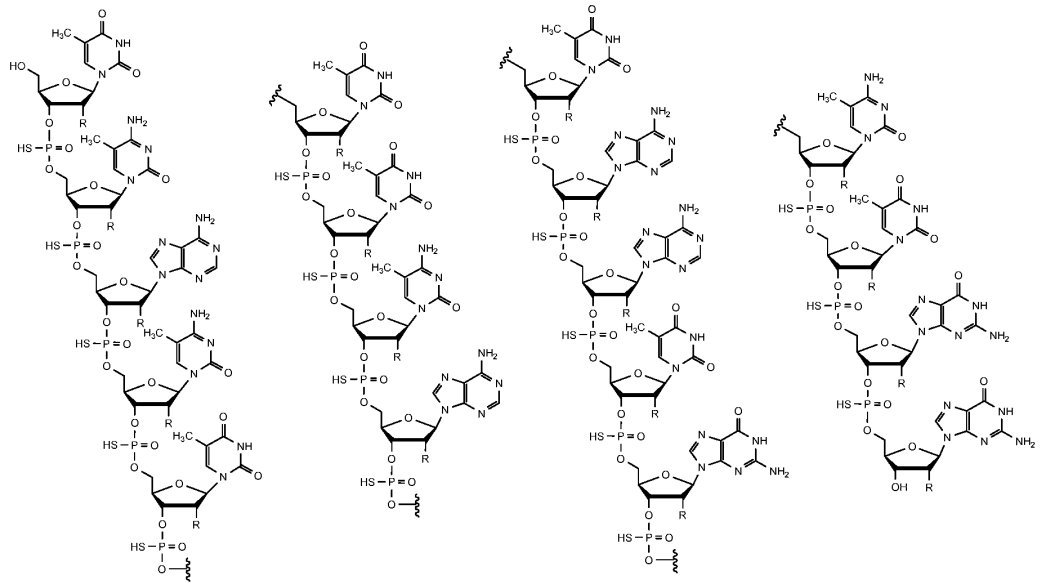
WHAT IS CLAIMED IS:

1. A method for treating spinal muscular atrophy (SMA) in a human subject in need thereof, the method comprising administering to the human subject at least two loading doses of an antisense compound having the following structure:



R = $OCH_2CH_2OCH_3$

or a salt thereof,

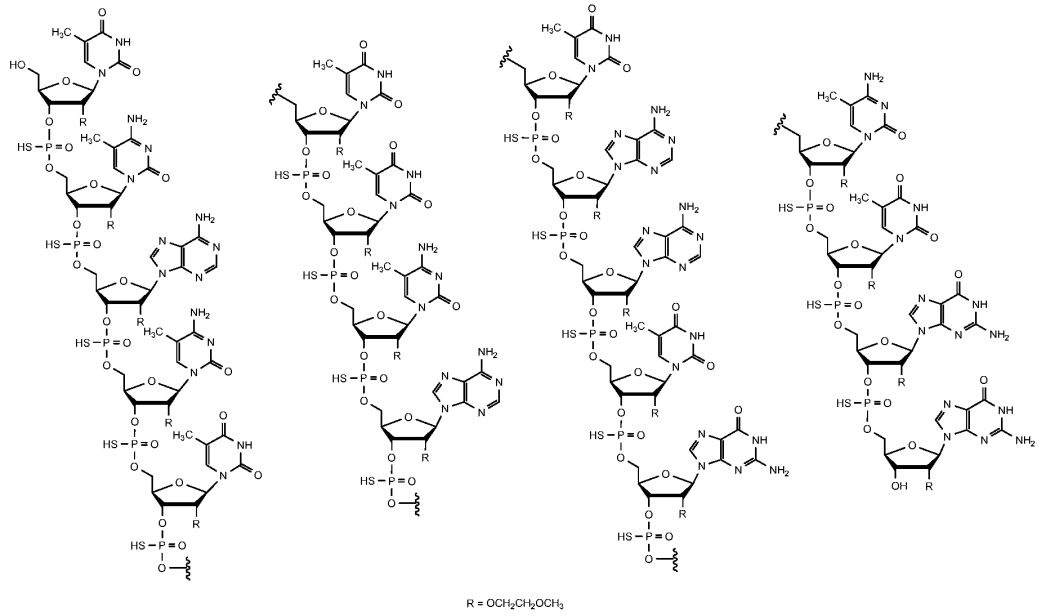
wherein the method comprises administering to the human subject by intrathecal injection:

(i) a first loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound; and

(ii) a second loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 10 to 20 days after administration of the first loading dose.

2. A method for increasing levels of survival motor neuron-2 (SMN2) messenger ribonucleic acid (mRNA) containing exon 7 in a human subject having mutations in chromosome 5q that are associated with SMN protein deficiency, the method comprising administering to the

human subject at least two loading doses of an antisense compound having the following structure:



or a salt thereof,

wherein the method comprises administering to the human subject by intrathecal injection:

(i) a first loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound; and

(ii) a second loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 10 to 20 days after administration of the first loading dose.

3. The method of claim 1 or 2, further comprising administering to the human subject by intrathecal injection at least one maintenance dose, wherein the at least one maintenance dose is equivalent to about 28 mg of the antisense compound.

4. The method of claim 1 or 2, wherein the method further comprises administering to the human subject by intrathecal injection maintenance doses of the antisense compound or the

salt thereof, beginning about 4 months after administration of the second loading dose and continuing once about every 4 months thereafter, wherein each maintenance dose is equivalent to about 28 mg of the antisense compound.

5. The method of claim 4, wherein the second loading dose is administered about 14 days after administration of the first loading dose.

6. The method of claim 1 or 2, wherein the method further comprises administering to the human subject by intrathecal injection:

(iii) a third loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 10 to 20 days after administration of the second loading dose; and

(iv) maintenance doses of the antisense compound or the salt thereof, beginning about 4 months after administration of the third loading dose and continuing once about every 4 months thereafter, wherein each maintenance dose is equivalent to about 28 mg of the antisense compound.

7. The method of claim 6, wherein the second loading dose is administered about 14 days after administration of the first loading dose and the third loading dose is administered about 14 days after administration of the second loading dose.

8. The method of claim 1 or 2, wherein the method further comprises administering to the human subject by intrathecal injection:

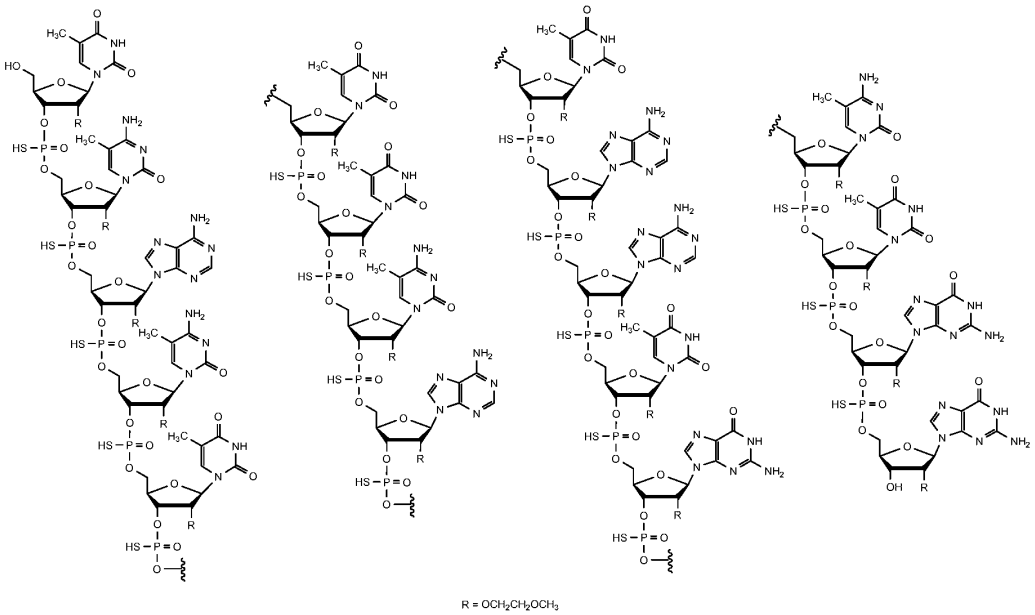
(iii) a third loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 10 to 20 days after administration of the second loading dose;

(iv) a fourth loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 10 to 20 days after administration of the third loading dose; and

(v) maintenance doses of the antisense compound or the salt thereof, beginning about 4 months after administration of the fourth loading dose and continuing once about every 4 months thereafter, wherein each maintenance dose is equivalent to about 28 mg of the antisense compound.

9. The method of claim 8, wherein the second loading dose is administered about 14 days after administration of the first loading dose, the third loading dose is administered about 14 days after administration of the second loading dose, and the fourth loading dose is administered about 14 days after administration of the third loading dose.

10. A method for treating spinal muscular atrophy (SMA) in a human subject in need thereof, the method comprising administering to the human subject an antisense compound having the following structure:



or a salt thereof,

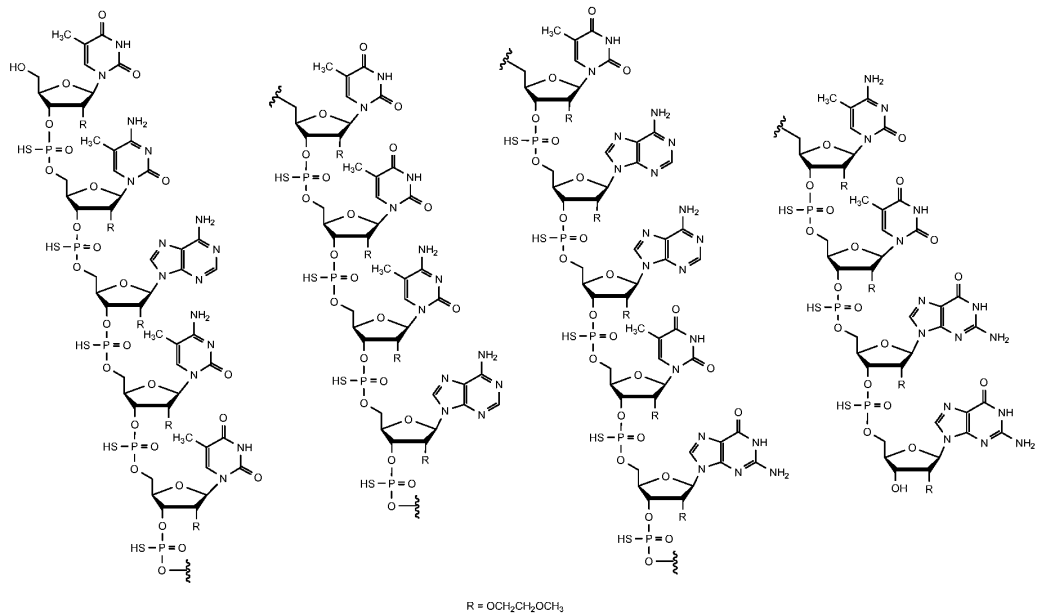
wherein the human subject was previously administered one or more doses of the antisense compound or the salt thereof, wherein the one or more previously administered

doses were equivalent to about 12 mg of the antisense compound, wherein the method comprises administering to the human subject by intrathecal injection:

(i) a loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 4 months after administration of the last previously administered dose equivalent to about 12 mg of the antisense compound; and

(ii) maintenance doses of the antisense compound or the salt thereof, beginning about 4 months after administration of the loading dose and continuing once about every 4 months thereafter, wherein each maintenance dose is equivalent to about 28 mg of the antisense compound.

11. A method for increasing levels of survival motor neuron-2 (SMN2) messenger ribonucleic acid (mRNA) containing exon 7 in a human subject having mutations in chromosome 5q that are associated with SMN protein deficiency, the method comprising administering to the human subject an antisense compound having the following structure:



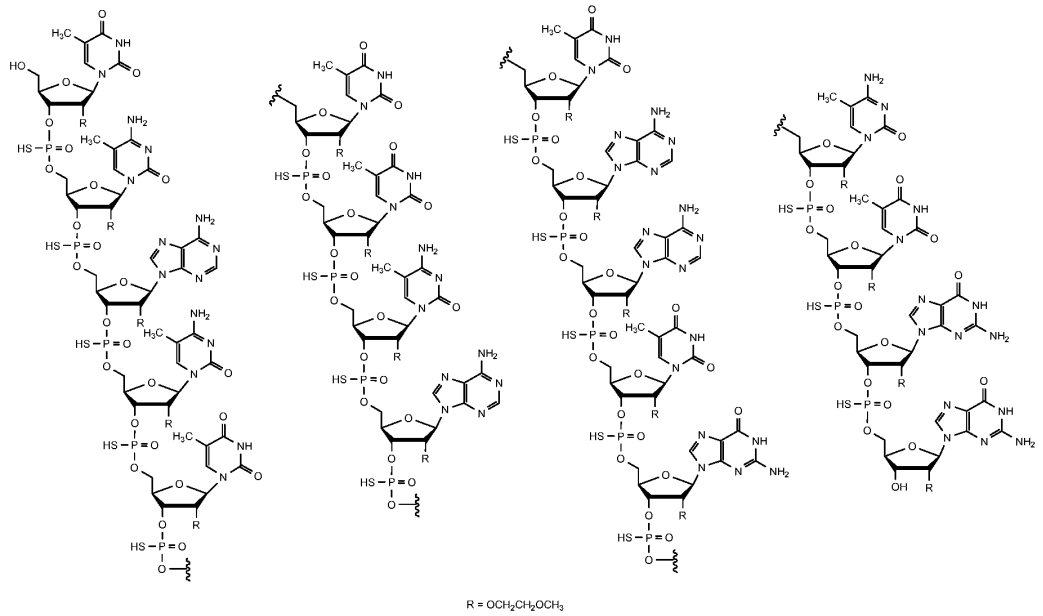
or a salt thereof,

wherein the human subject was previously administered one or more doses of the antisense compound or the salt thereof, wherein the one or more previously administered doses were equivalent to about 12 mg of the antisense compound, wherein the method comprises administering to the human subject by intrathecal injection:

(i) a loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 4 months after administration of the last previously administered dose equivalent to about 12 mg of the antisense compound; and

(ii) maintenance doses of the antisense compound or the salt thereof, beginning about 4 months after administration of the loading dose and continuing once about every 4 months thereafter, wherein each maintenance dose is equivalent to about 28 mg of the antisense compound.

12. A method for treating spinal muscular atrophy (SMA) in a human subject in need thereof, the method comprising administering to the human subject an antisense compound having the following structure:



or a salt thereof,

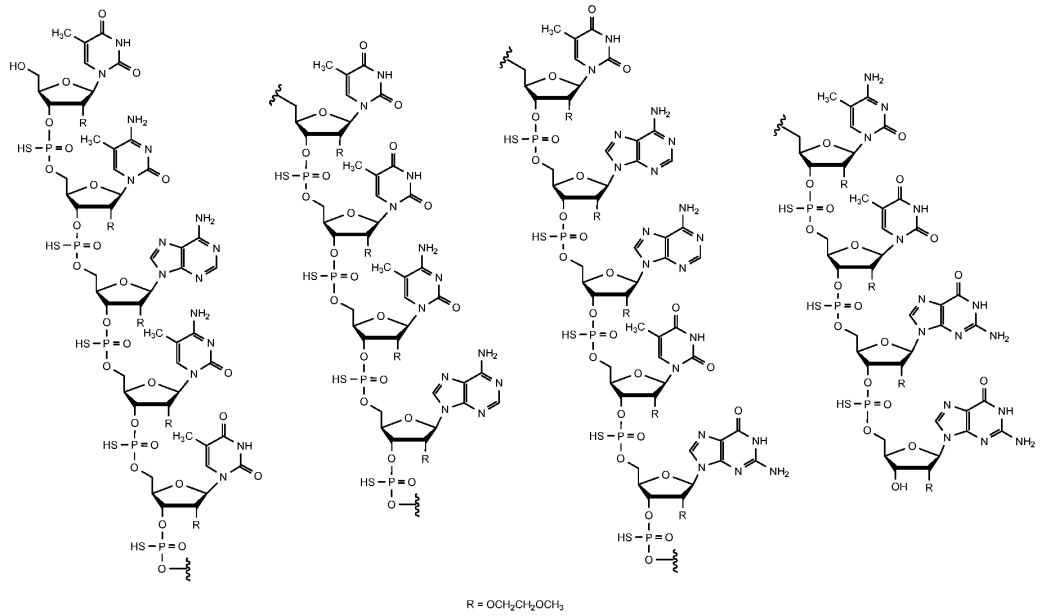
wherein the human subject was previously administered one or more doses of the antisense compound or the salt thereof, wherein the one or more previously administered doses were equivalent to about 12 mg of the antisense compound, wherein the method comprises administering to the human subject by intrathecal injection:

(i) a first loading dose of the antisense compound or the salt thereof that is equivalent to about 28 mg of the antisense compound, administered about 4 months after administration of the last previously administered dose equivalent to about 12 mg of the antisense compound;

(ii) a second loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 4 months after administration of the first loading dose; and

(iii) maintenance doses of the antisense compound or the salt thereof, beginning about 4 months after administration of the second loading dose and continuing once about every 4 months thereafter, wherein each maintenance dose is equivalent to about 28 mg of the antisense compound.

13. A method for increasing levels of survival motor neuron-2 (SMN2) messenger ribonucleic acid (mRNA) containing exon 7 in a human subject having mutations in chromosome 5q that are associated with SMN protein deficiency, the method comprising administering to the human subject an antisense compound having the following structure:



or a salt thereof,

wherein the human subject was previously administered one or more doses of the antisense compound or the salt thereof, wherein the one or more previously administered doses were equivalent to about 12 mg of the antisense compound, wherein the method comprises administering to the human subject by intrathecal injection:

(i) a first loading dose of the antisense compound or the salt thereof that is equivalent to about 28 mg of the antisense compound, administered about 4 months after administration of the last previously administered dose equivalent to about 12 mg of the antisense compound;

(ii) a second loading dose of the antisense compound or the salt thereof that is equivalent to about 50 mg of the antisense compound, administered about 4 months after administration of the first loading dose; and

(iii) maintenance doses of the antisense compound or the salt thereof, beginning about 4 months after administration of the second loading dose and continuing once about every 4 months thereafter, wherein each maintenance dose is equivalent to about 28 mg of the antisense compound.

14. The method of any one of claims 10 to 13, wherein the human subject was previously administered at least five doses of the antisense compound or the salt thereof, wherein each of the at least five previously administered doses was equivalent to about 12 mg of the antisense compound.

15. The method of any one of claims 1 to 14, wherein the human subject has (i) type I SMA; (ii) type II SMA; (iii) type III SMA; or (iv) type IV SMA.

16. The method of any one of claims 1 to 14, wherein the human subject is presymptomatic for SMA.

17. The method of any one of claims 1 to 16, wherein the human subject is administered the antisense compound or the salt thereof using a spinal anesthesia needle.

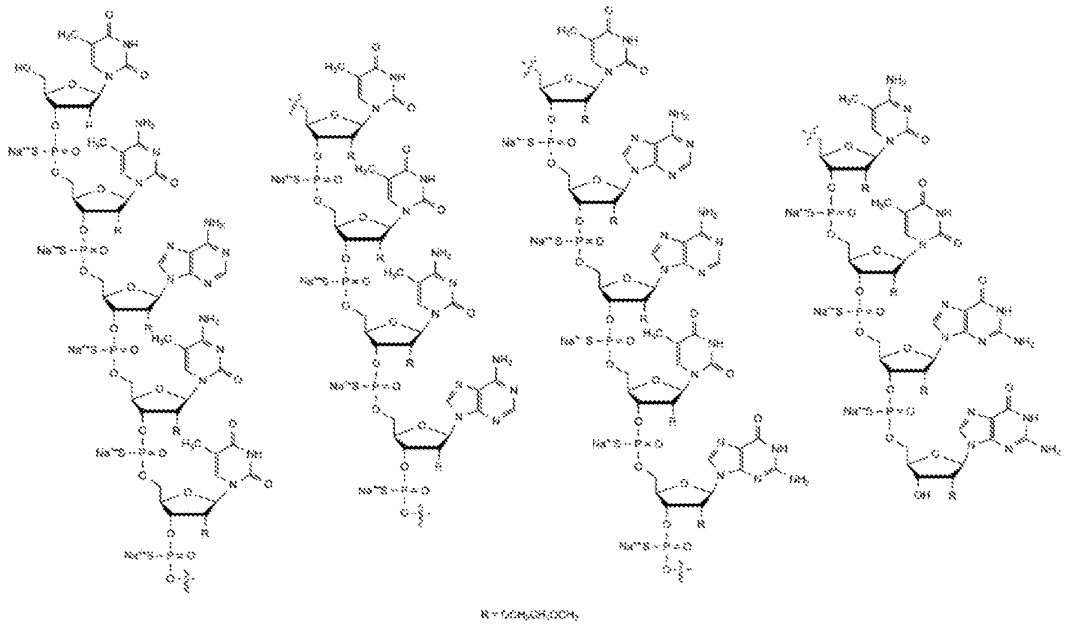
18. The method of any one of claims 1 to 17, wherein the antisense compound or the salt thereof is administered in an injection volume of 5.0 mL

19. The method of claim 18, wherein the antisense compound or the salt thereof is dissolved in phosphate buffered saline (PBS).

20. The method of claim 18, wherein the antisense compound or the salt thereof is dissolved in artificial cerebrospinal fluid (aCSF).

21. The method of any one of claims 1 to 20, wherein the salt of the antisense compound is a sodium salt.

22. The method of any one of claims 1 to 20, wherein the salt of the antisense compound has the following structure:



23. The method of any one of claims 1 to 22, wherein the method comprises detecting a neurofilament level in the human subject before and/or after initiation of treatment.

24. The method of claim 23, comprising:

measuring a first neurofilament level in a first biological sample obtained from the human subject before initiation of treatment;

administering the antisense compound or salt thereof to the human subject according to any one of the preceding claims; and

measuring at least one subsequent neurofilament level in a second biological sample obtained from the human subject after administering all loading doses and at least one maintenance dose of the antisense compound or salt thereof.

25. The method of claim 23, comprising:

measuring a first neurofilament level in a first biological sample obtained from the human subject before initiation of treatment;

administering a first loading dose of the antisense compound or salt thereof to the human subject according to any one of the preceding claims; and

measuring at least one subsequent neurofilament level in a biological sample obtained from the human subject after administering said first loading dose of the antisense compound or salt thereof.

26. The method of claim 23, comprising:

measuring a first neurofilament level in a first biological sample obtained from the human subject before initiation of treatment;

administering a first loading dose and a second loading dose of the antisense compound or salt thereof to the human subject according to any one of the preceding claims; and

measuring at least one subsequent neurofilament level in a biological sample obtained from the human subject after administering said first loading dose and said second loading dose of the antisense compound or salt thereof.

27. The method of any one of claims 24-26, wherein the subsequent neurofilament level is reduced by at least 50% compared to the first neurofilament level.

28. The method of any one of claims 25-26, wherein the subsequent neurofilament level is equal to or higher than the first neurofilament level and the method further comprises administering further doses of the antisense compound or salt thereof to the human subject.

29. The method of any one of claims 23 to 28, wherein the neurofilament is a neurofilament heavy chain (NF-H), medium/intermediate chain (NF-M), or light chain (NF-L).

30. The method of claims 23 to 29, wherein the first and second biological samples are blood, serum, plasma, or cerebrospinal fluid.