What is claimed is:

1. 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,

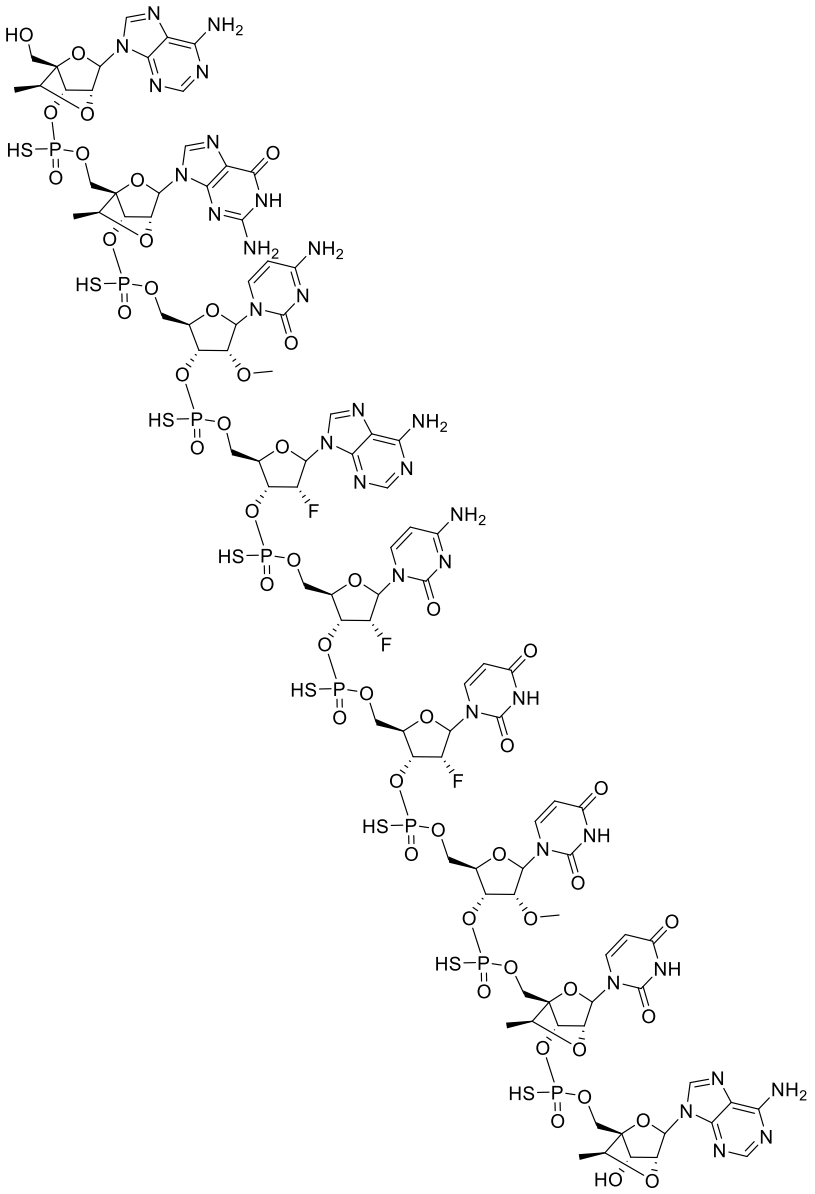
wherein the modified oligonucleotide has the structure 5'-$A_SG_SC_MA_FC_FU_FU_MU_SA_S$-3',

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.

2. The use of claim 1, wherein the modified oligonucleotide or a pharmaceutically acceptable salt thereof is to be administered at a dose of 1 mg/kg, 2 mg/kg, or 3 mg/kg.

3. The use of claim 1 or 2, wherein the pharmaceutically acceptable salt is a sodium salt.

4. 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.

5. The method of claim 4, wherein the modified oligonucleotide is to be administered at a dose of 1 mg/kg, 2 mg/kg, or 3 mg/kg.

6. The method of claim 4 or 5, wherein pharmaceutically acceptable salt is a sodium salt.

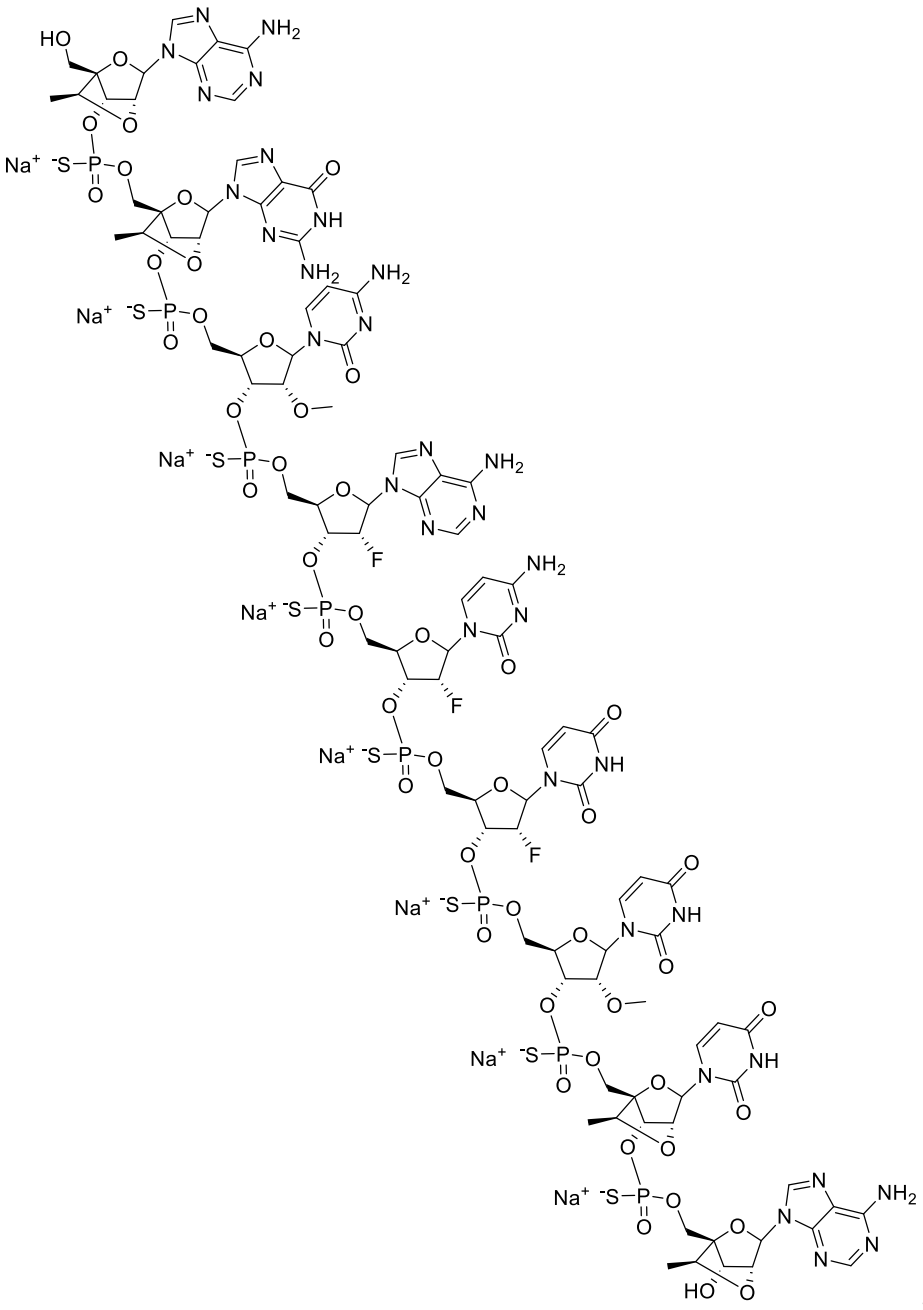
7. The method of any one of claims 1-6, wherein the modified oligonucleotide is present in a pharmaceutical composition comprising a pharmaceutically acceptable diluent.

8. The method of claim 7, wherein the pharmaceutically acceptable diluent is a sterile aqueous solution.

9. The method of claim 8, wherein the sterile aqueous solution is a saline solution.

10. 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: .

11. The use of claim 10, wherein the modified oligonucleotide is to be administered at a dose of 1 mg/kg, 2 mg/kg, or 3 mg/kg.

12. The use of claim 10 or 11, wherein the modified oligonucleotide is present in a pharmaceutical composition comprising a pharmaceutically acceptable diluent.

13. The use of claim 12, wherein the pharmaceutically acceptable diluent is a sterile aqueous solution.

14. The use of claim 13, wherein the sterile aqueous solution is a saline solution.

15. The use of any one of claims 1-14, wherein the subject has polycystic kidney disease.

16. The use of any one of claims 1-15, wherein the subject has been diagnosed as having polycystic kidney disease using clinical, histopathologic, and/or genetic criteria.

17. The use of any one of claims 1-16, wherein the polycystic kidney disease is autosomal dominant polycystic kidney disease (ADPKD).

18. The use of claim 17, wherein the subject has Mayo Imaging Classification 1C, 1D, or 1E of ADPKD.

19. The use of any one of claims 1-18, wherein the subject, prior to administration of the modified oligonucleotide, has an estimated glomerular filtration rate (eGFR) between 30-90 mL/min/1.73 m^2.

20. The use of any one of claims 1-19, wherein the subject, prior to administration of the modified oligonucleotide, was determined to have a decreased level of polycystin-1 (PC1) and/or polycystin-2 (PC2) in the kidney, urine or blood of the subject.

21. The use of any one of claims 1-20, wherein the subject has a mutation selected from a mutation in the *PKD1* gene or a mutation in the *PKD2* gene.

22. The use of any one of claims 1-21, wherein the subject has increased total kidney volume.

23. The use of any one of claims 1-22, wherein the subject has hypertension.

24. The use of any one of claims 1-23, wherein the subject has impaired kidney function.

25. The use of any one of claims 1-24, wherein the modified oligonucleotide is to be administered at a dose of 1 mg/kg.

26. The use of any one of claims 1-24, wherein the modified oligonucleotide is to be administered at a dose of 2 mg/kg.

27. The use of any one of claims 1-24, wherein the modified oligonucleotide is to be administered at a dose of 3 mg/kg.

28. The use of any one of claims 1-27, wherein the modified oligonucleotide is to be administered once every 2 weeks.

29. The use of any one of claims 1-28, wherein the modified oligonucleotide is to be administered at least 7 times.

30. The use of any one of claims 1-29, wherein the modified oligonucleotide is to be administered subcutaneously.

31. The use of any one of claims 1-30, wherein the treatment reduces total kidney volume in the subject.

32. The use of any one of claims 1-31, wherein the treatment slows the rate of increase of total kidney volume in the subject.

33. The use of claim 31 or 32, wherein the total kidney volume is height-adjusted total kidney volume (htTKV).

34. The use of any one of claims 1-33, wherein the treatment slows the rate of decline of glomerular filtration rate in the subject.

35. The use of any one of claims 1-34, wherein the treatment increases glomerular filtration rate in the subject.

36. The use of claim 34 or 35, wherein the glomerular filtration rate is estimated glomerular filtration rate.

37. The use of any one of claims 1-36, wherein the treatment inhibits or slows the increase in the growth of cysts in the kidney and/or liver of the subject.

38. The use of claim 37, wherein the treatment inhibits or slows the increase in total cyst volume, number and/or size distribution.

39. The use of any one of claims 1-38, wherein the treatment:

a) improves or slows the rate of decrease of creatinine clearance in the subject;

b) reduces or slows the rate of increase of albumin:creatinine ratio in the subject;

c) reduces or slows the rate of increase of blood urine nitrogen (BUN) level in the subject;

d) reduces or slows the rate of increase of serum creatinine (SCr) level in the subject;

e) increases polycystin-1 (PC1) in the urine of the subject;

f) increases polycystin-2 (PC2) in the urine of the subject;

g) reduces or slows the rate of increase of neutrophil gelatinase-associated lipocalin (NGAL) protein in the urine of the subject; and/or

h) reduces or slows the rate of increase of kidney injury molecule-1 (KIM-1) protein in the urine of the subject.

40. The use of any one of claims 1-39, wherein the treatment:

a) reduces or slows the rate of increase of monocyte chemoattractant protein-1 (MCP-1) in the urine of the subject;

b) reduces or slows the rate of increase of beta-2 microglobulin (B2M) in the urine of the subject;

c) reduces or slows the rate of increase of complement split products C3a and/or Bb in the plasma of the subject;

d) reduces or slows the rate of increase of serum insulin-like growth factor binding protein acid labile subunit (IGFALS) in the subject;

e) reduces or slows the rate of increase of serum copeptin (CT-proAVP) in the subject;

f) reduces or slows the rate of increase of serum N-acetyl-1-methylhistidine in the subject; and/or

g) reduces or slows the rate of increase of acute phase proteins in the subject.

41. The use of any one of claims 1-40, wherein the treatment results in little to no CNS impairment in the subject.

42. The use of claim 41, wherein the treatment results in little to no change in the Scale for the Assessment and Rating of Ataxia (SARA) test score for the subject.

43. The use of any one of claims 1-42, wherein

a) height-adjusted total kidney volume (HtTKV) is to be measured in the subject;

b) polycystin-1 (PC1) is to be measured in the urine of the subject;

c) polycystin-2 (PC2) is to be measured in the urine of the subject;

d) blood urea nitrogen (BUN) level is to be measured in the subject;

e) serum creatinine (SCr) level is to be measured in the subject;

f) creatinine clearance is to be measured in the subject;

g) urine albumin:creatinine ratio (UACR) is to be measured in the subject;

h) estimated glomerular filtration rate (eGFR) is to be measured in the subject;

i) neutrophil gelatinase-associated lipocalin (NGAL) protein is to be measured in the urine of the subject;

j) kidney injury molecule-1 (KIM-1) protein is to be measured in the urine of the subject;

k) monocyte chemoattractant protein-1 (MCP-1) is to be measured in the urine of the subject;

l) beta-2 microglobulin (B2M) is to be measured in the urine of the subject;

m) serum insulin-like growth factor binding protein acid labile subunit (IGFALS) is to be measured in the subject;

n) serum copeptin (CT-proAVP) is to be measured in the subject;

o) serum N-acetyl-1-methylhistidine is to be measured in the subject;

p) complement split products C3a and/or Bb is to be measured in the plasma of the subject; and/or

q) total cyst volume, number and/or size distribution is to be measured in the subject; and/or

r) SARA test score for the subject is to be measured.

44. The use of any one of claims 1-43, wherein the subject is a human subject.

45. The use of any one of claims 1-44, which has an acceptable safety and tolerability profile.