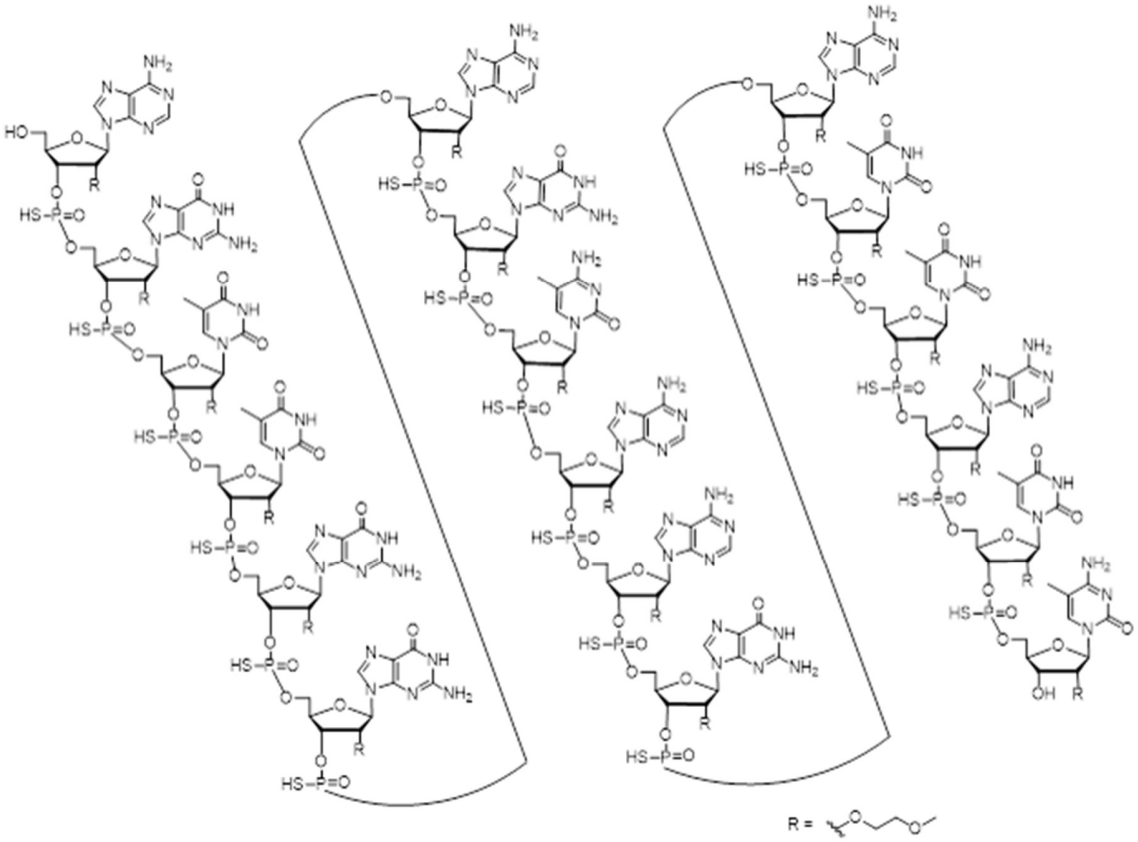
## CLAIMS

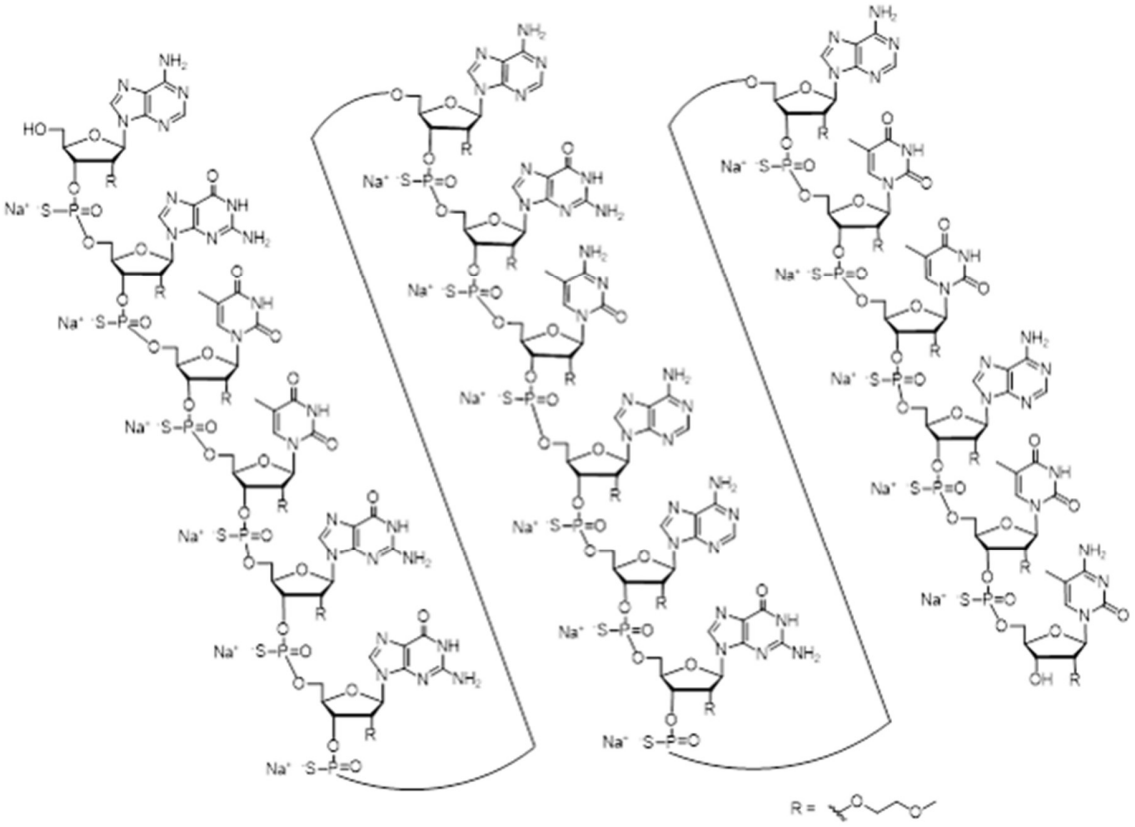
WHAT IS CLAIMED IS:

1. A compound according to the following chemical structure:



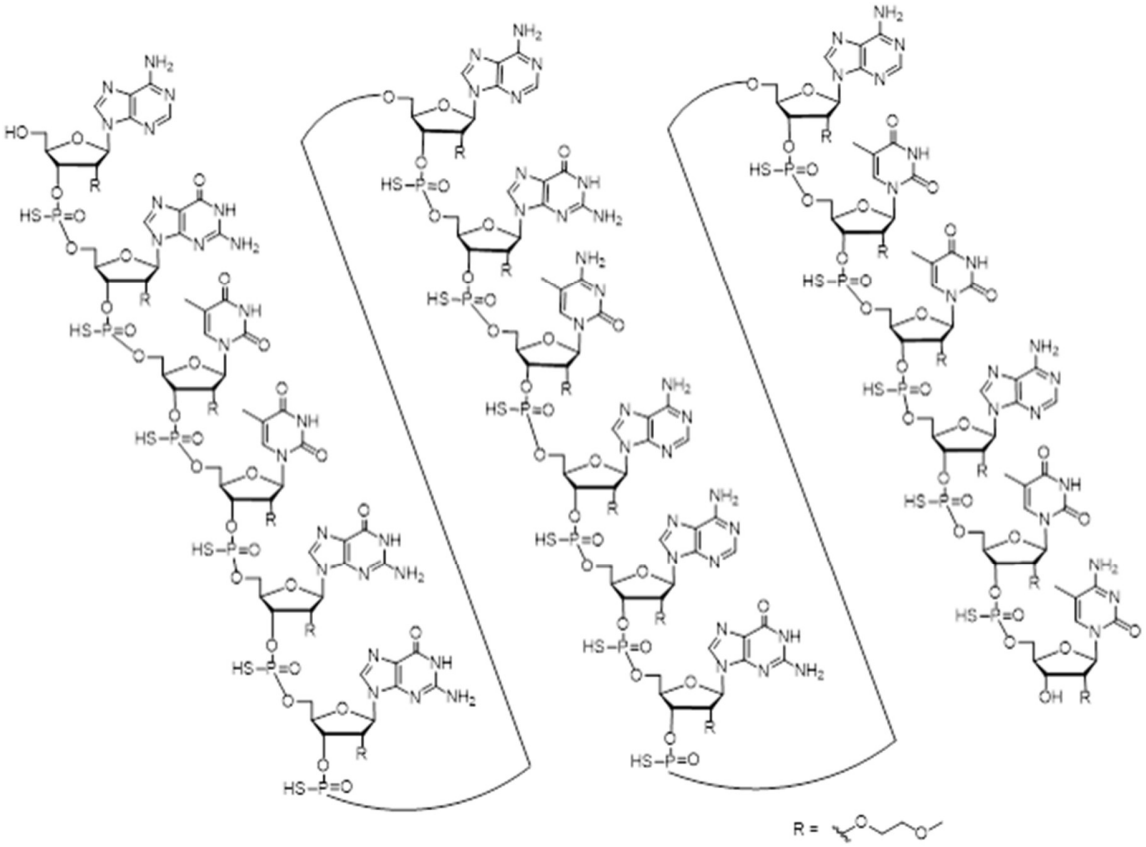
(I), or a salt thereof.

2. The compound of claim 1, wherein the compound has the following chemical structure:



(II).

3. Use of a pharmaceutical composition in the manufacture of a medicament for treating or reducing the likelihood of developing a disease or condition characterized by a reduced expression or function of $Na_V1.1$ protein in a human subject in need thereof, wherein the pharmaceutical composition is to be administered to the human subject, wherein the pharmaceutical composition comprises a compound according to the following chemical structure:



(I), or a salt thereof.

4. The use according to claim 3, wherein the pharmaceutical composition comprises the compound at a first dose of from about 0.5 milligrams to about 500 milligrams.

5. The use according to claim 3, wherein the human subject is at most 18 years old at first dose.

6. The use according to any one of claims 3-5, wherein a pharmaceutical composition comprising the compound at a first dose of about 0.1, 0.5, 1, 2.5, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 22.5, 25, 27.5, 30, 32.5, 35, 37.5, 40, 42.5, 45, 47.5, 50, 52.5, 55, 57.5, 60, 62.5, 65, 67.5, 70, 72.5, 75, 77.5, 80, 82.5, 85, 87.5, 90, 92.5, 95, 97.5, 100, 102.5, 105, 107.5, 110, 112.5, 115, 117.5, 120, 122.5, 125, 127.5, 130, 132.5, 135, 137.5, 140, 142.5, 145, 147.5, 150, 152.5, 155, 157.5, 160, 162.5, 165, 167.5, 170, 172.5, 175, 177.5, 180, 182.5, 185, 187.5, 190, 192.5, 195, 197.5, 200, 202.5, 205, 207.5, 210, 212.5, 215, 217.5, 220, 222.5, 225, 227.5, 230, 232.5, 235, 237.5, 240, 242.5, 245, 247.5, or 250 mg is to be administered to the human subject.

7. The use according to any one of claims 3-6, wherein the disease or condition is Dravet Syndrome.

8. The use according to any one of claims 3-7, wherein the subject is characterized by having:
   (i) seizure onset prior to 12 months of age with recurrent focal motor or hemiconvulsive or generalized tonic-clonic seizures, which are often prolonged and triggered by hyperthermia;
   (ii) no past history of causal magnetic resonance imaging lesion;
   (iii) no other known etiology of any diseases or conditions except Dravet Syndrome;
   (iv) normal development at seizure onset;
   (v) a pathogenic variant, or variant of uncertain significance in an SCN1A gene;
   (vi) at least 2 prior treatments for epilepsy that either had lack of adequate seizure control;
   (vii) 4 or more convulsive seizures during the 28 days prior to administration, wherein the convulsive seizures is any one selected from Hemiclonic, Focal With Motor Signs, Focal To Bilateral Tonic Clonic Convulsion, Generalized Tonic Clonic Convulsion, Tonic, Tonic or Atonic (Drop Attacks), and Clonic;
   (viii) a current intervention for epilepsy or medication with at least one antiepileptic drug at a dose which has been stable for at least 4 weeks, wherein the interventions for epilepsy is a ketogenic diet, a vagal nerve stimulator, or a cannabinoid or marijuana-derived product; or
   (ix) any combination of (i) – (viii).

9. The use according to any one of claims 3-8, wherein the subject is additionally characterized by not having one or more of the following:
   (a) one of the following mutations in the SCN1A gene: Thr226Met, Leu263Val, Val422Leu, Thr1174Ser, Trp1204Arg, Pro1345Ser, Gln1489Lys, Phe1499Leu, Arg1575Cys, Val1611Phe, Leu1624Pro, Arg1648Cys, Leu1649Gln, Leu1670Trp, Gly1674Arg, and Asp1866Tyr;
   (b) a known pathogenic mutation in another gene that causes epilepsy, wherein the pathogenic mutation is homozygous in cases of known recessive disease;
   (c) currently treated with a sodium channel blocker as maintenance treatment and an anticoagulant, wherein the sodium channel blocker is phenytoin, carbamazepine, oxcarbazepine, lamotrigine, lacosamide, or rufinamide, and wherein the anticoagulant is not an aspirin;
   (d) clinically, significantly unstable medical conditions other than epilepsy;
   (e) clinically, relevant symptoms or a clinically significant illness in the 4 weeks prior to administration, other than epilepsy;
   (f) a history of brain or spinal cord disease other than epilepsy, Dravet Syndrome or a history of bacterial meningitis or brain malformation;
   (g) a spinal deformity or other condition that alters the free flow of cerebrospinal fluid (CSF) or having an implanted CSF drainage shunt;

(h) clinically significant abnormal laboratory values prior to administration;

(i) aspartate aminotransferase or alanine aminotransferase >2.5-fold upper limit of normal, serum creatinine greater than an upper limit of normal or platelet count less than a lower limit of normal;

(j) clinically relevant abnormalities in the 12-lead electrocardiogram (ECG) measured at prior to administration;

(k) a psychiatric or behavioral disorder;

(l) currently or in the past 4 weeks, medication of an anticoagulant, wherein the anticoagulant is not aspirin; or

(m) any combination of (a) – (l).

10. The use according to any one of claims 3-9, wherein:

(i) the human subject is from 1 to 18, from 2 to 18, from 3 to 18, from 4 to 18, from 5 to 18, from 6 to 18, from 7 to 18, from 8 to 18, from 9 to 18, from 10 to 18, from 11 to 18, from 12 to 18, from 13 to 18, from 14 to 18, from 15 to 18, from 16 to 18, or from 17 to 18 years old;

(ii) the human subject is a human from 1 to 17, from 1 to 16, from 1 to 15, from 1 to 14, from 1 to 13, from 1 to 12, from 1 to 11, from 1 to 10, from 1 to 9, from 1 to 8, from 1 to 7, from 1 to 6, from 1 to 5, from 1 to 4, from 1 to 3, or from 1 to 2 years old; or

(iii) the human subject is less than a year old or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18 years old.

11. The use according to any one of claims 3-10, wherein the pharmaceutical composition is to be administered into:

(i) the intrathecal space of the human subject;

(ii) the cerebrospinal fluid of the human subject;

(iii) the brain of the human subject; and/or

(iv) the cerebrospinal fluid in the brain of the subject.

12. The use according to any one of claims 3-11, wherein the pharmaceutical composition is to be administered:

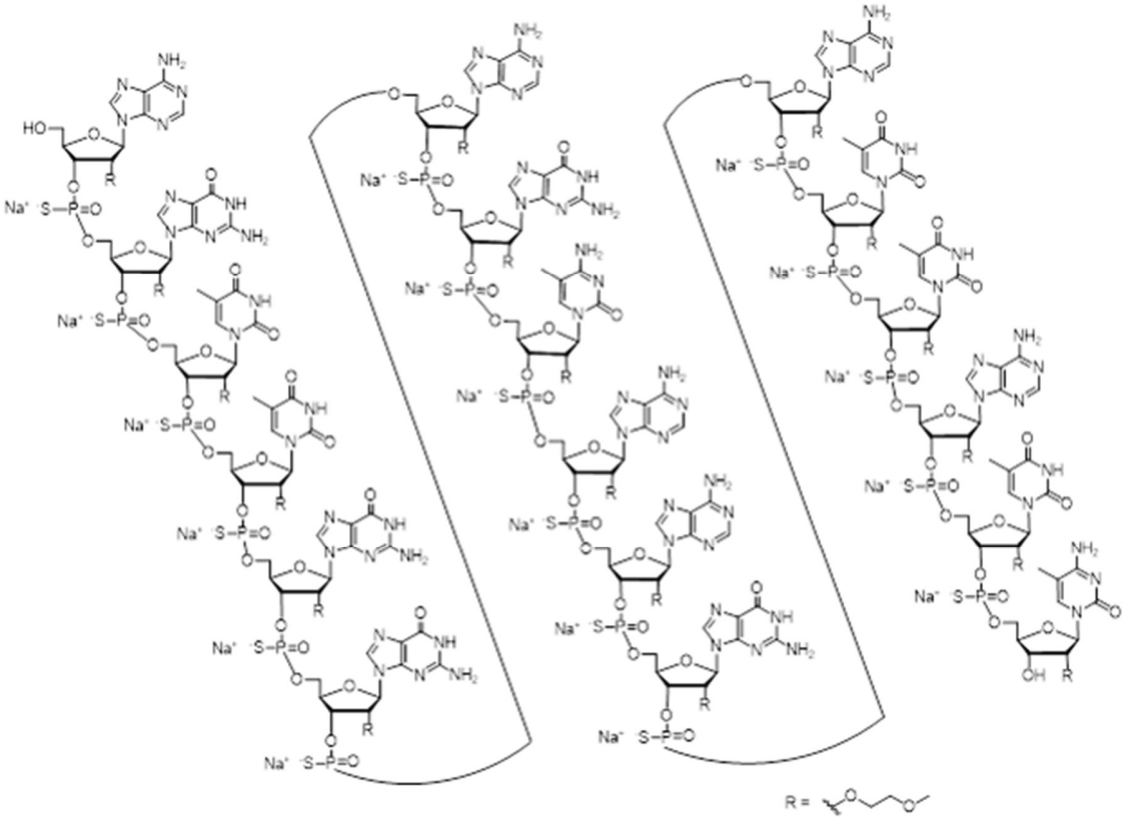
(i) as a bolus injection;

(ii) with a delivery pump;

(iii) by intracerebroventricular injection; and/or

(iv) by intrathecal injection.

13. The use according to any one of claims 3-12, wherein the compound has the following structure:



(II).

14. The use according to any one of claims 3-13, wherein a pharmaceutical composition comprising the compound at subsequent doses of from about 0.5 milligrams to about 500 milligrams is to be further administered to the human subject.

15. The use according to claim 14, wherein the subsequent dose is 0.1, 0.5, 1, 2.5, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 22.5, 25, 27.5, 30, 32.5, 35, 37.5, 40, 42.5, 45, 47.5, 50, 52.5, 55, 57.5, 60, 62.5, 65, 67.5, 70, 72.5, 75, 77.5, 80, 82.5, 85, 87.5, 90, 92.5, 95, 97.5, 100, 102.5, 105, 107.5, 110, 112.5, 115, 117.5, 120, 122.5, 125, 127.5, 130, 132.5, 135, 137.5, 140, 142.5, 145, 147.5,

150, 152.5, 155, 157.5, 160, 162.5, 165, 167.5, 170, 172.5, 175, 177.5, 180, 182.5, 185, 187.5, 190, 192.5, 195, 197.5, 200, 202.5, 205, 207.5, 210, 212.5, 215, 217.5, 220, 222.5, 225, 227.5, 230, 232.5, 235, 237.5, 240, 242.5, 245, 247.5, or 250 mg.

16. The use according to claim 14 or 15, wherein:

(i) the subsequent dose is lower than the previous dose following an indication that administration of the previous dose is not tolerated;

(ii) the subsequent dose is the same as the previous dose following an indication that administration of the previous dose is tolerated;

(iii) the subsequent dose is higher than the previous dose following an indication that administration of the previous dose is tolerated;

(iv) the subsequent dose is the same as the previous dose following an indication that administration of the previous dose is effective;

(v) the subsequent dose is lower than the previous dose following an indication that administration of the previous dose is effective;

(vi) the subsequent dose is higher than the previous dose following an indication that administration of the previous dose is not effective;

(vii) the subsequent doses are to be administered at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 months after administration of the previous dose;

(viii) dose frequency is maintained or reduced following an indication that the previous dose is effective; and/or

(ix) dose frequency is increased following an indication that the previous dose is not effective.

17. The use according to any one of claims 3-16, wherein the pharmaceutical composition comprises a pharmaceutically acceptable excipient, carrier or diluent.

18. The use according to any one of claims 3-17, wherein the pharmaceutical composition is a liquid composition.

19. The use according to claim 18, wherein the pharmaceutical composition comprises the compound in a volume of 5 mL or more, 10 mL or more, 15 mL or more, or 20 mL or more.

20. The use according to any one of claims 3-19, wherein the pharmaceutical composition comprises from 0.1 mL to 50 mL of a diluent, wherein the compound is solubilized or diluted in the diluent.

21. The use according to claim 20, wherein the pharmaceutical composition comprises:

    (i) about 0.1, 0.5, 1, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45 or 50 mL of the diluent;

    (ii) 1 mL to 20 mL of the diluent, 2 mL to 10 mL of the diluent or 1 mL to 5 mL of the diluent;

    (iii) at least 5, 6, 7, 8, 9, or 10 mL of the diluent; and/or

    (iv) a cerebral spinal fluid (CSF) sample from the subject or an artificial cerebral spinal fluid (aCSF) solution.

22. The use according to any one of claims 3-21, wherein:

    (i) a cerebral spinal fluid sample is to be first obtained from the subject;

    (ii) the compound in a CSF sample from the subject is to be solubilized or diluted;

    (iii) the pharmaceutical composition is to be administered as a bolus injection;

    (iv) the pharmaceutical composition is to be administered as a bolus injection over 1 to 60 minutes, 1 to 50 minutes, 1 to 40 minutes, 1 to 30 minutes, 1 to 20 minutes, 1 to 10 minutes, 1 to 5 minutes, or 1 to 3 minutes; and/or

    (v) the pharmaceutical composition is to be administered as a bolus injection using a spinal anesthesia needle.

23. The use according to any one of claims 3-22, wherein:

    (i) the compound is solubilized or diluted in an artificial cerebral spinal fluid (aCSF) solution;

(ii) the solution comprises a cerebral spinal fluid (CSF) sample from the subject;

(iii) the compound is solubilized or diluted in an isotonic solution;

(iv) the compound is solubilized or diluted in a phosphate-buffered solution with at least pH 5.8;

(v) the compound is solubilized or diluted in a phosphate-buffered (pH 6.6 – 7.6) solution;

(vi) the compound is solubilized or diluted in a buffer comprising 25-250 mM NaCl;

(vii) the compound is solubilized or diluted in a buffer comprising 0.1-20 mM KCl;

(viii) the compound is solubilized or diluted in a buffer comprising 0.1-50 mM $Na_2HPO_4$;

(ix) the compound is solubilized or diluted in a buffer comprising 0.1-50 mM $NaH_2PO_4$;

(x) the compound is solubilized or diluted in a buffer comprising 0.1-50 mM $CaCl_2$;

(xi) the compound is solubilized or diluted in a buffer comprising 0.1-50 mM $MgCl_2$;

(xii) the compound is solubilized or diluted in a buffer comprising 25-250 mM NaCl, 0.1-20 mM KCl, 0.1-50 mM $Na_2HPO_4$, 0.1-50 mM $NaH_2PO_4$, 0.1-50 mM $CaCl_2$, and 0.1-50 mM $MgCl_2$; and/or

(xiii) the compound is solubilized or diluted in a buffer comprising 150 mM NaCl, 3.0 mM KCl, 0.7 mM $Na_2HPO_4$, 0.3 mM $NaH_2PO_4$, 0.79 mM $MgCl_2$, and 1.4 mM $CaCl_2$.

24. The use according to any one of claims 3-23, wherein:

(i) the compound is solubilized or diluted in a buffer further comprising carbohydrates;

(ii) the compound is solubilized or diluted in a buffer further comprising 1-100 mM D-glucose;

(iii) the compound is solubilized or diluted in a buffer further comprising 1-100 mM $NaHCO_3$, 1-100 mM $KHCO_3$, or a combination thereof;

(iv) the compound is solubilized or diluted in a buffer further comprising an antioxidant, optionally wherein the antioxidant is t-butylhydroxyquinoline (TBHQ), buylated

hydroxytolune (BHT), butylated hydroxyanisole (BHA), vitamin E, or any combination thereof; and/or

(v) the pharmaceutical formulation does not comprise a preservative.

25. The use according to any one of claims 3-24, wherein the compound is present in the pharmaceutical composition at a concentration of:

(i) from 0.1 mg/mL to 250 mg/mL;

(ii) about 0.1 mg/mL, 0.5 mg/mL, 1 mg/mL, 2 mg/mL, 2.5 mg/mL, 3 mg/mL, 4 mg/mL, 5 mg/mL, 6 mg/mL, 7 mg/mL, 8 mg/mL, 9 mg/mL, 10 mg/mL, 11 mg/mL, 12 mg/mL, 13 mg/mL, 14 mg/mL, 15 mg/mL, 16 mg/mL, 17 mg/mL, 18 mg/mL, 19 mg/mL, or 20 mg/mL;

(iii) about 22.5 mg/mL, 25 mg/mL, 27.5 mg/mL, 30 mg/mL, 32.5 mg/mL, 35 mg/mL, 37.5 mg/mL, 40 mg/mL, 42.5 mg/mL, 45 mg/mL, 47.5 mg/mL, 50 mg/mL, 52.5 mg/mL, 55 mg/mL, 57.5 mg/mL, 60 mg/mL, 62.5 mg/mL, 65 mg/mL, 67.5 mg/mL, 70 mg/mL, 72.5 mg/mL, 75 mg/mL, 77.5 mg/mL, 80 mg/mL, 82.5 mg/mL, 85 mg/mL, 87.5 mg/mL, 90 mg/mL, 92.5 mg/mL, 95 mg/mL, 97.5 mg/mL, 100 mg/mL, 102.5 mg/mL, 105 mg/mL, 107.5 mg/mL, 110 mg/mL, 112.5 mg/mL, 115 mg/mL, 117.5 mg/mL, 120 mg/mL, 122.5 mg/mL, 125 mg/mL, 127.5 mg/mL, 130 mg/mL, 132.5 mg/mL, 135 mg/mL, 137.5 mg/mL, 140 mg/mL, 142.5 mg/mL, 145 mg/mL, 147.5 mg/mL, 150 mg/mL, 152.5 mg/mL, 155 mg/mL, 157.5 mg/mL, 160 mg/mL, 162.5 mg/mL, 165 mg/mL, 167.5 mg/mL, 170 mg/mL, 172.5 mg/mL, 175 mg/mL, 177.5 mg/mL, 180 mg/mL, 182.5 mg/mL, 185 mg/mL, 187.5 mg/mL, 190 mg/mL, 192.5 mg/mL, 195 mg/mL, 197.5 mg/mL, 200 mg/mL, 202.5 mg/mL, 205 mg/mL, 207.5 mg/mL, 210 mg/mL, 212.5 mg/mL, 215 mg/mL, 217.5 mg/mL, 220 mg/mL, 222.5 mg/mL, 225 mg/mL, 227.5 mg/mL, 230 mg/mL, 232.5 mg/mL, 235 mg/mL, 237.5 mg/mL, 240 mg/mL, 242.5 mg/mL, 245 mg/mL, 247.5 mg/mL, or 250 mg/mL; or

(iv) 11 mg/mL, 22 mg/mL, 33 mg/mL, 44 mg/mL, 55 mg/mL, 66 mg/mL, 77 mg/mL, 88 mg/mL, 99 mg/mL, or 100 mg/mL.

26. The use according to any one of claims 3-24, wherein the reduced expression or function of $Na_V1.1$ protein is associated with an altered splicing of a non-sense mediated RNA decay-inducing exon from a pre-mRNA that contains the NMD exon and encodes $Na_V1.1$ protein.

27. The use according to any one of claims 3-25, wherein the compound:

(i) promotes exclusion of the NMD exon from the pre-mRNA that contains the NMD exon and that encodes the Nav1.1 protein;

(ii) binds to a targeted portion of a pre-mRNA that contains the NMD exon and that encodes the Nav1.1 protein;

(iii) increases a level of processed mRNA encoding the $Na_V1.1$ protein when the ASO is introduced into the cell; and/or

(iv) increases a level of the $Na_V1.1$ protein when the compound is introduced into the cell.

28. The use according to claim 27, wherein the targeted portion:

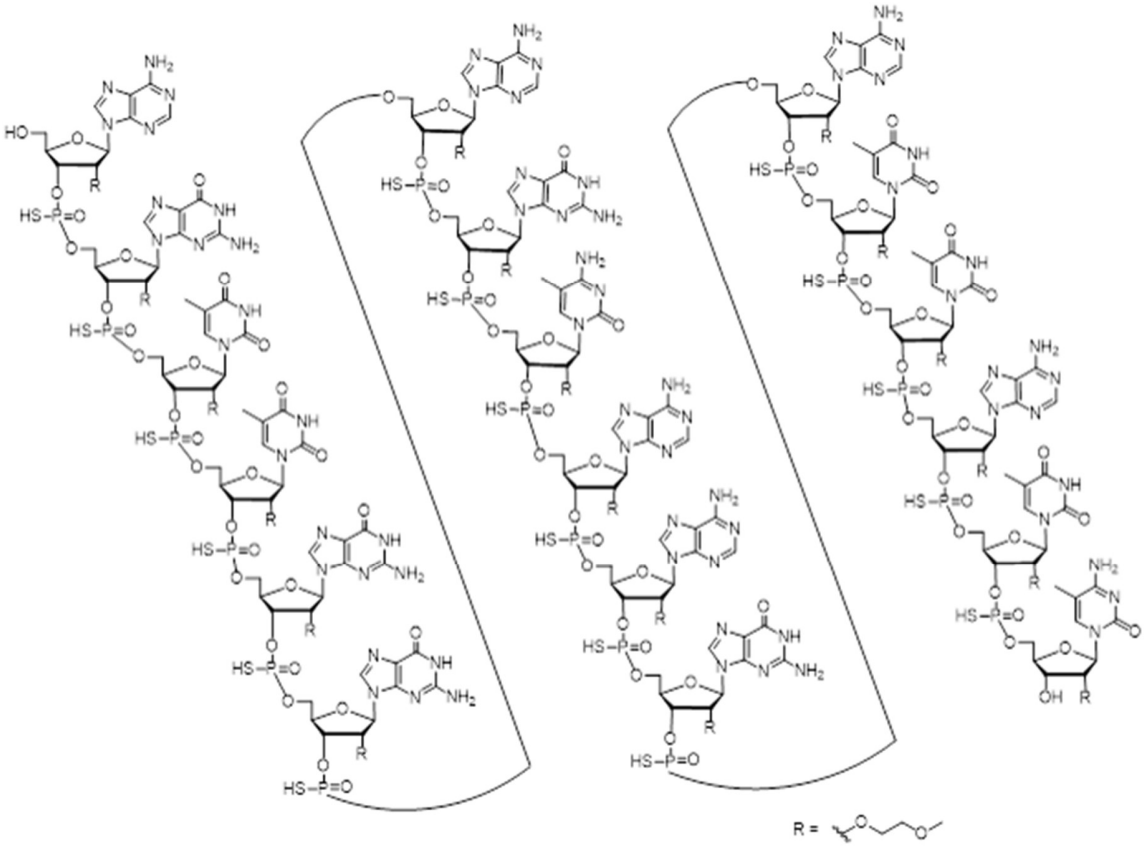
(i) is within an intron sequence flanking the NMD exon;

(ii) comprises at least one nucleotide of the NMD exon; and/or

(iii) is within the NMD exon.

29. The use according to any one of claims 3-28, wherein the disease or condition is treated.

30. A pharmaceutical composition comprising a compound according to the following chemical structure:



(I), or a salt thereof for use in therapy.