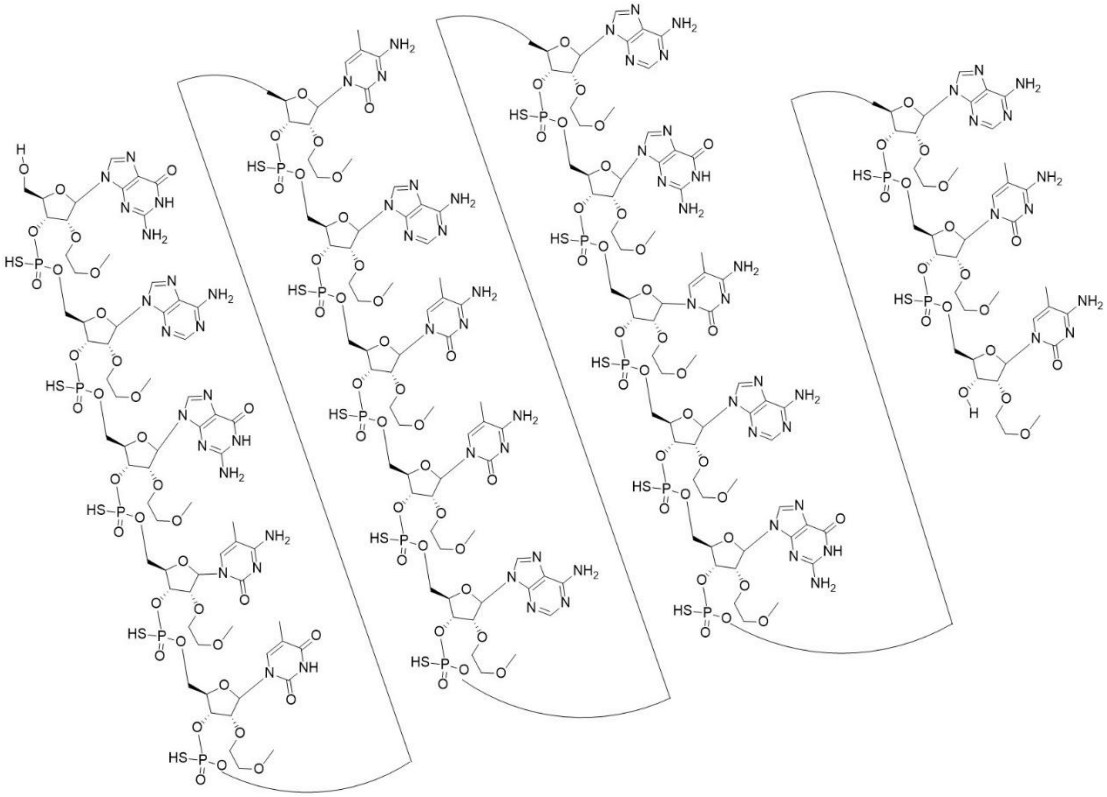
CLAIMS

What is claimed is:

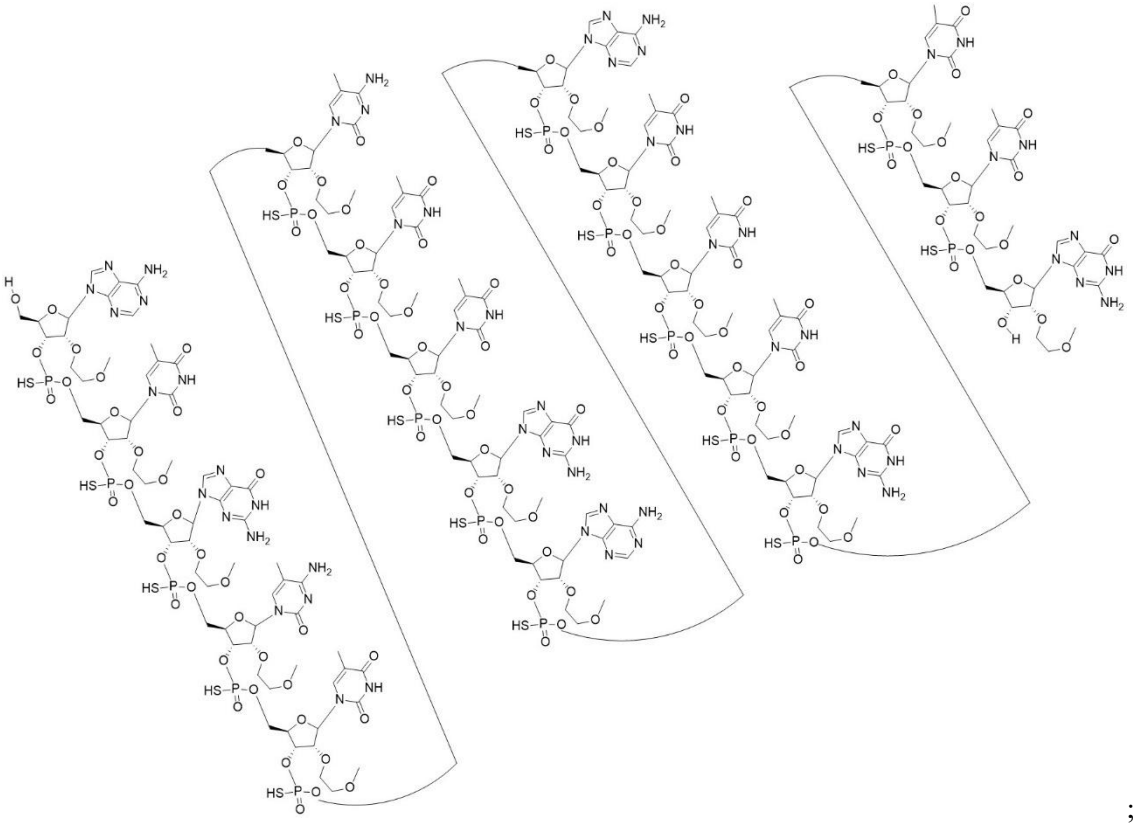
1. An antisense oligomer that is a compound according to any one of the following chemical structures (SEQ ID NOs: 313-317, respectively, in order of appearance):



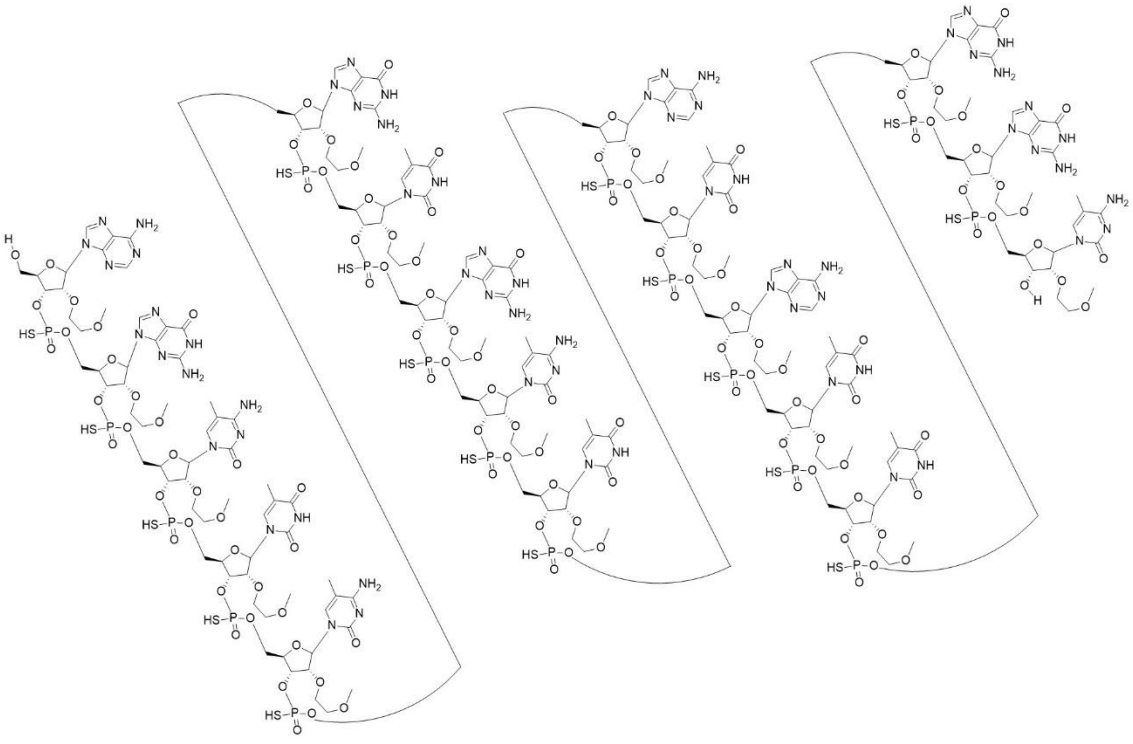
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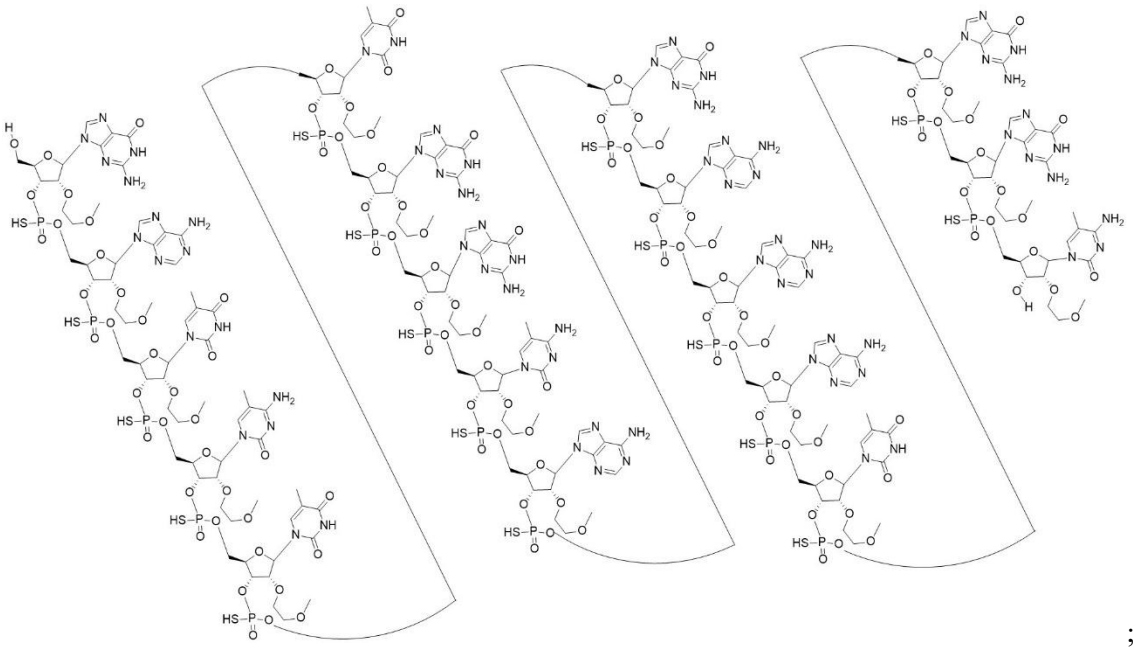
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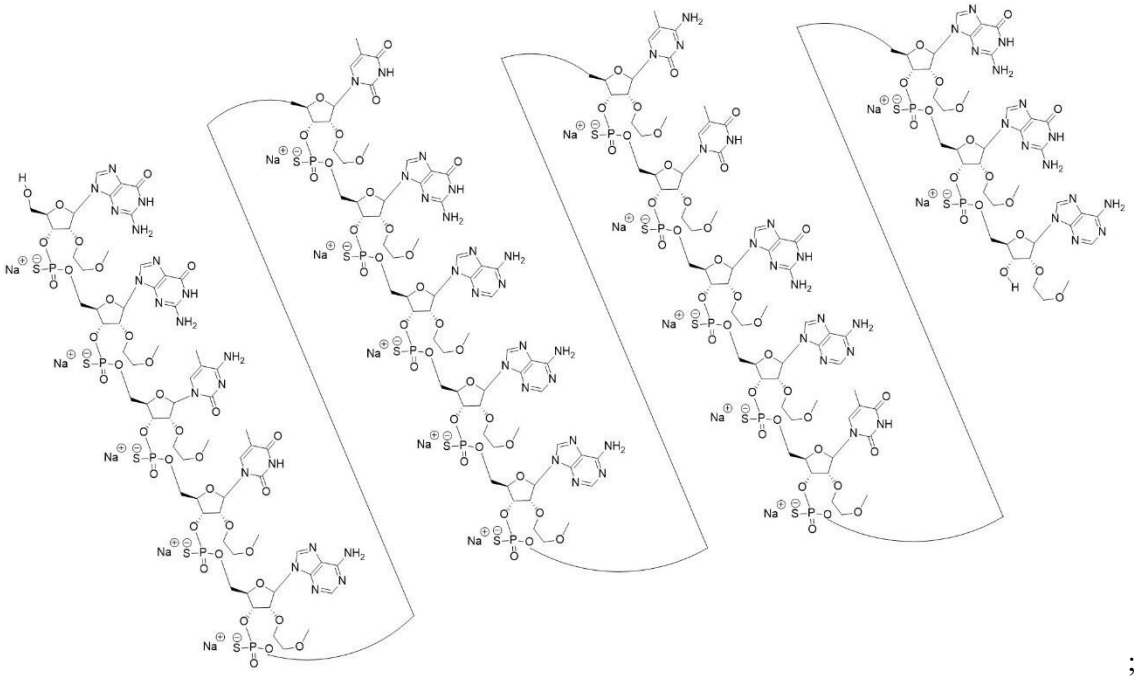
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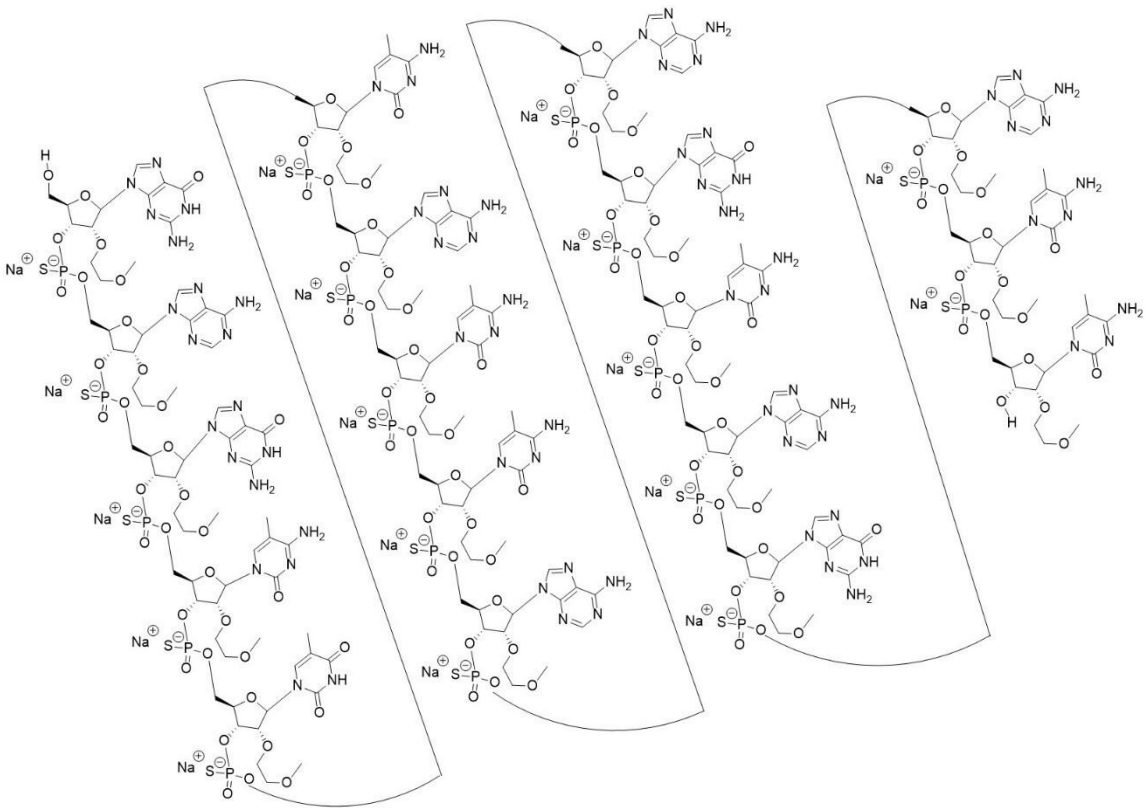
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or a pharmaceutically acceptable salt thereof;

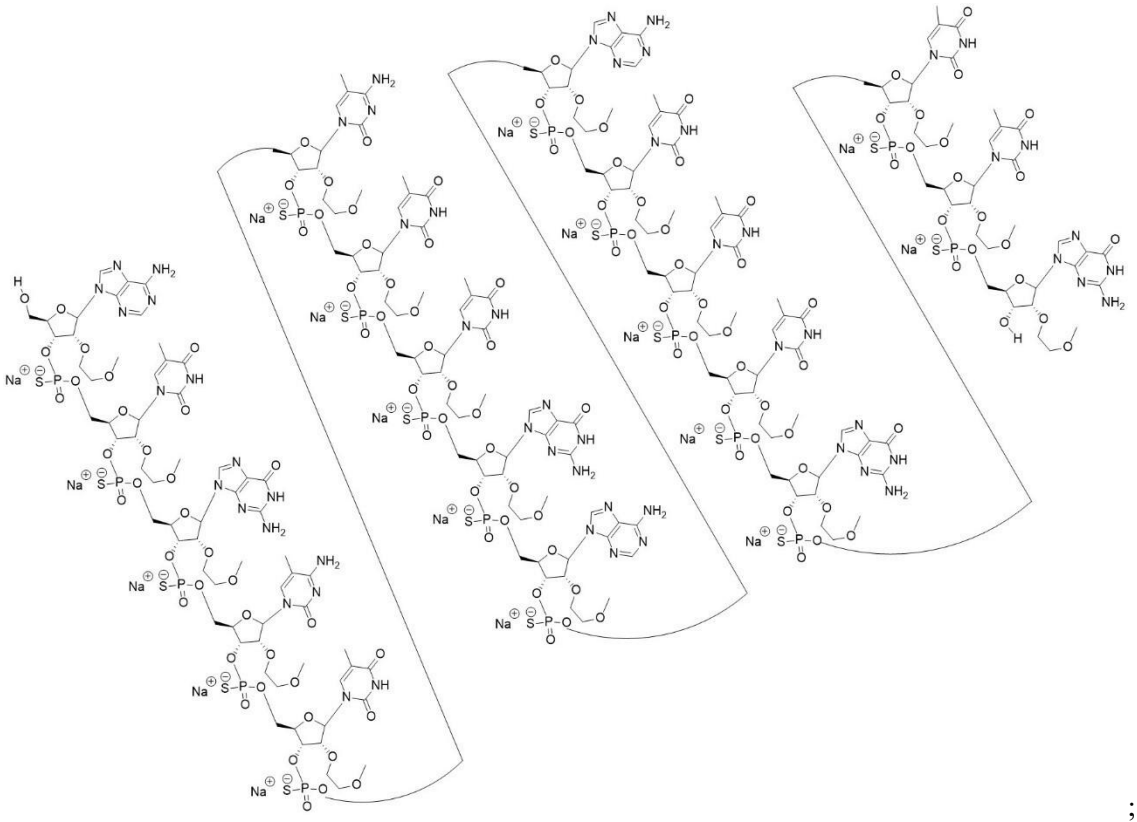
or a compound according to any one of the following chemical structures (SEQ ID NOs: 313-317, respectively, in order of appearance):



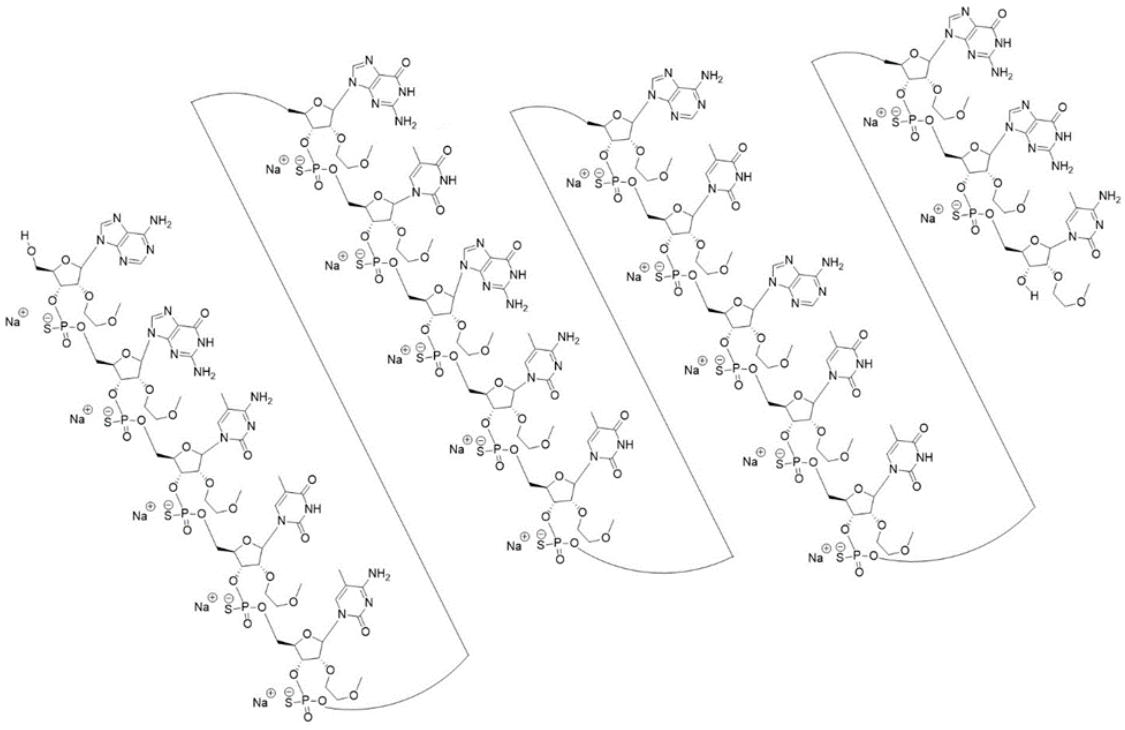
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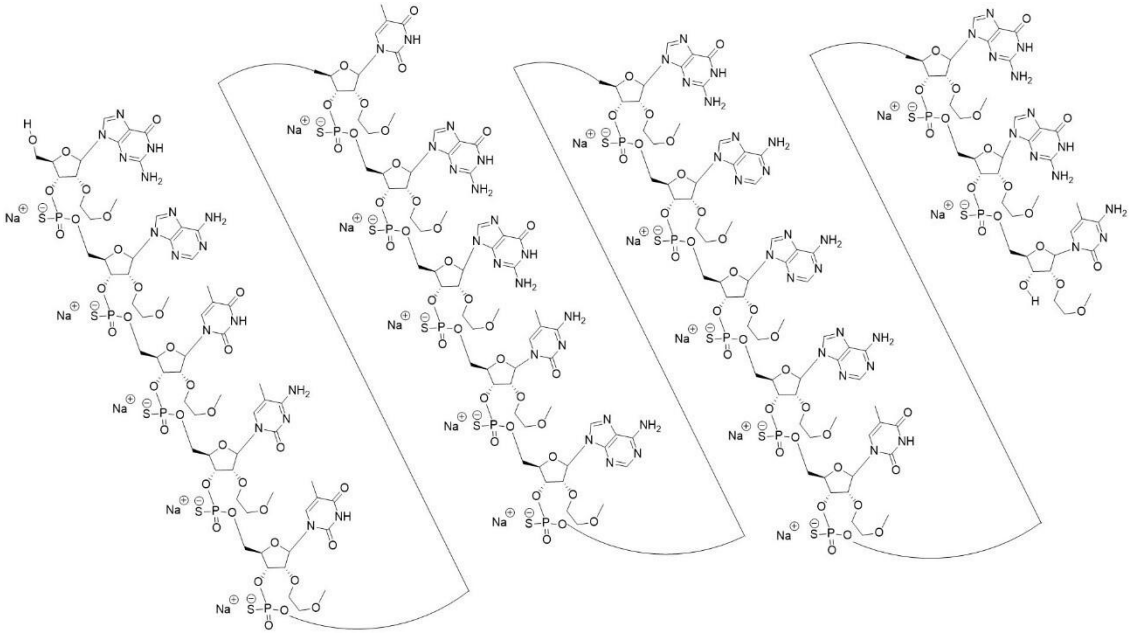
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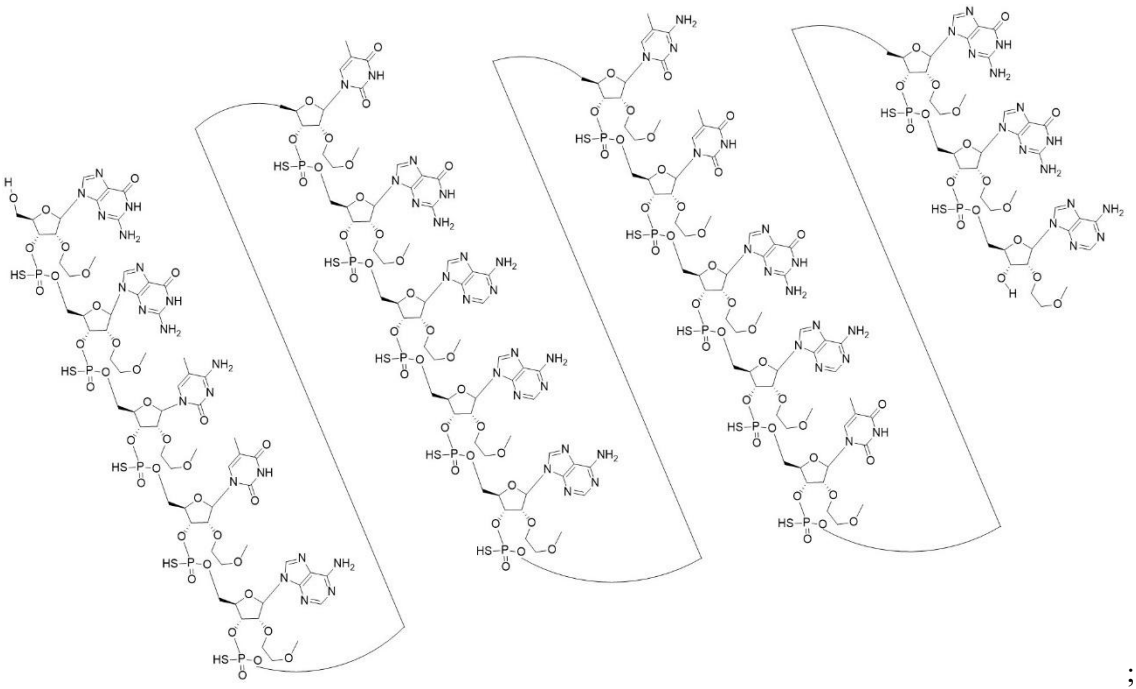


; or



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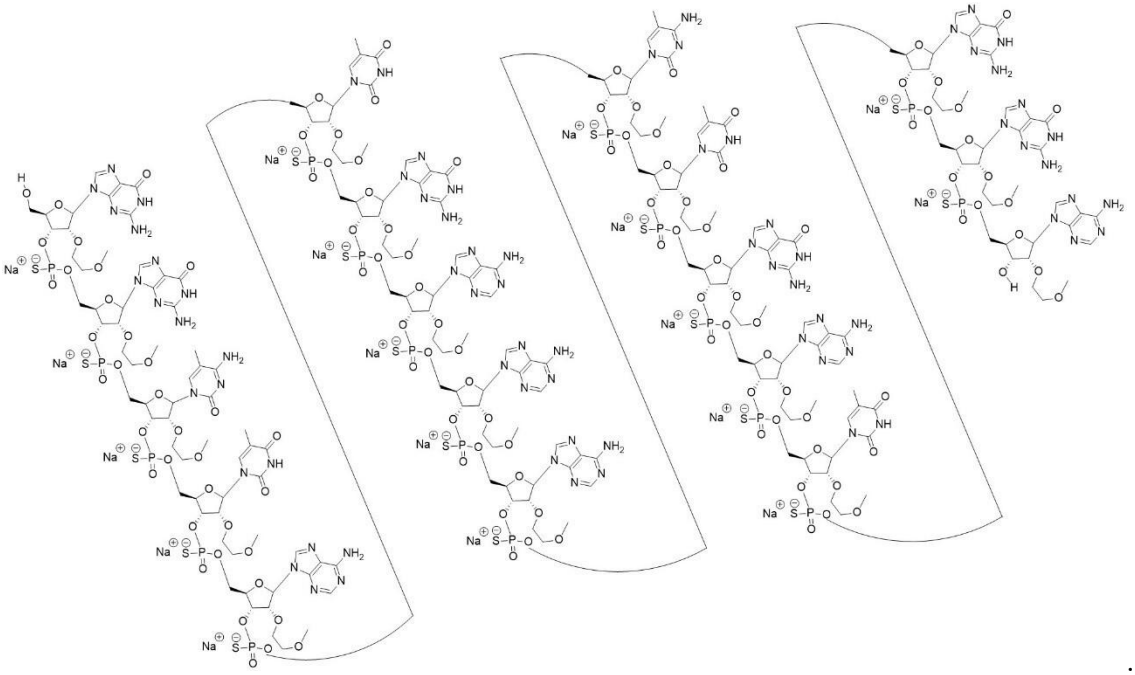
2. The antisense oligomer of claim 1, wherein the antisense oligomer is a compound according to the following chemical structure:



;

or a pharmaceutically acceptable salt thereof;

or a compound according to the chemical structure



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3. A pharmaceutical composition comprising:

(a) an antisense oligomer; and

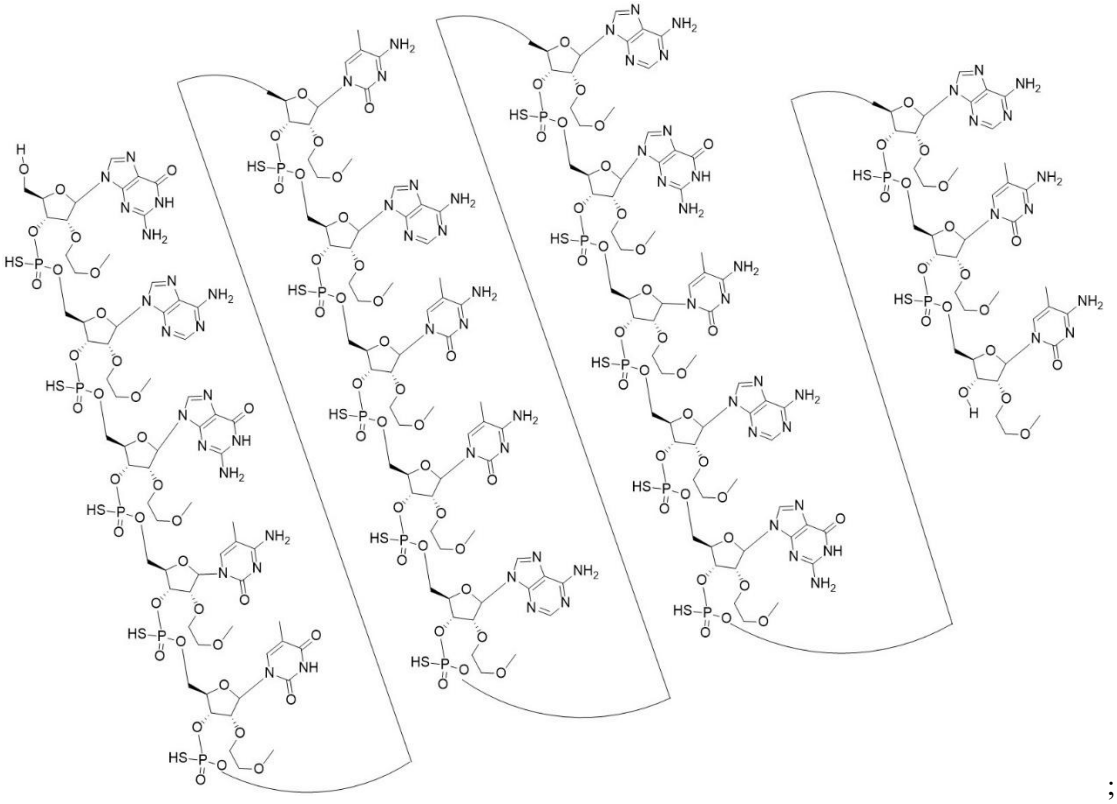
(b) a pharmaceutically acceptable diluent;

wherein the antisense oligomer is dissolved or suspended in a solution, and

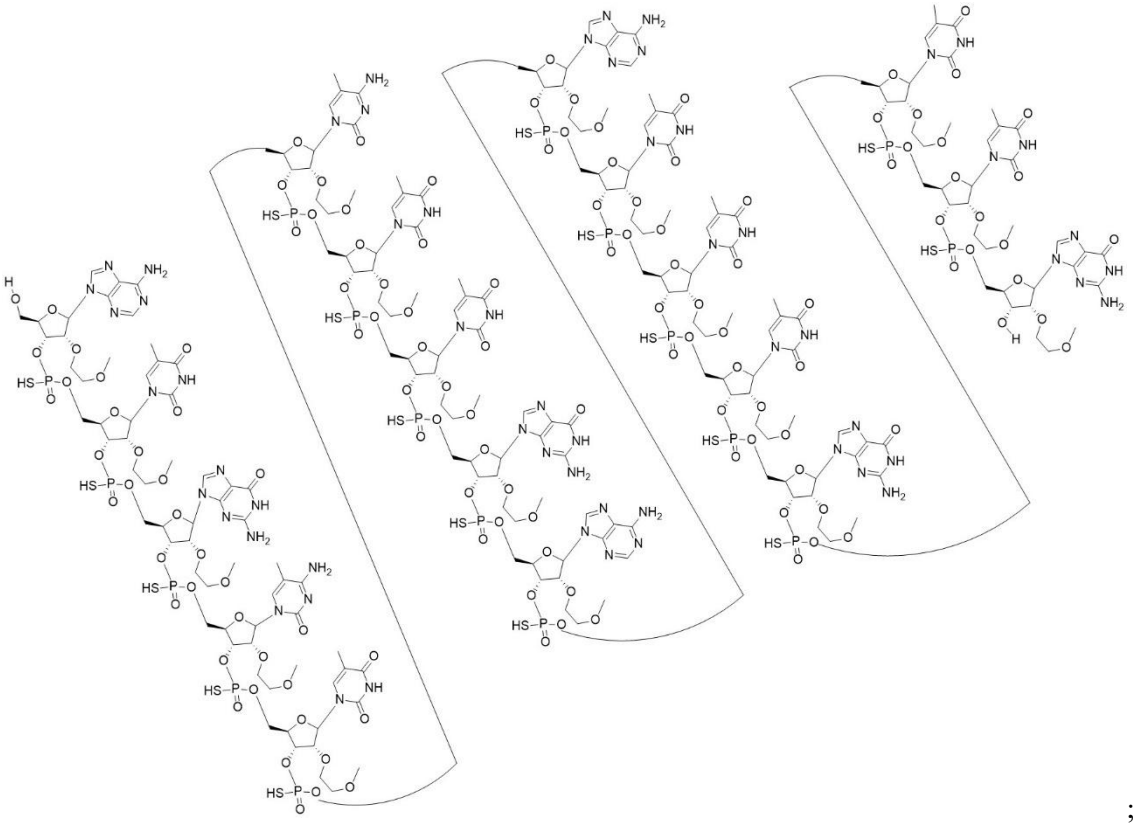
wherein the antisense oligomer is a compound according to any one of the following chemical structures (SEQ ID NOs: 313-317, respectively, in order of appearance):



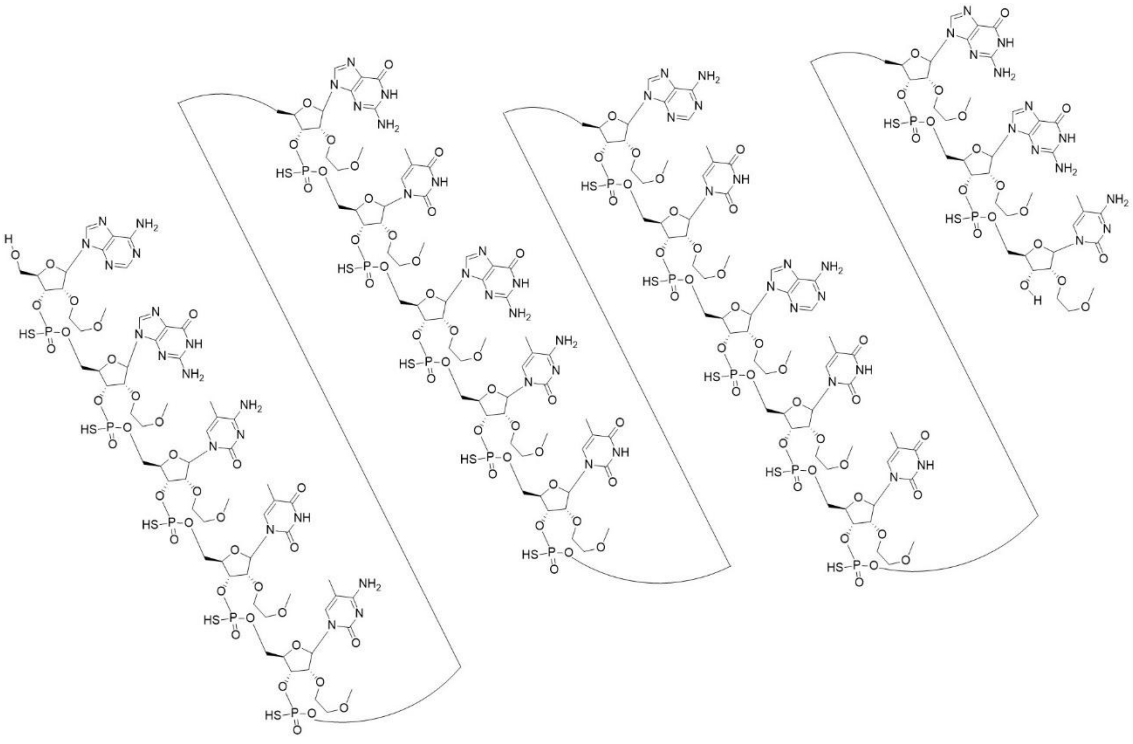
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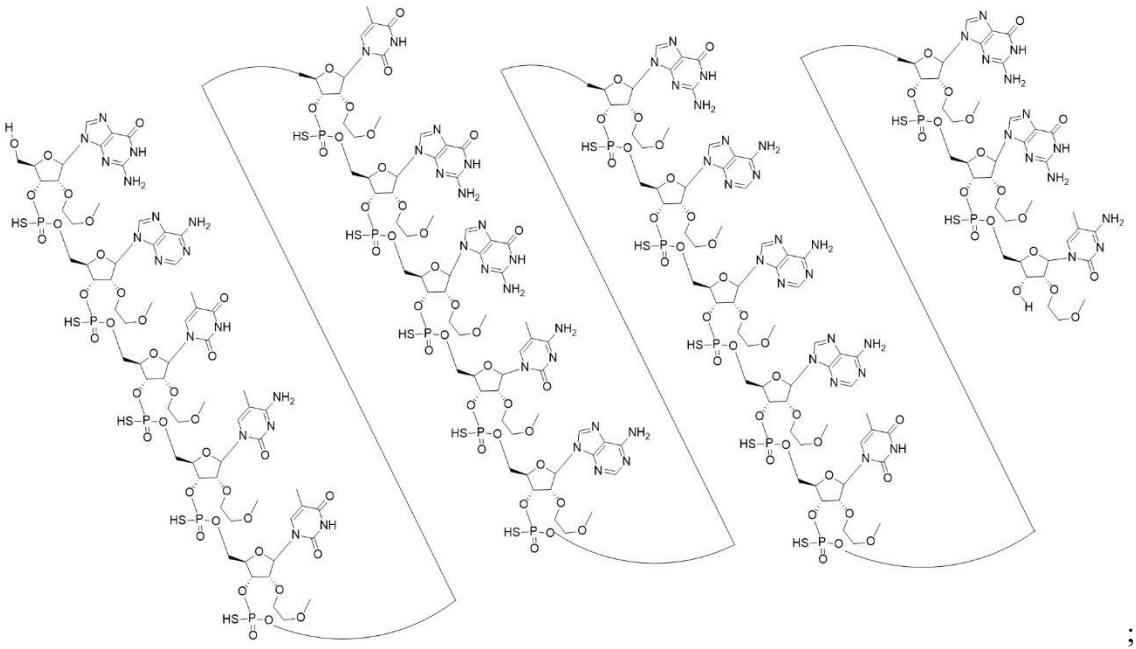
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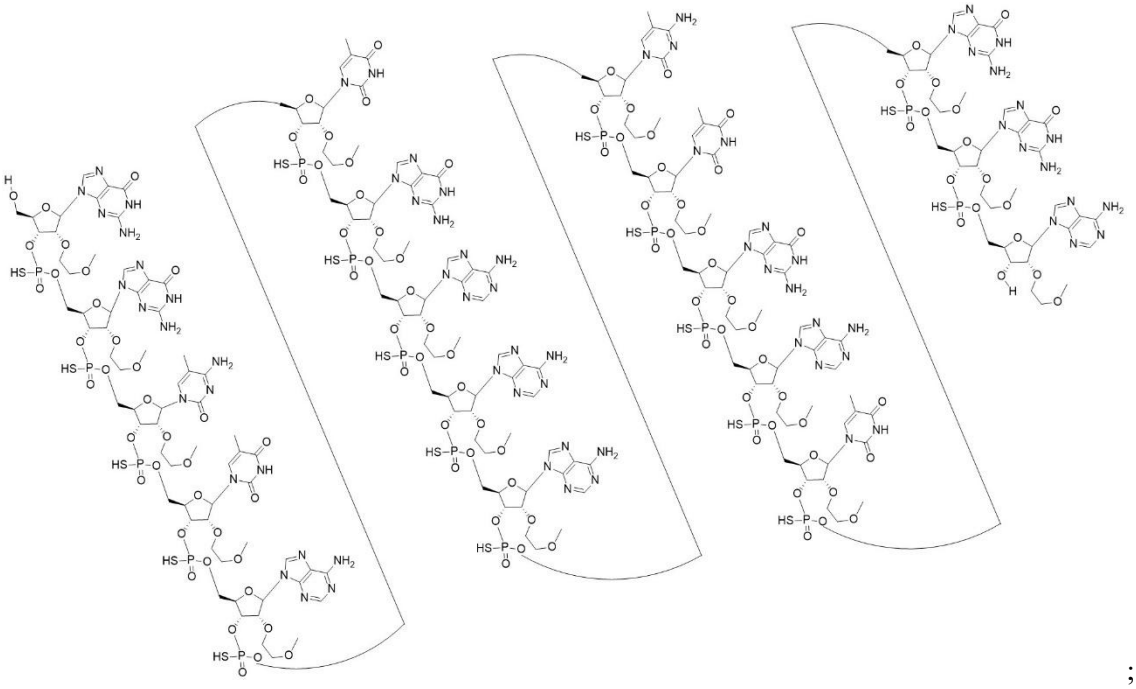
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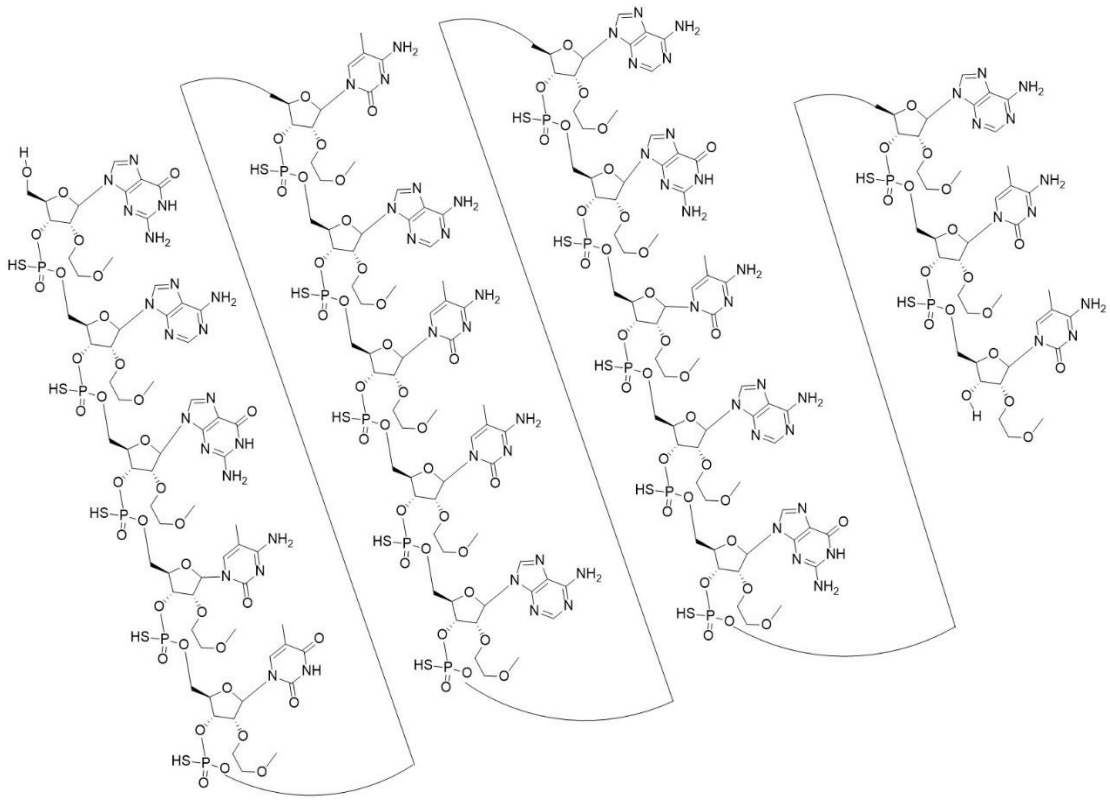
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or a pharmaceutically acceptable salt thereof.

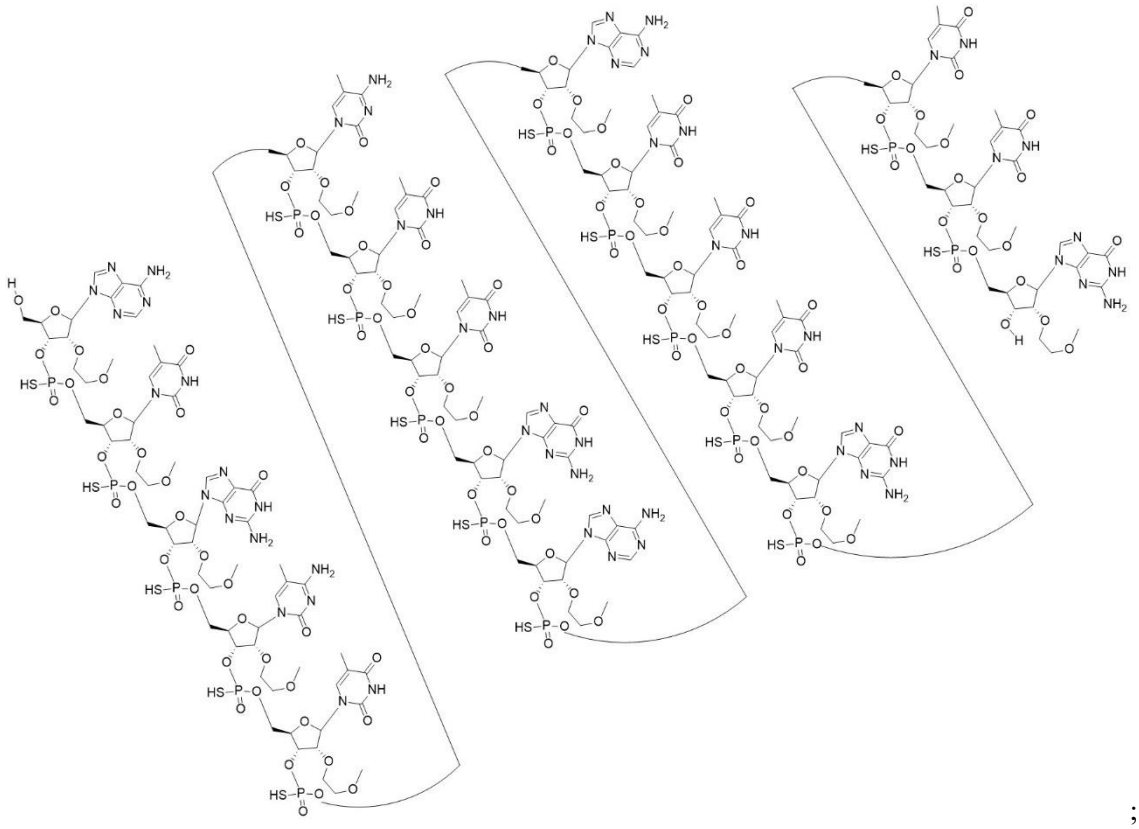
4. Use of a pharmaceutical composition in the manufacture of a medicament for the treatment of a disease or condition or reducing likelihood of developing the disease or condition in a subject in need thereof, wherein the disease or condition comprises an eye disease or condition, wherein the pharmaceutical composition comprises an antisense oligomer, and wherein the antisense oligomer is a compound according to any one of the following chemical structures (SEQ ID NOs: 313-317, respectively, in order of appearance):



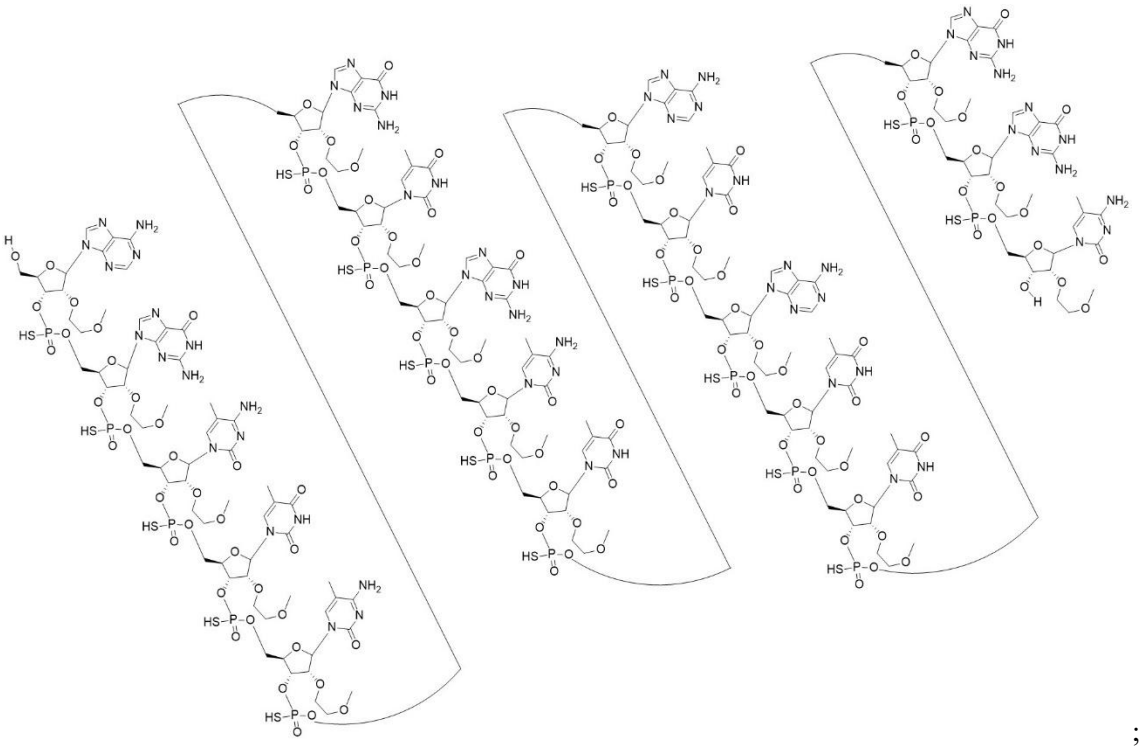
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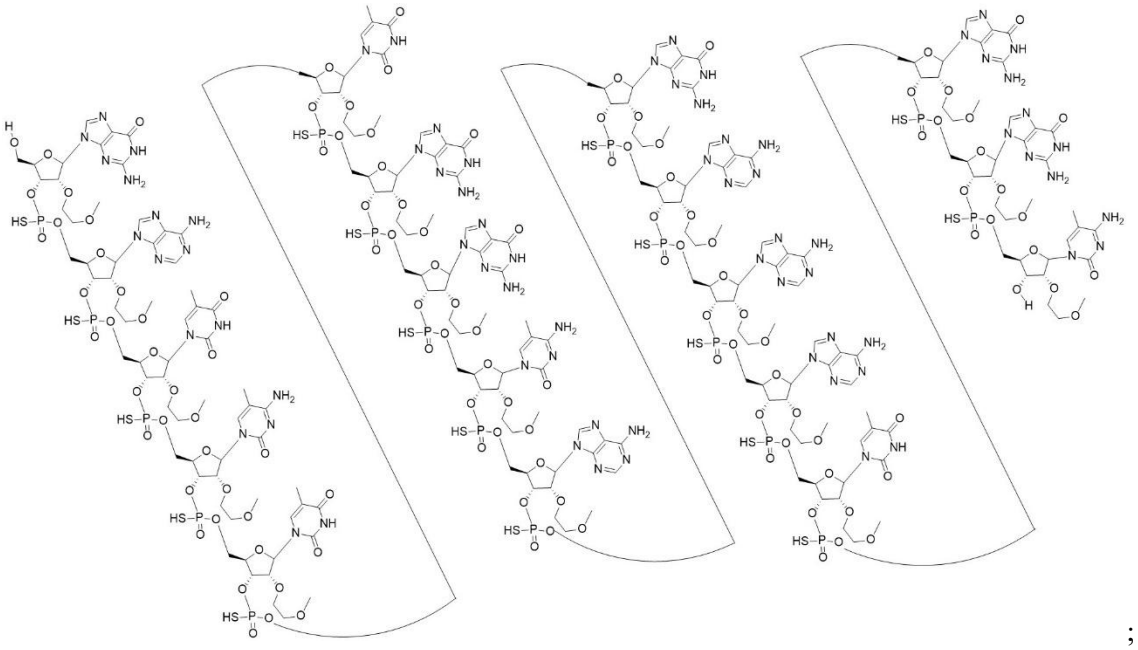
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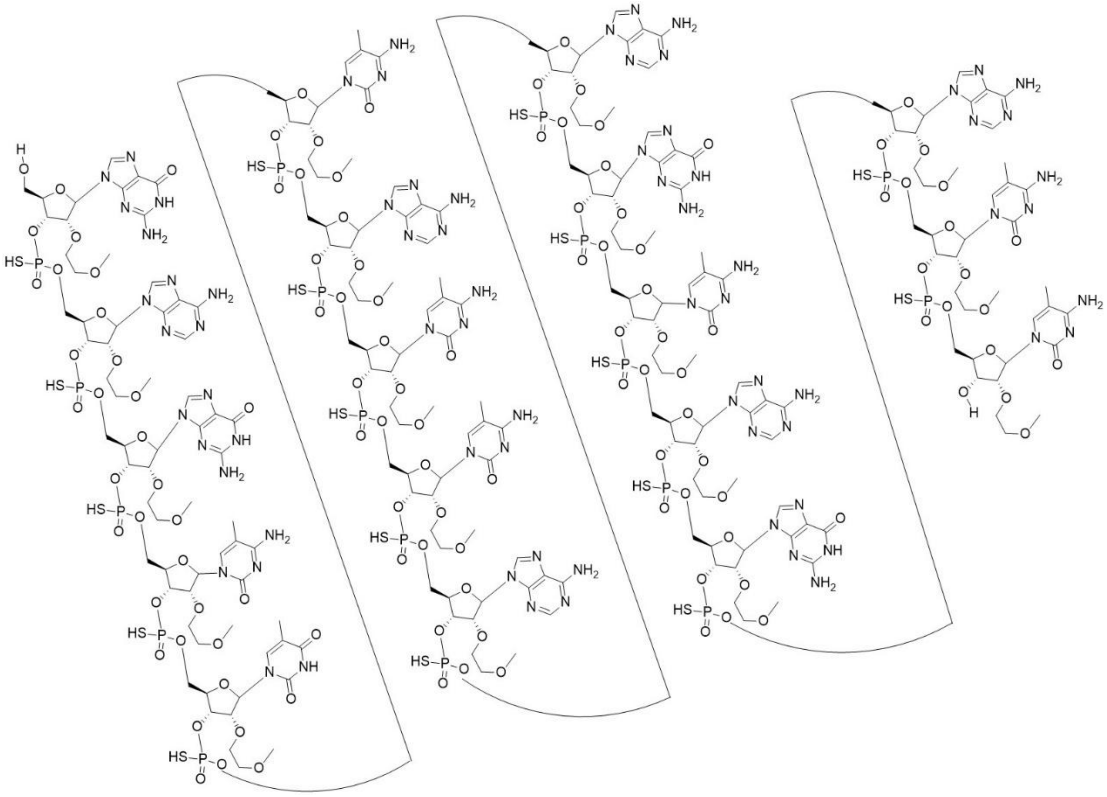
or a pharmaceutically acceptable salt thereof.

5. Use of a pharmaceutical composition of the manufacture of a medicament for treating a disease or condition or reducing likelihood of developing the disease or condition in a human subject in need thereof, wherein the disease or condition is characterized by a reduced expression or function of

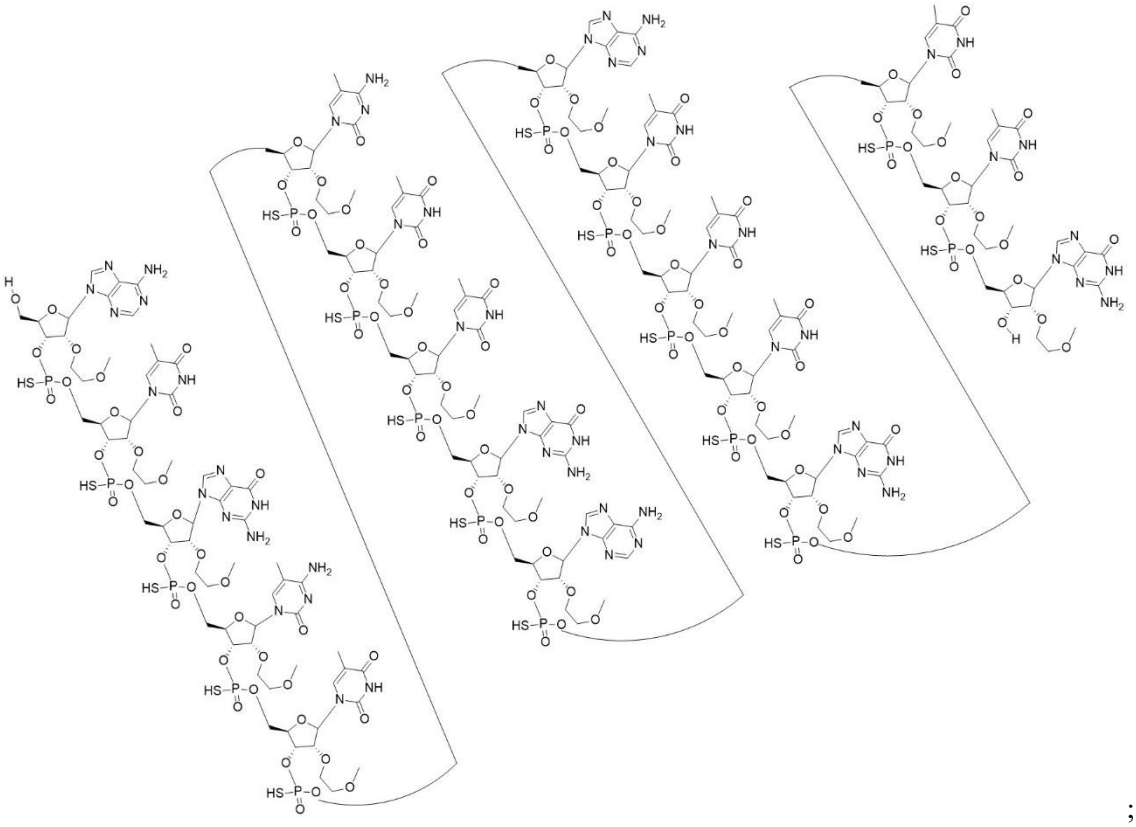
OPA1 protein, wherein the pharmaceutical composition comprises an antisense oligomer, and wherein the antisense oligomer is a compound according to any one of the following chemical structures (SEQ ID NOs: 313-317, respectively, in order of appearance):



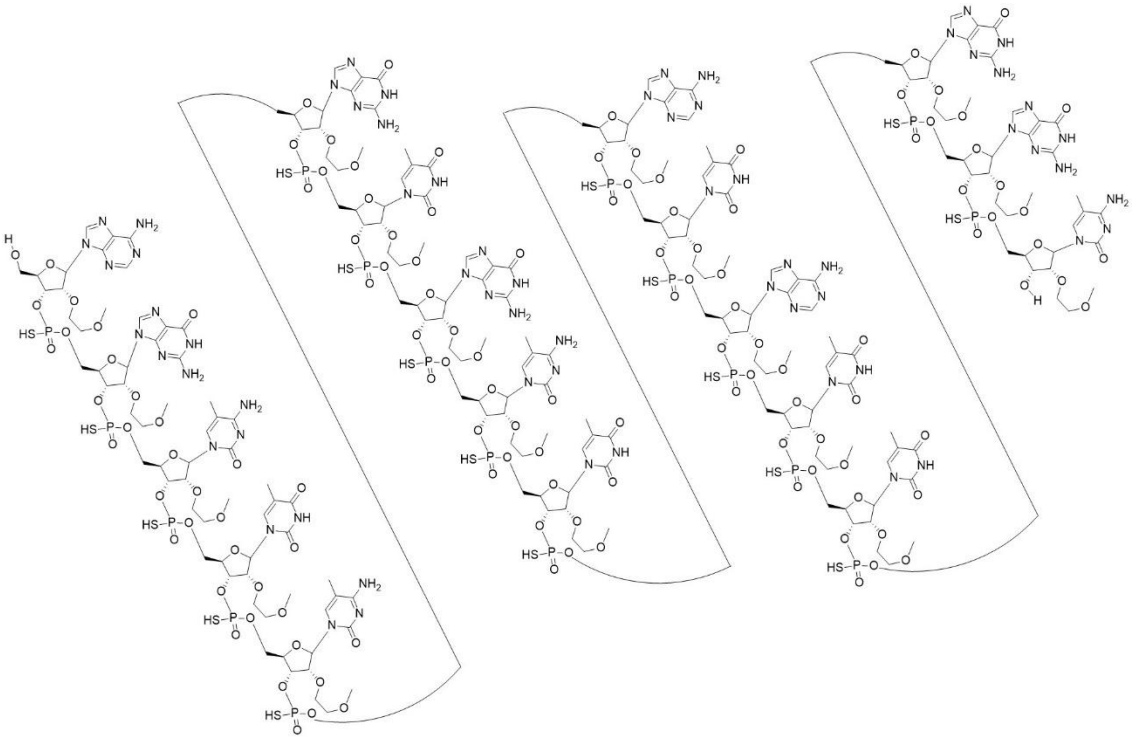
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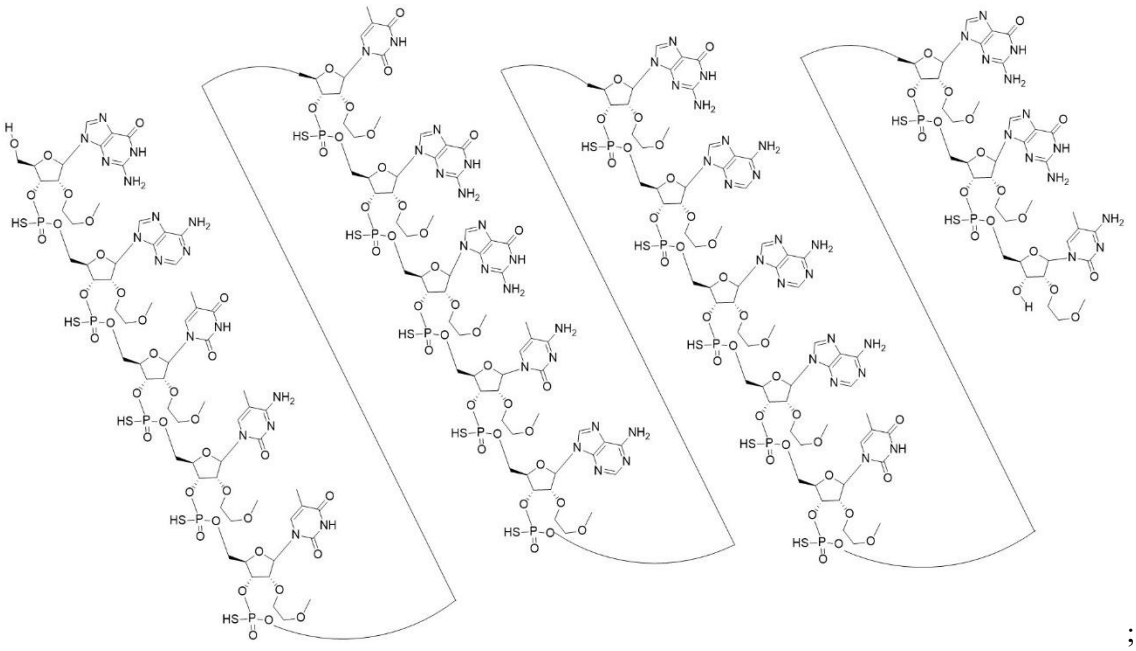
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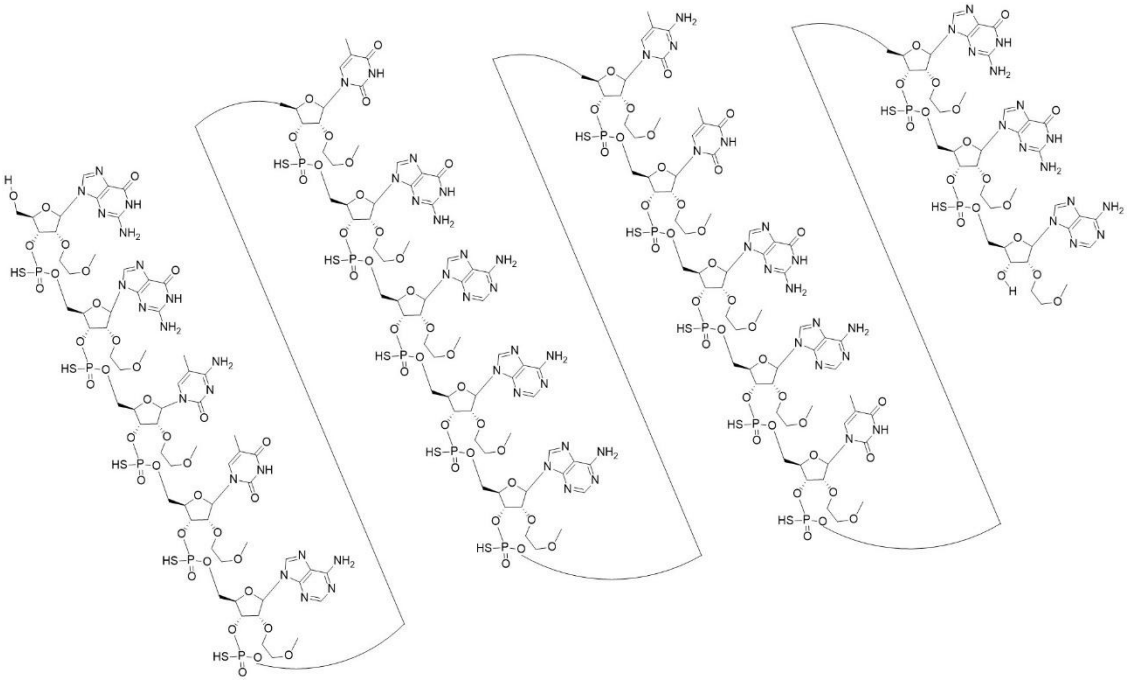
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or a pharmaceutically acceptable salt thereof.

6. The pharmaceutical composition of claim 2, or the use of claim 4 or 5, wherein the antisense oligomer is the compound according the chemical structure



(SEQ ID NO: 313) or a pharmaceutically acceptable salt thereof, and

wherein the antisense oligomer is dissolved or suspended in a solution at a concentration of from about 1 mg/mL to about 200 mg/mL.

7. The use of any one of claims 4-6, wherein the disease or condition comprises ADOA-plus syndrome; a mitochondrial disorder; glaucoma; normal tension glaucoma; Charcot-Marie-Tooth disease; mitochondria dysfunction; diabetic retinopathy; age-related macular degeneration; retinal ganglion cell death; mitochondrial fission-mediated mitochondrial dysfunction; progressive external ophthalmoplegia; deafness; ataxia; motor neuropathy; sensory neuropathy; myopathy; Behr syndrome; brain dysfunction; encephalopathy; peripheral neuropathy; fatal infantile mitochondrial encephalomyopathy; hypertrophic cardiomyopathy; spastic ataxic syndrome; sensory motor peripheral neuropathy; hypotonia; gastrointestinal dysmotility and dysphagia; optic atrophy; optic atrophy plus syndrome; Mitochondrial DNA depletion syndrome 14; late-onset cardiomyopathy; diabetic cardiomyopathy; Alzheimer's Disease; focal segmental glomerulosclerosis; kidney disease; Huntington's Disease; cognitive function decline in healthy aging; Prion diseases; late onset dementia and parkinsonism; mitochondrial myopathy; Leigh syndrome; Friedreich's ataxia; Parkinson's disease; MELAS (Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes); pyruvate dehydrogenase complex deficiency; chronic kidney disease; Leber's hereditary optic neuropathy; obesity; age-related systemic neurodegeneration; skeletal muscle atrophy; heart and brain ischemic damage; or massive liver apoptosis.
8. The use of any one of claims 4-7, wherein the disease or condition comprises Optic atrophy type 1.
9. The use of any one of claims 4-8, wherein the disease or condition comprises autosomal dominant optic atrophy (ADOA).
10. The use of any one of claims 4-9, wherein the subject is characterized by having:
(i) a heterozygous *OPA1* gene variant;
(ii) clear ocular media to allow for adequate visualization of the vitreous and fundus and to achieve appropriate quality of all ophthalmic assessments;
(iii) an AREDS Clinical Lens Standard of <1 for posterior subcapsular (PSC) opacity;
(iv) a BCVA EDTRS letter score of ≥35 and ≤70 with each eye individually that is administered with the pharmaceutical composition; or (v) any combination of (i)-(iv).
11. The use of any one of claims 4-10, wherein the subject is characterized by:
(1) not having a gain-of-function variant, or compound heterozygous or homozygous pathogenic or likely pathogenic variant in *OPA1* gene;
(2) not having only benign or likely benign variants in the *OPA1* gene;
(3) not having extraocular phenotypic manifestations of (syndromic) ADOA (ADOA-plus);
(4) not having been diagnosed with Behr syndrome;
(5) not having a known pathogenic mutation in another gene implicated in optic atrophy or retinal diseases;

(6) not having diabetic retinopathy with potential for development of proliferative diabetic retinopathy, diabetic macular edema, or optic neuropathy;
(7) not having or having a history of any ocular condition in either eye;
(8) not having a history of intraocular surgery or corneal surgery including refractive surgery in either eye within 12 weeks prior to the administering;
(9) not having a history of retinal photocoagulation;
(10) not having a history or presence of retinal vein occlusion;
(11) not being considered to be at risk for uveitis or ocular infection because of having any of the following: an active flare of non-infectious uveitis or an episode of infectious uveitis or other ocular infection in either eye within 12 months prior to the administering;
(12) not having dry age-related macular degeneration in either eye;
(13) not having high myopia (>6 diopters);
(14) not having a history of cancer (except a diagnosis of basal cell, squamous cell skin cancer, or carcinoma in situ of the cervix that has been successfully treated);
(15) not taking, or having taken at any time, any medication or treatment that can or might cause an optic neuropathy;
(16) not having any history of nutritional deficiency (including B12 and/or folate deficiencies), or not having a known deficiency in serum B12 or folate, not having had bariatric surgery; or
(17) any combination of (1)-(16).

12. The use of any one of claims 4-11, wherein the pharmaceutical composition is formulated for intravitreal injection.

13. The use of any one of claims 4-12, wherein pharmaceutical composition is formulated for administration to an eye of the subject
(a) at a dose of from about 0.005 to about 20 mg of the antisense oligomer, and/or
(b) in a volume of from about 5 µL to about 250 µL.

14. The use of any one of claims 4-13, wherein the pharmaceutical composition is formulated for administration as a first dose and a subsequent dose to an eye of the subject.

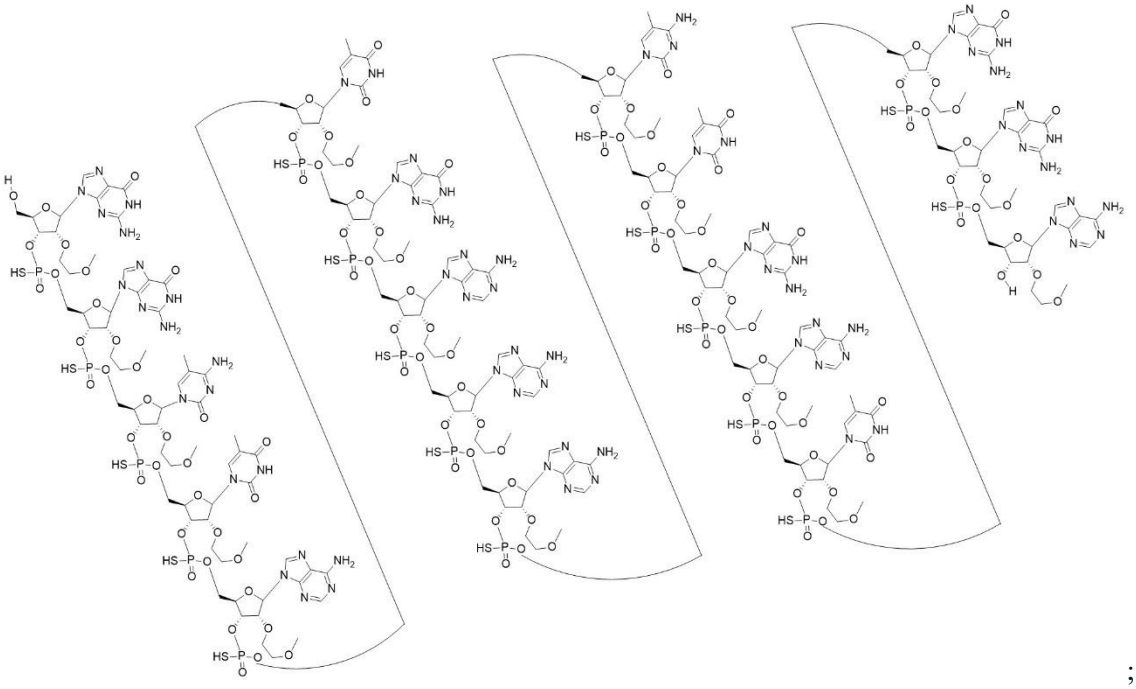
15. The use of any one of claims 4-14, wherein the pharmaceutical composition is formulated for administration at the same dose of the antisense oligomer to both the left eye and the right eye of the subject.

16. The use of any one of claims 4-15, wherein the pharmaceutical composition is formulated for administration at a different dose of the antisense oligomer to each of the left eye and the right eye of the subject.

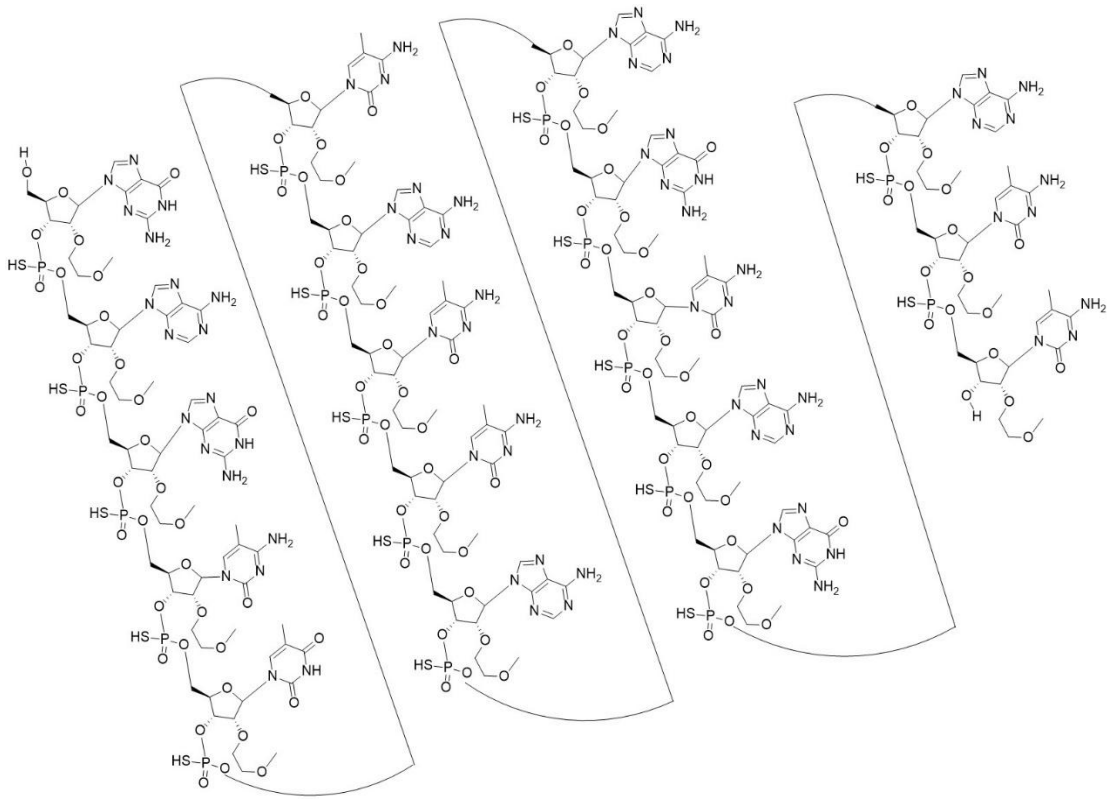
17. The use of any one of claims 4-16, wherein the antisense oligomer promotes splicing of a nonsense-mediated RNA decay-inducing exon (NMD exon) from a pre-mRNA in a cell of the subject, thereby increasing a level of processed mRNA that is processed from the pre-mRNA, and increasing expression of the OPA1 protein in the cell; wherein the pre-mRNA encodes the OPA1 protein and comprises the NMD exon; and wherein the NMD exon has genomic coordinates GRCh38/hg38: chr3 193628509 to 193628616.

18. The use of claim 17, wherein the OPA1 protein expressed from the processed mRNA is
(a) a full-length OPA1 protein,
(b) a wild-type OPA1 protein,
(c) a functional OPA1 protein,
(d) at least partially functional as compared to a wild-type OPA1 protein,
(e) at least partially functional as compared to a full-length wild-type OPA1 protein, or
(f) a combination thereof.

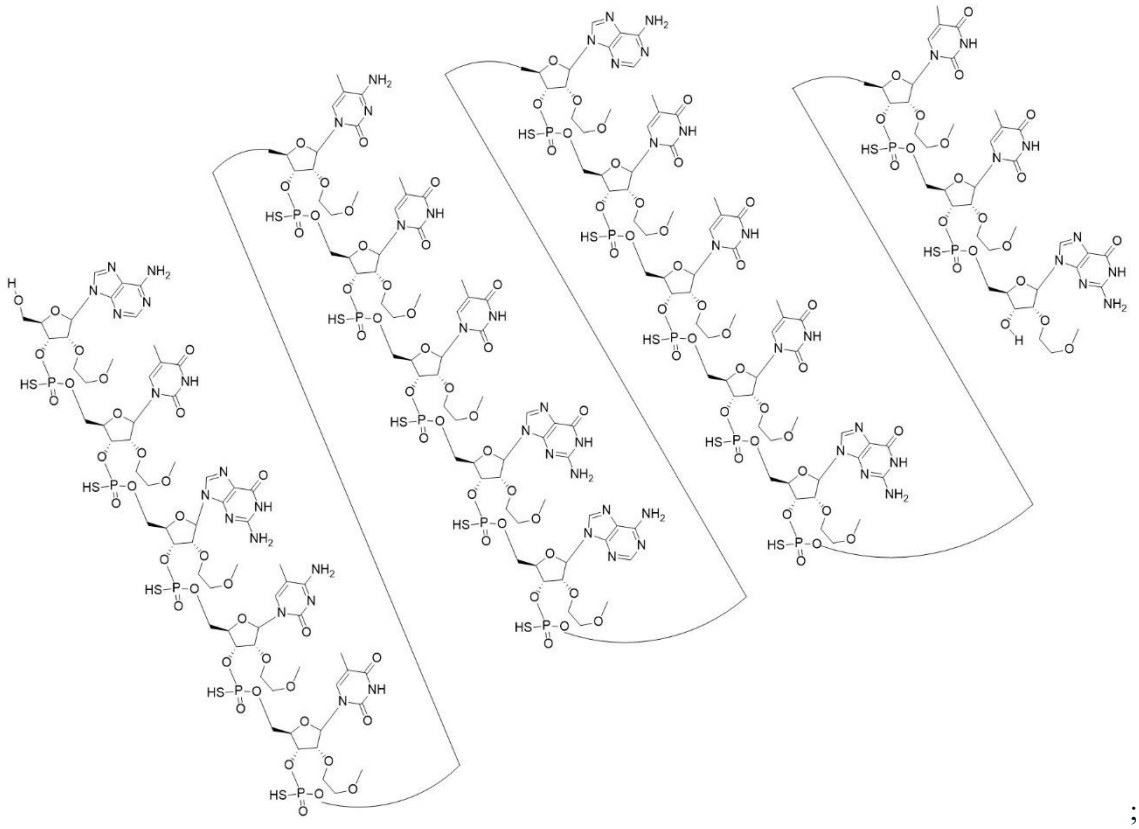
19. A pharmaceutical composition for use in therapy, wherein the pharmaceutical composition comprises an antisense oligomer, and wherein the antisense oligomer is a compound according to any one of the following chemical structures (SEQ ID NOs: 313-317, respectively, in order of appearance):



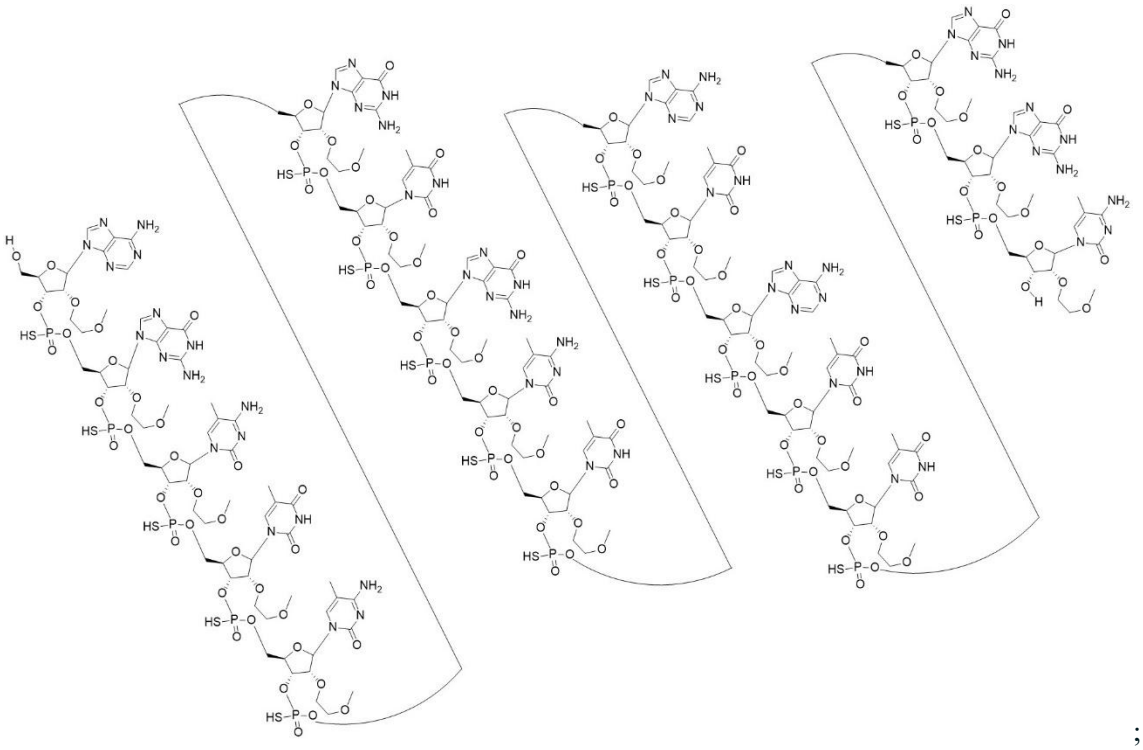
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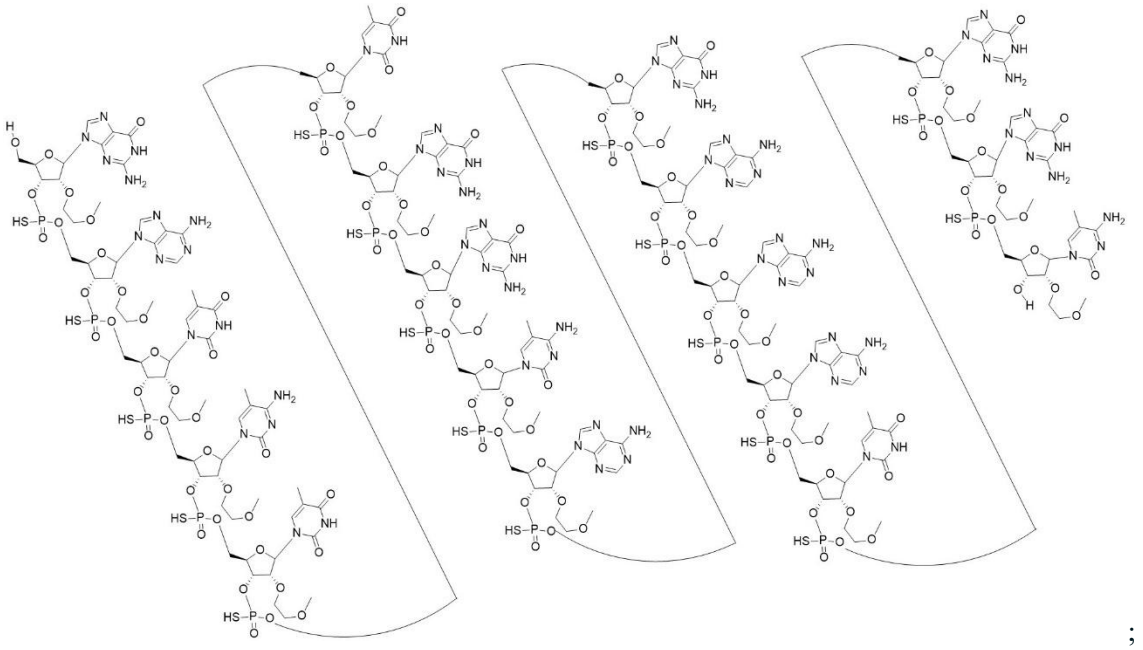
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or a pharmaceutically acceptable salt thereof.