Embodiment 52. The modified oligonucleotide for use of any one of embodiments 46-51, wherein the modified oligonucleotide is administered at least seven times.

Embodiment 53. Use of a modified oligonucleotide or a pharmaceutically acceptable salt thereof for the preparation of a medicament for treating polycystic kidney disease, wherein the modified oligonucleotide has the structure 5'-$A_SG_SC_MA_FC_FU_FU_MU_SA_S$-3',

wherein nucleosides followed by subscript "M" are 2'-O-methyl nucleosides; nucleosides followed by subscript "F" are 2'-fluoro nucleosides; and nucleosides followed by subscript "S" are S-cEt nucleosides, and wherein each cytosine is a non-methylated cytosine;

wherein the modified oligonucleotide is formulated for administration at a dose of 0.5 - 5 mg/kg, 0.5 - 4.5 mg/kg, 0.5 - 4 mg/kg, 0.5 - 3.5 mg/kg, 0.5 - 3 mg/kg, 1 - 5 mg/kg, 1 - 4.5 mg/kg, 1 - 4 mg/kg, 1 - 3.5 mg/kg, or 1 - 3 mg/kg.

Embodiment 54. The use of embodiment 53, wherein the modified oligonucleotide is administered at a dose of 1 mg/kg, 2 mg/kg, or 3 mg/kg.

Embodiment 55. The use of embodiment 53 or 54, wherein the pharmaceutically acceptable salt is a sodium salt.

Embodiment 56. The use of any one of embodiments 53-55, wherein the modified oligonucleotide is present in a pharmaceutical composition comprising a sterile saline solution.

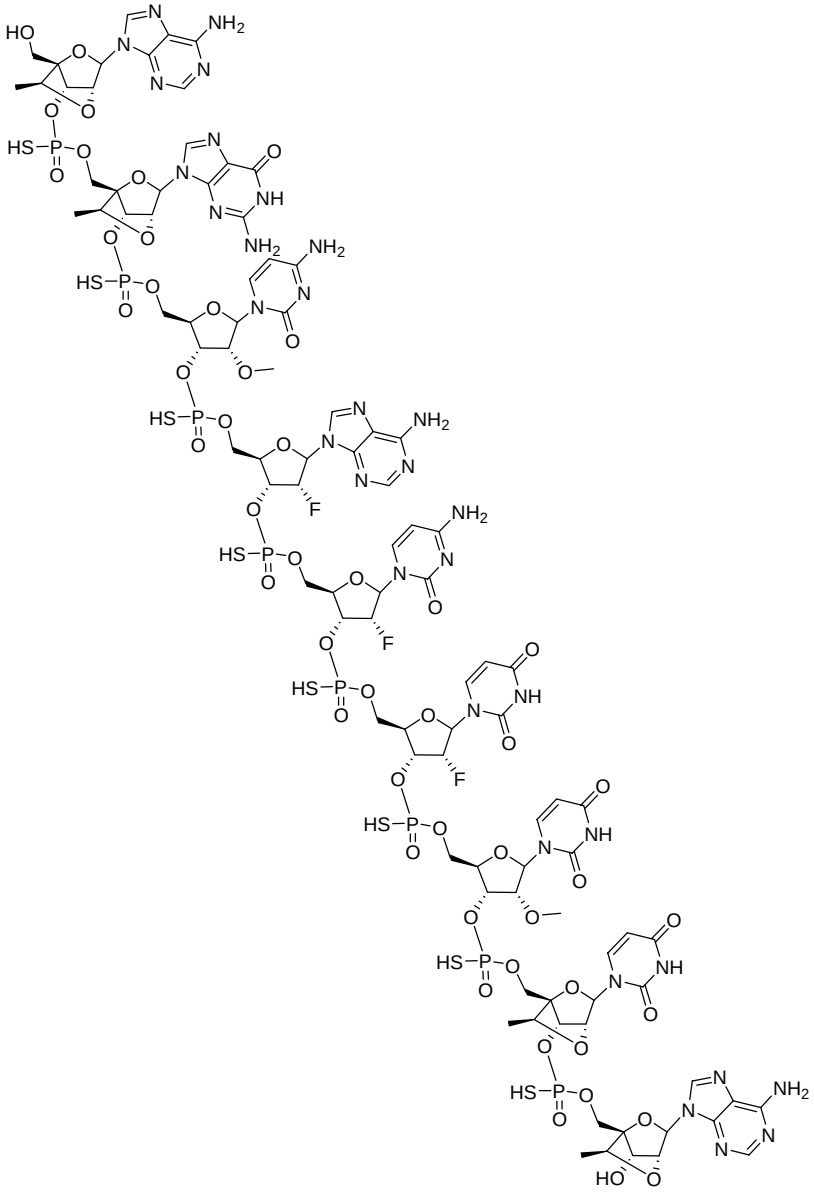
Embodiment 57. The use of any one of embodiments 53-56, wherein the polycystic kidney disease is autosomal dominant polycystic kidney disease (ADPKD).

Embodiment 58. The use of any one of embodiments 53-57, wherein the modified oligonucleotide is administered at least once every two weeks.

Embodiment 59. The use of any one of embodiments 53-58, wherein the modified oligonucleotide is administered at least seven times.

[0006a] In one aspect, the present disclosure refers to use of a modified oligonucleotide or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating polycystic kidney disease, wherein the modified oligonucleotide or a pharmaceutically acceptable salt thereof is to be administered to a subject in need thereof at a dose of 0.5 - 5 mg/kg, 0.5 - 4.5 mg/kg, 0.5 - 4 mg/kg, 0.5 - 3.5 mg/kg, 0.5 - 3 mg/kg, 1 - 5 mg/kg, 1 - 4.5 mg/kg, 1 - 4 mg/kg, 1 - 3.5 mg/kg, or 1 - 3 mg/kg,
wherein the modified oligonucleotide has the structure 5'-$A_SG_SC_MA_FC_FU_FU_MU_SA_S$-3',
wherein nucleosides followed by subscript "M" are 2'-O-methyl nucleosides; nucleosides followed by subscript "F" are 2'-fluoro nucleosides; and nucleosides followed by subscript "S" are S-cEt nucleosides, and wherein each cytosine is a non-methylated cytosine.
[0006b] In another aspect, the present disclosure refers to use of a modified oligonucleotide in the manufacture of a medicament for treating polycystic kidney disease, wherein the modified oligonucleotide is to be administered to a subject in need thereof at a dose of 0.5 - 5 mg/kg, 0.5 - 4.5

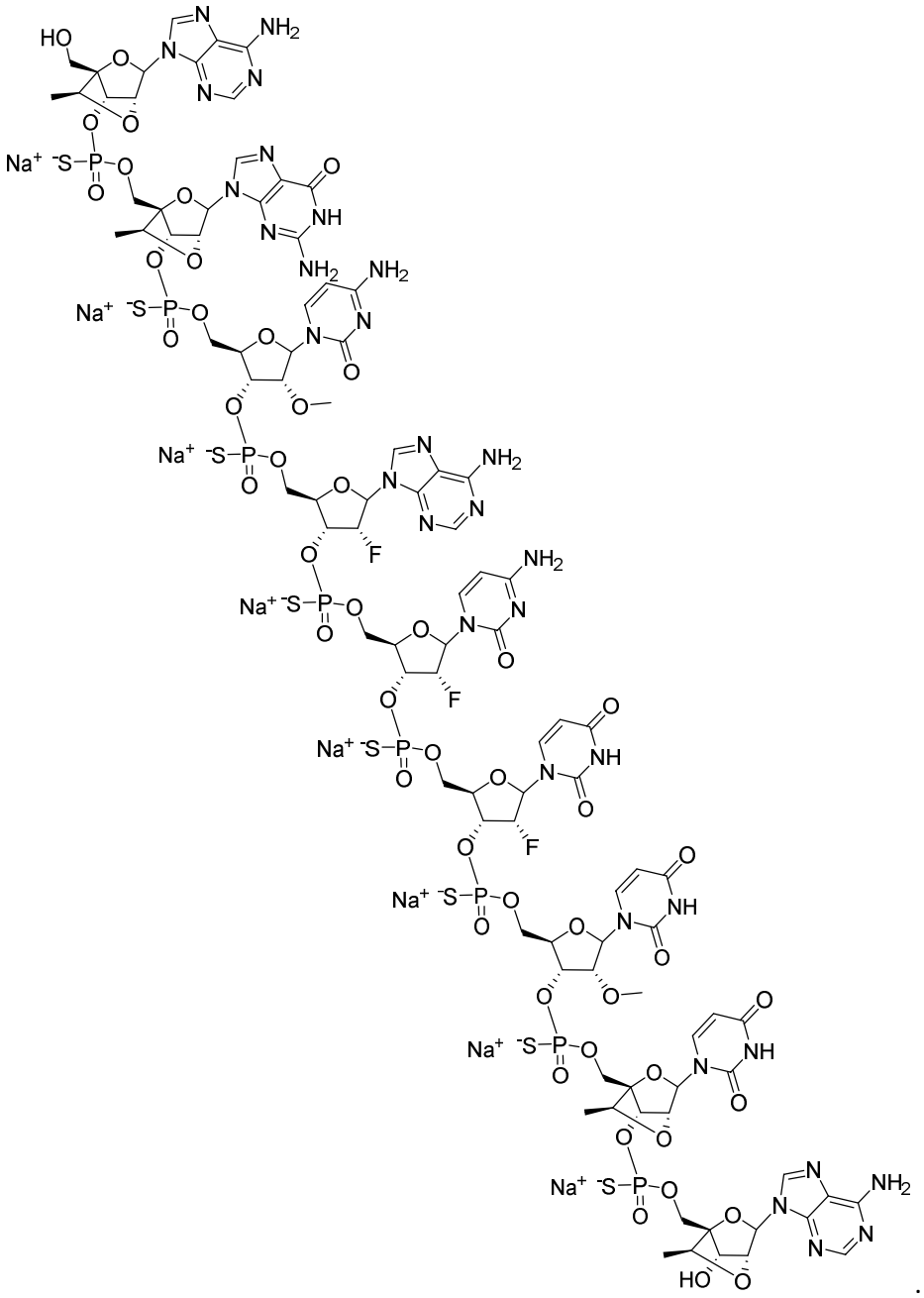
mg/kg, 0.5 - 4 mg/kg, 0.5 - 3.5 mg/kg, 0.5 - 3 mg/kg, 1 - 5 mg/kg, 1 - 4.5 mg/kg, 1 - 4 mg/kg, 1 - 3.5 mg/kg, or 1 - 3 mg/kg, wherein the modified oligonucleotide has the structure:



or a pharmaceutically acceptable salt thereof.

[0006c] In another aspect, the present disclosure refers to use of a modified oligonucleotide in the manufacture of a medicament for treating polycystic kidney disease, wherein the modified oligonucleotide is to be administered to a subject in need thereof at a dose of 0.5 - 5 mg/kg, 0.5 - 4.5 mg/kg, 0.5 - 4 mg/kg, 0.5 - 3.5 mg/kg, 0.5 - 3 mg/kg, 1 - 5 mg/kg, 1 - 4.5 mg/kg, 1 - 4 mg/kg, 1 - 3.5

mg/kg, or 1 - 3 mg/kg, wherein the modified oligonucleotide has the structure:



BRIEF DESCRIPTION OF FIGURES

[0007] **Figure 1.** Purine nucleobase structures.

[0008] **Figure 2A-2C**. Efficacy of RG-NG-1015 in the *Pkd1*-F/RC model of PKD. Effects of treatment on (2A) kidney-to-body weight ratio, (2B) blood urea nitrogen (BUN) level, and (2C) blood creatinine level.

[0009] **Figure 3**. Maximum Tolerated Dose (MTD) study and Comparative Dose Assessment of RG-NG-1001, RGLS4326, and RG-NG-1017. 6–7-week-old male C57BL/6J mice were dosed with a single intracerebroventricular (ICV) injection of RG-NG-1001 and RGLS4326 (anti-miR-17 oligos that inhibit AMPA-R) and RG-NG-1017 (anti-miR-17 oligos that does not inhibit AMPA-R; RG-NG-1017) at different dose levels in 4 µLvolume and monitored for 7 days. Mortality of the mice is indicated for the three different compounds at different dosages.