherein the X is O, and wherein the dsRNA molecule is at a salt form concentration of 106 mg/mL.

3. The pharmaceutical composition of claim 2, wherein the salt form is a sodium salt form.

4. The pharmaceutical composition of claim 3, wherein substantially all of the phosphodiester and/or phosphorothioate groups in the molecule comprise a sodium counterion, optionally wherein all of the phosphodiester and/or phosphorothioate groups in the molecule comprise a sodium counterion.

5. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule in a phosphate buffered saline (PBS),

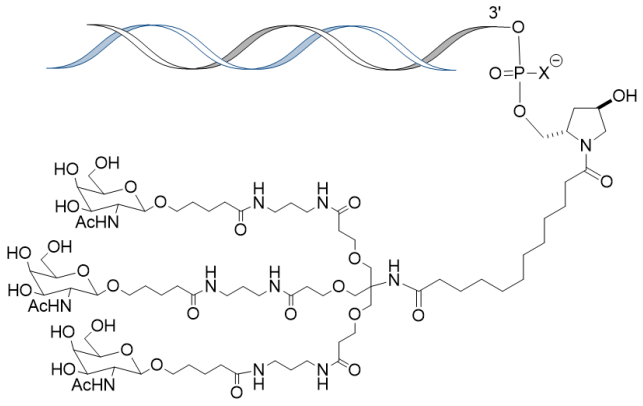
wherein the PBS is at a concentration of 5 mM,

wherein the pH of the pharmaceutical composition is 6.8 to 7.2,

wherein the dsRNA molecule has a sense strand and an antisense strand, wherein the nucleotide sequence of the sense strand consists of 5'-GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:13) and the nucleotide sequence of the antisense strand consists of 5'- usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:14),

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

wherein a ligand is conjugated to the 3' end of the sense strand as shown in the following structure:




, wherein the X is O, and wherein the dsRNA molecule is at a free acid form concentration of 100 mg/mL.

6. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule in a phosphate buffered saline (PBS),

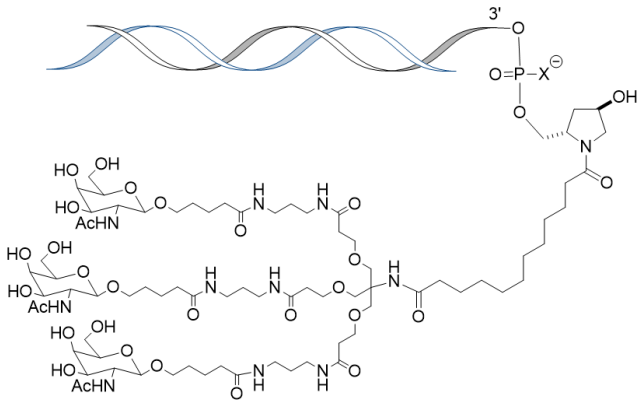
wherein the PBS is at a concentration of 5 mM,

wherein the pH of the pharmaceutical composition is 6.8 to 7.2,

wherein the dsRNA molecule has a sense strand and an antisense strand, wherein the nucleotide sequence of the sense strand consists of 5'-GfsgsUfuAfaCfaCfCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:13) and the nucleotide sequence of the antisense strand consists of 5'- usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:14),

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

wherein a ligand is conjugated to the 3' end of the sense strand as shown in the following structure:




, wherein the X is O, and wherein the dsRNA molecule is at a salt form concentration of 106 mg/mL.

7. The pharmaceutical composition of claim 5 or 6, wherein the osmolality of the composition is

(i) between 50 and 400 mOsm/kg,

(ii) between 100 and 400 mOsm/kg,

(iii) between 240 and 390 mOsm/kg, or

(iv) between 290 and 320 mOsm/kg.

8. The pharmaceutical composition of claim 5 or 6, wherein the osmolality of the pharmaceutical composition is 300 mOsm/kg.

9. The pharmaceutical composition of any one of claims 1-8, wherein the PBS comprises 0.64 mM $NaH_2PO_4$, 4.36 mM $Na_2HPO_4$, and 84 mM NaCl, optionally pH 7.0.

10. The pharmaceutical composition of any one of claims 1-9, wherein the PBS comprises 0.0885 mg/mL monosodium phosphate monohydrate, 1.169 mg/mL disodium phosphate heptahydrate, and 4.909 mg/mL sodium chloride, optionally pH 7.0.

11. The pharmaceutical composition of any one of claims 1-10, wherein the composition consists of the dsRNA molecule in 5 mM PBS.

12. The pharmaceutical composition of any one of claims 1-11, wherein the composition

(i) is stable for up to 36 months when stored at 2°C to 8°C,

(ii) is stable for up to 36 months when stored at 25°C and 60% relative humidity (RH),

(iii) is stable for up to 6 months when stored at 40°C and 75% relative humidity (RH),

(iv) comprises not less than (NLT) 95.0 area % duplex and not more than (NMT) 5 area% single strands as determined by purity non-denaturing IPRP-HPLC,

(v) comprises not less than (NLT) 85.0 area % total single strands as determined by purity denaturing AX-HPLC, or

(vi) comprises not less than (NLT) 80.0 area % total single strands as determined by purity denaturing IPRP-HPLC.

13. The pharmaceutical composition of any one of claims 1-12, wherein the pharmaceutical composition is for inhibiting expression of a SERPINC1 gene.

14. A vial comprising the pharmaceutical composition of any one of claims 1-13, optionally wherein

(i) the vial comprises 0.5 mL to 2.0 ml of the pharmaceutical composition or

(ii) the vial comprises 0.8 ml of the pharmaceutical composition.

15. A syringe comprising the pharmaceutical composition of any one of claims 1-13, optionally wherein

(i) the syringe is a 1 ml syringe,

(ii) the syringe is a 3 ml syringe,

(iii) the syringe comprises a 29 G needle,

(iv) the syring comprises a 30 G needle,

(v) the syringe is a pre-filled syringe, or

(vi) the syringe is a single-use syringe.

16. An injection device comprising the pharmaceutical composition of any one of claims 1-13, optionally wherein the injection device is an automatic injection device.

17. The injection device of claim 16, wherein the injection device is an autoinjector pen.

18. The injection device of claim 16 or 17, wherein the injection device is pre-filled or single-use.