Claims

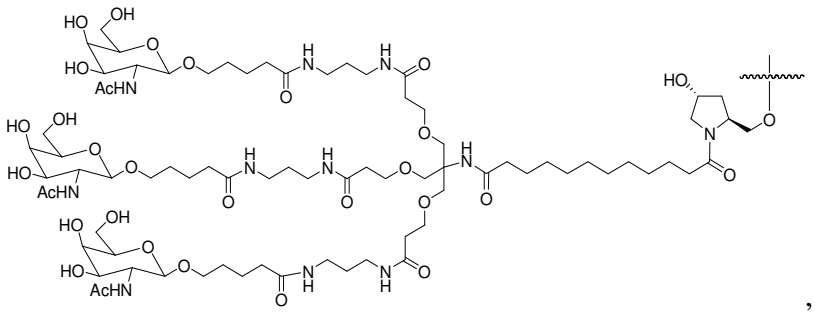
1. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule at a concentration of about 50 mg/mL to about 200 mg/mL and phosphate buffered saline (PBS) at a concentration of about 1 mM to about 10 mM,

wherein the pH and the osmolality of the pharmaceutical composition are suitable for subcutaneous administration to a subject,

wherein the dsRNA molecule comprises a sense strand having the nucleotide sequence 5'- GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:941) and an antisense strand having the nucleotide sequence 5'-usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:960),

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, U, respectively; and s is a phosphorothioate linkage, and

wherein a ligand is conjugated to the 3' end of the sense strand via a linker, and wherein the ligand and the linker comprise the following structure:



, wherein the dsRNA molecule is in a free acid form.

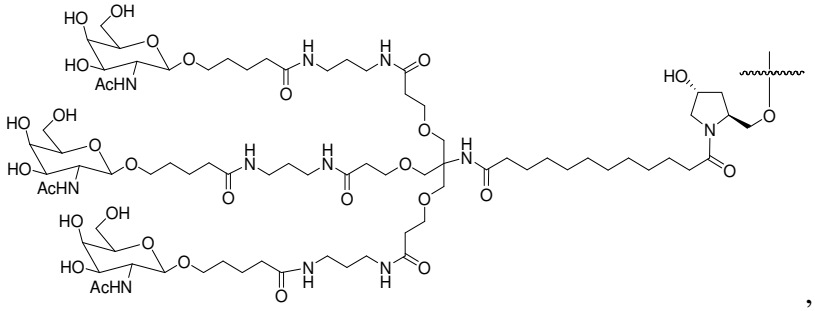
2. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule at a concentration of about 50 mg/mL to about 200 mg/mL and phosphate buffered saline (PBS) at a concentration of about 1 mM to about 10 mM,

wherein the pH and the osmolality of the pharmaceutical composition are suitable for subcutaneous administration to a subject,

wherein the dsRNA molecule comprises a sense strand having the nucleotide sequence 5'- GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (ID NO:941) and an antisense strand having the nucleotide sequence of 5'- usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:960),

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, U, respectively; and s is a phosphorothioate linkage, and

wherein a ligand is conjugated to the 3' end of the sense strand via a linker, and wherein the ligand and the linker comprise the following structure:



, wherein the dsRNA molecule is in a salt form.

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 phosphorothiotate groups in the molecule comprise a sodium counterion, optionally wherein all of the phosphodiester and/or phosphorothiotate groups in the molecule comprise a sodium counterion.

5. The pharmaceutical composition of any one of claims 1-4, wherein the concentration of PBS is

(i) between about 2 mM and about 7 mM,

(ii) between about 3 mM and about 6 mM, or

(iii) about 5 mM.

6. The pharmaceutical composition of any one of claims 1-5, wherein the pH of the composition is

(i) between about 5.0 to about 8.0,

(ii) between about 6.0 to about 8.0,

(iii) between about 6.5 to about 7.5, or

(iv) between about 6.8 to about 7.2.

7. The pharmaceutical composition of any one of claims 1-6, wherein the osmolality of the composition is

(i) between about 50 and about 400 mOsm/kg,

(ii) between about 100 and about 400 mOsm/kg,

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

(iv) between about 290 and about 320 mOsm/kg.

8. The pharmaceutical composition of any one of claims 1-7, wherein the concentration of the dsRNA molecule in the pharmaceutical composition is

(i) between about 50 mg/mL and about 150 mg/mL,

(ii) between about 80 mg/mL and about 110 mg/mL, or

(iii) about 100 mg/mL.

9. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule at a concentration of about 100 mg/mL and phosphate buffered saline (PBS) at a concentration of about 5 mM,

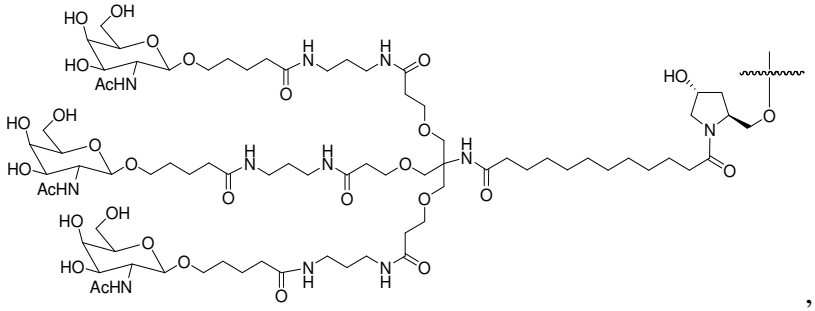
wherein the pH of the pharmaceutical composition is about 6.8 to about 7.2,

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

wherein the dsRNA molecule comprises a sense strand having the nucleotide sequence 5'- GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:941) and an antisense strand having the nucleotide sequence 5'-usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:960),

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, U, respectively; and s is a phosphorothioate linkage, and

wherein a ligand is conjugated to the 3' end of the sense strand via a linker, and wherein the ligand and the linker comprise the following structure:



, wherein the dsRNA molecule is in a free acid form.

10. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule at a concentration of about 106 mg/mL and phosphate buffered saline (PBS) at a concentration of about 5 mM,

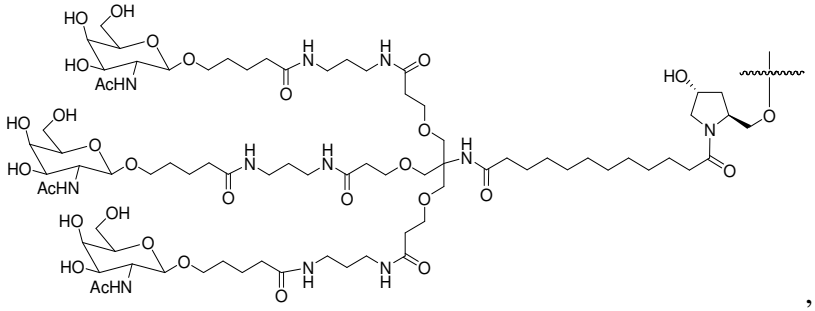
wherein the pH of the pharmaceutical composition is about 6.8 to about 7.2,

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

wherein the dsRNA molecule comprises a sense strand having the nucleotide sequence 5'- GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:941) and an antisense strand having the nucleotide sequence 5'-usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:960),

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, U, respectively; and s is a phosphorothioate linkage, and

wherein a ligand is conjugated to the 3' end of the sense strand via a linker, and wherein the ligand and the linker comprise the following structure:



, wherein the dsRNA molecule is in a salt form.

11. The pharmaceutical composition of claim 10, wherein the salt form is a sodium salt form.

12. The pharmaceutical composition of claim 11, 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.

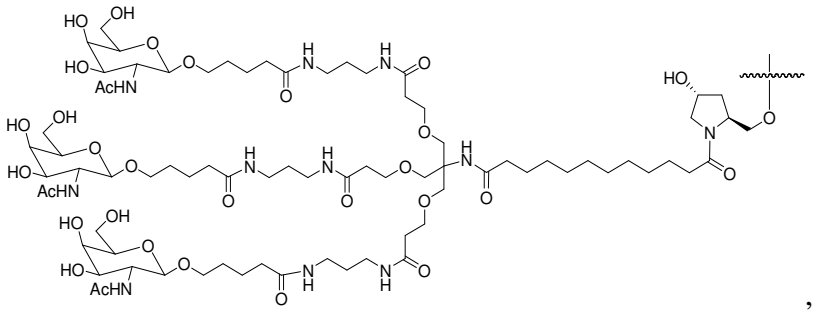
13. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule at a concentration of about 100 mg/mL and phosphate buffered saline (PBS) at a concentration of about 5 mM,

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

wherein the dsRNA molecule comprises a sense strand having the nucleotide sequence 5'- GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:941) and an antisense strand having the nucleotide sequence 5'-usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:960),

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, U, respectively; and s is a phosphorothioate linkage, and

wherein a ligand is conjugated to the 3' end of the sense strand via a linker, and wherein the ligand and the linker comprise the following structure:



, wherein the dsRNA molecule is in a free acid form.

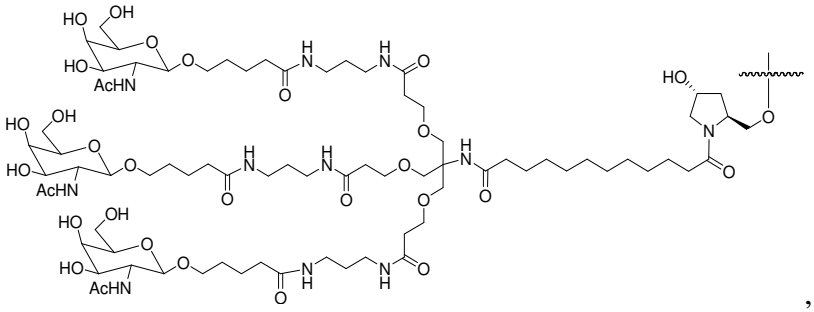
14. A pharmaceutical composition comprising a double-stranded ribonucleic acid (dsRNA) molecule at a concentration of about 106 mg/mL and phosphate buffered saline (PBS) at a concentration of about 5 mM,

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

wherein the dsRNA molecule comprises a sense strand having the nucleotide sequence 5'- GfsgsUfuAfaCfaCfCfAfuUfuAfcUfuCfaAf – 3' (SEQ ID NO:941) and an antisense strand having the nucleotide sequence 5'- usUfsgAfaGfuAfaAfuggUfgUfuAfaCfcsasg – 3' (SEQ ID NO:960),

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, U, respectively; and s is a phosphorothioate linkage, and

wherein a ligand is conjugated to the 3' end of the sense strand via a linker, and wherein the ligand and the linker comprise the following structure:



, wherein the dsRNA molecule is in a salt form.

15. The pharmaceutical composition of any one of claims 1-14, wherein the composition

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

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

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

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

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

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

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

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

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

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

(i) the syringe is a 1 ml syringe,

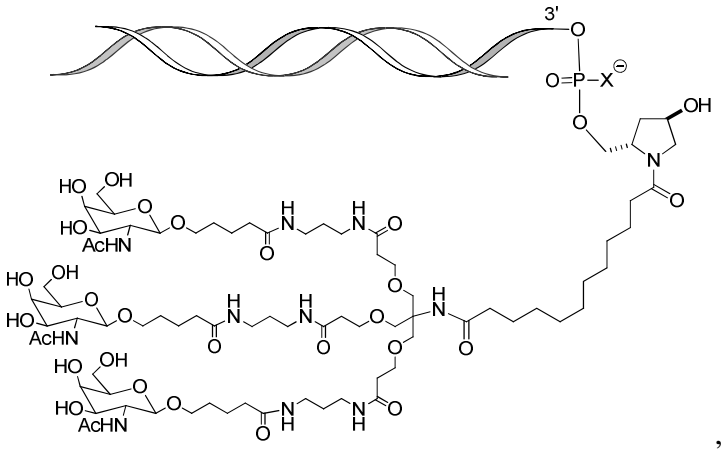
(ii) the syringe is a 3 ml syringe,

(iii) the syringe comprises a 29 G needle,

(iv) the syring comprises a 30 G needle, or

(v) the syringe is a pre-filled syringe.

18. The pharmaceutical composition, vial, or syringe of any one of the preceding claims, wherein the ligand is conjugated to the 3' end of the sense strand via the linker as shown in the following structure:



, wherein the X is O.

19. The pharmaceutical composition, vial, or syringe of any one of claims 1-18, wherein the PBS comprises 0.64 mM NaH_2PO_4, about 4.36 mM Na_2HPO_4, and about 84 mM NaCl, optionally pH 7.0.

20. The pharmaceutical composition, vial, or syringe of any one of claims 1-18, wherein the PBS is obtainable by mixing 0.0885 mg monosodium phosphate monohydrate, 1.169 mg disodium phosphate heptahydrate, and 4.909 mg sodium chloride for every 1 ml of the PBS, optionally pH 7.0.

21. The pharmaceutical composition, vial, or syringe of any one of the preceding claims, wherein the pharmaceutical composition is for inhibiting expression of a *SERPINC1* gene.