What is claimed is:

1. Use of a modified oligonucleotide in the manufacture of a medicament for treating Alport syndrome, wherein two or more doses of the modified oligonucleotide are to be administered to a subject having Alport syndrome, wherein the modified oligonucleotide consists of 19 linked nucleosides and has the structure 5'-$A_EC_SATC_SAGTC_STGAU_SAAGC_STA_E$-3' (SEQ ID NO: 3), where nucleosides not followed by a subscript are β-D-deoxyribonucleosides; nucleosides followed by a subscript "E" are 2'-MOE nucleosides; nucleosides followed by a subscript "S" are S-cEt nucleosides, and each internucleoside linkage is a phosphorothioate internucleoside linkage, and wherein a dose of 1.5 mg/kg is to be administered at a frequency of two weeks between doses.

2. The use of claim 1, wherein the dose is to be delivered in a pharmaceutically acceptable diluent.

3. The use of claim 2, wherein the pharmaceutically acceptable diluent is a saline solution.

4. The use of claim 3, wherein the saline solution is a 0.3% sodium chloride solution.

5. The use of any one of claims 2 to 4, wherein the concentration of the modified oligonucleotide in the pharmaceutically acceptable diluent is at least 110 mg/mL.

6. The use of any one of claims 1 to 5, wherein the dose is a single bolus injection of 110 mg/mL of the modified oligonucleotide.

7. The use of any one of claims 1 to 6, wherein the modified oligonucleotide is to be administered as a subcutaneous injection.

8. The use of claim 7, wherein the subcutaneous injection is to be administered in the anterior abdominal wall of the subject.

9. The use of any one of claims 1 to 8, wherein the subject has been diagnosed with Alport syndrome by clinical, histopathologic, and/or genetic criteria.

10. The use of any of claims 1 to 9, wherein the subject has an estimated glomerular filtration rate of 30 ml/min/1.73 m^2 prior to receiving the first dose of the modified oligonucleotide.

11. The use of claim 15, wherein the subject has an estimated glomerular filtration rate (eGFR) between 45 and 90 ml/min/1.73 m^2 prior to receiving the first dose of the modified oligonucleotide.

12. The use of any one of claims 1 to 11, wherein the estimated glomerular filtration rate of the subject is declining at a rate ≥5 ml/min/1.73 m^2/year prior to receiving the first dose of the modified oligonucleotide.

13. The use of any one of claims 1 to 12, wherein the subject is male, has been diagnosed with X-linked Alport syndrome, and is between 18 and 30 years of age.

14. The use of any one of claims 1 to 13, wherein the subject has proteinuria of greater than 300 milligrams of protein per gram of creatinine prior to receiving the first dose of the modified oligonucleotide.

15. The use of any one of claims 1 to 14, wherein the subject, following administration of the modified oligonucleotide, experiences an improvement in one or more parameters associated with Alport syndrome selected from the group consisting of:
    a. estimated glomerular filtration rate;
    b. rate of decline in estimated glomerular filtration rate; and
    c. quality of life using the Short Form 36 Health Survey®.

16. The use of any one of claims 1 to 15, wherein the subject, following administration of the modified oligonucleotide, exhibits an improvement in one or more renal biomarkers selected from the group consisting of:
    a. miR-21 in biopsy tissue;
    b. blood urea nitrogen;
    c. urine protein/albumin ratio;
    d. urine albumin/creatine ratio;
    e. creatinine;
    f. urine podocyturia;
    g. kidney injury molecule-1;
    h. beta-2 microglobulin;
    i. clusterin;
    j. cystatin C;
    k. asymmetric dimethylarginine;
    l. transforming growth factor-beta;
    m. connective tissue growth factor; and
    n. neutrophil gelatinase-associated lipocalin.

17. The use of any one of claims 1 to 16, wherein one or more of creatinine, cystatin C, kidney injury molecule-1, beta-2 microglobulin, and/or clusterin is measured in a blood sample of the subject.

18. The use of any one of claims 1 to 16, wherein one or more of creatinine, cystatin C, kidney injury molecule-1, beta-2 microglobulin, and/or clusterin is measured in a urine sample of the subject.

19. The use of any one of claims 1 to 18, wherein the subject has been treated with an angiotensin II converting enzyme (ACE) inhibitor for at least 30 days prior to receiving the first dose of the oligonucleotide.

20. The use of any one of claims 1 to 19, wherein the subject has been treated with an angiotensin II receptor blocker (ARB) for at least 30 days prior to receiving the first dose of the oligonucleotide.

21. The use of claim 19 wherein the angiotensin II converting enzyme (ACE) inhibitors is selected from captopril, enalapril, lisinopril, benazepril, quinapril, fosinopril, and ramipril.

22. The use of claim 20 wherein the angiotensin II receptor blockers (ARB) is selected from candesartan, irbesartan, olmesartan, losartan, valsartan, telmisartan, and eprosartan.

23. The use of any one of claims 1 to 22, wherein at least 24 doses are to be administered to the subject.

24. Use of a pharmaceutical composition comprising a modified oligonucleotide in the manufacture of a medicament for treating Alport syndrome in a subject, wherein:

a. the subject has been diagnosed with Alport syndrome using clinical, histopathologic, and/or genetic criteria;

b. two or more doses of the pharmaceutical composition are to be administered to the subject, wherein the modified oligonucleotide consists of 19 linked nucleosides and has the structure 5'-$A_EC_SATC_SAGTC_STGAU_SAAGC_STA_E$-3' (SEQ ID NO: 3), where nucleosides not followed by a subscript are β-D-deoxyribonucleosides; nucleosides followed by a subscript "E" are 2'-MOE nucleosides; nucleosides followed by a subscript "S" are S-cEt nucleosides, and each internucleoside linkage is a phosphorothioate internucleoside linkage, wherein the dose of the modified oligonucleotide is 1.5 mg/kg and wherein the doses are to be administered with a frequency of two weeks between doses, and

c. the subject, following administration of the pharmaceutical composition, exhibits an improvement in one or more AS associated parameters selected from:
    i. estimated glomerular filtration rate (eGFR);
    ii. rate of decline of eGFR; and
    iii. quality of life (QOL) as measured by the Short Form 36 Health Survey®.

25. Use of a pharmaceutical composition comprising a modified oligonucleotide in the manufacture of a medicament for treating Alport syndrome in a subject, wherein:

a. the subject has been diagnosed with Alport syndrome using clinical, histopathologic, and/or genetic criteria, and has:
    i. an estimated glomerular filtration rate of at least 30 ml/min/1.73 m^2;
    ii. a decline in the rate of estimated glomerular filtration rate of ≥5 ml/min/1.73 m^2/year;
    iii. proteinuria greater equal to or greater than 300 mg protein/g creatinine; and
    iv. been treated with a stable dosing regimen of an ACE inhibitor and/or an ARB for at least 30 days;
b. two or more doses of the pharmaceutical composition are to be administered to the subject, wherein the modified oligonucleotide consists of 19 linked nucleosides and has the structure 5'-$A_ECsATC_SAGTC_STGAU_SAAGC_STA_E$-3' (SEQ ID NO: 3), where nucleosides not followed by a subscript are β-D-deoxyribonucleosides; nucleosides followed by a subscript "E" are 2'-MOE nucleosides; nucleosides followed by a subscript "S" are S-cEt nucleosides, and each internucleoside linkage is a phosphorothioate internucleoside linkage, wherein the dose of the modified oligonucleotide is 1.5 mg/kg and wherein the doses are to be administered with a frequency of two weeks between doses, and

c. the subject, following administration of the pharmaceutical composition, exhibits an improvement in one or more parameters associated with Alport syndrome selected from:
    i. estimated glomerular filtration rate (eGFR);
    ii. rate of decline of eGFR; and
    iii. quality of life (QOL) as measured by the Short Form 36 Health Survey®.

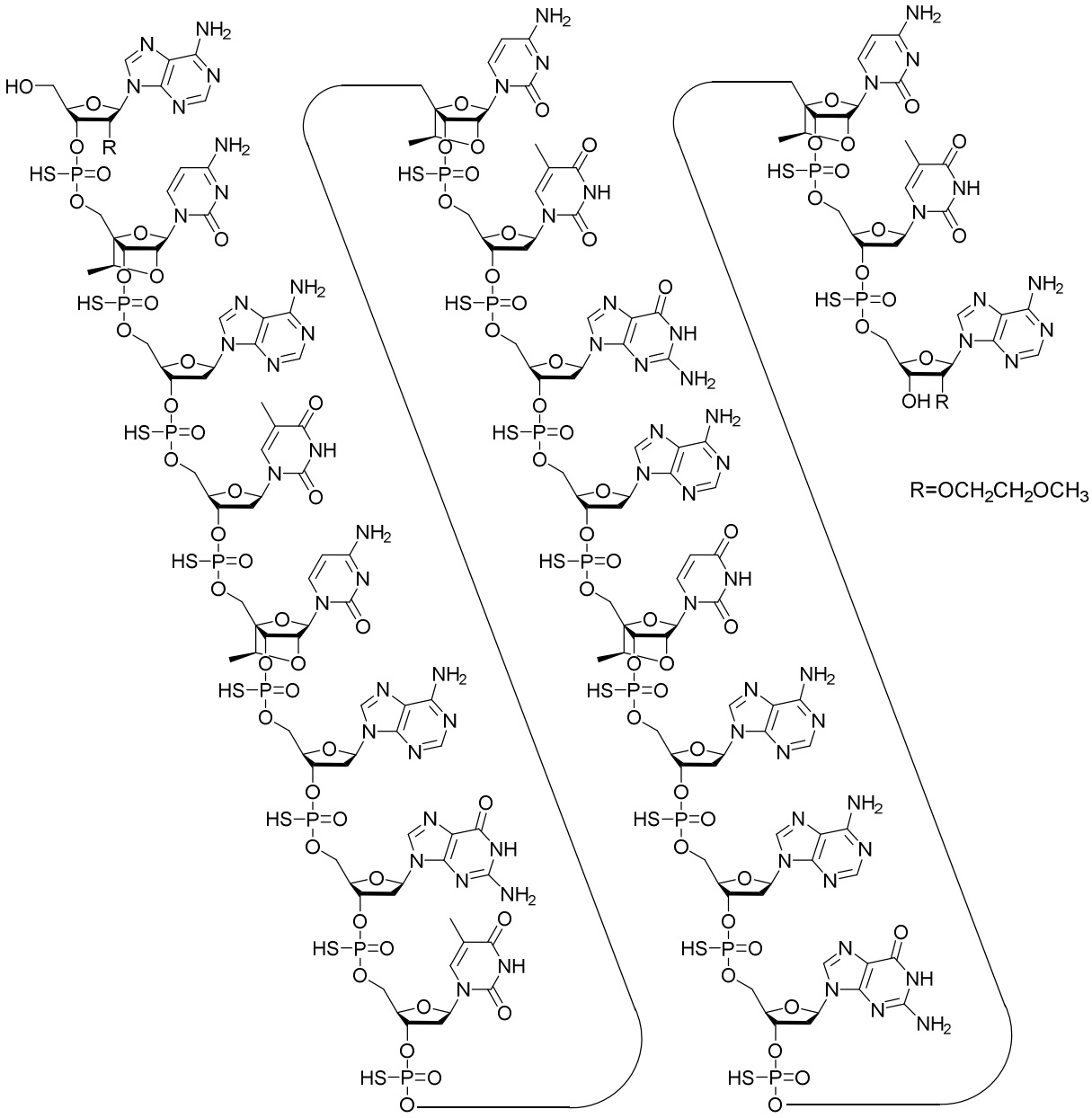
26. Use of a pharmaceutical composition comprising a modified oligonucleotide in the manufacture of a medicament for reducing decline in renal function over time in a subject with Alport syndrome, wherein:

a. the subject is diagnosed with Alport syndrome confirmed by clinical, histopathologic, and/or genetic criteria, and has:
    i. an estimated glomerular filtration rate of at least 30 ml/min/1.73 m^2;
    ii. a decline in the rate of estimated glomerular filtration rate of ≥5 ml/min/1.73 m^2/year;
    iii. proteinuria greater equal to or greater than 300 mg protein/g creatinine; and
    iv. been treated with a stable dosing regimen of an ACE inhibitor and/or an ARB for at least 30 days;

b. two or more doses of the pharmaceutical composition are to be administered to the subject, wherein the modified oligonucleotide consists of 19 linked nucleosides and has the structure 5'-$A_ECsATCsAGTCsTGAUsAAGCsTA_E$-3' (SEQ ID NO: 3), where nucleosides not followed by a subscript are β-D-deoxyribonucleosides; nucleosides followed by a subscript "E" are 2'-MOE nucleosides; nucleosides followed by a subscript "S" are S-cEt nucleosides, and each internucleoside linkage is a phosphorothioate internucleoside linkage, wherein the dose of the modified oligonucleotide is 1.5 mg/kg and wherein the doses are to be administered with a frequency of two weeks between doses, and

c. the subject, following administration of the pharmaceutical composition, exhibits an improvement in one or more Alport syndrome associated parameters selected from:
    i. estimated glomerular filtration rate (eGFR);
    ii. rate of decline of eGFR; and
    iii. quality of life (QOL) as measured by the Short Form 36 Health Survey®.

27. The use of any one of claims 1 to 26, wherein the modified oligonucleotide has the structure:

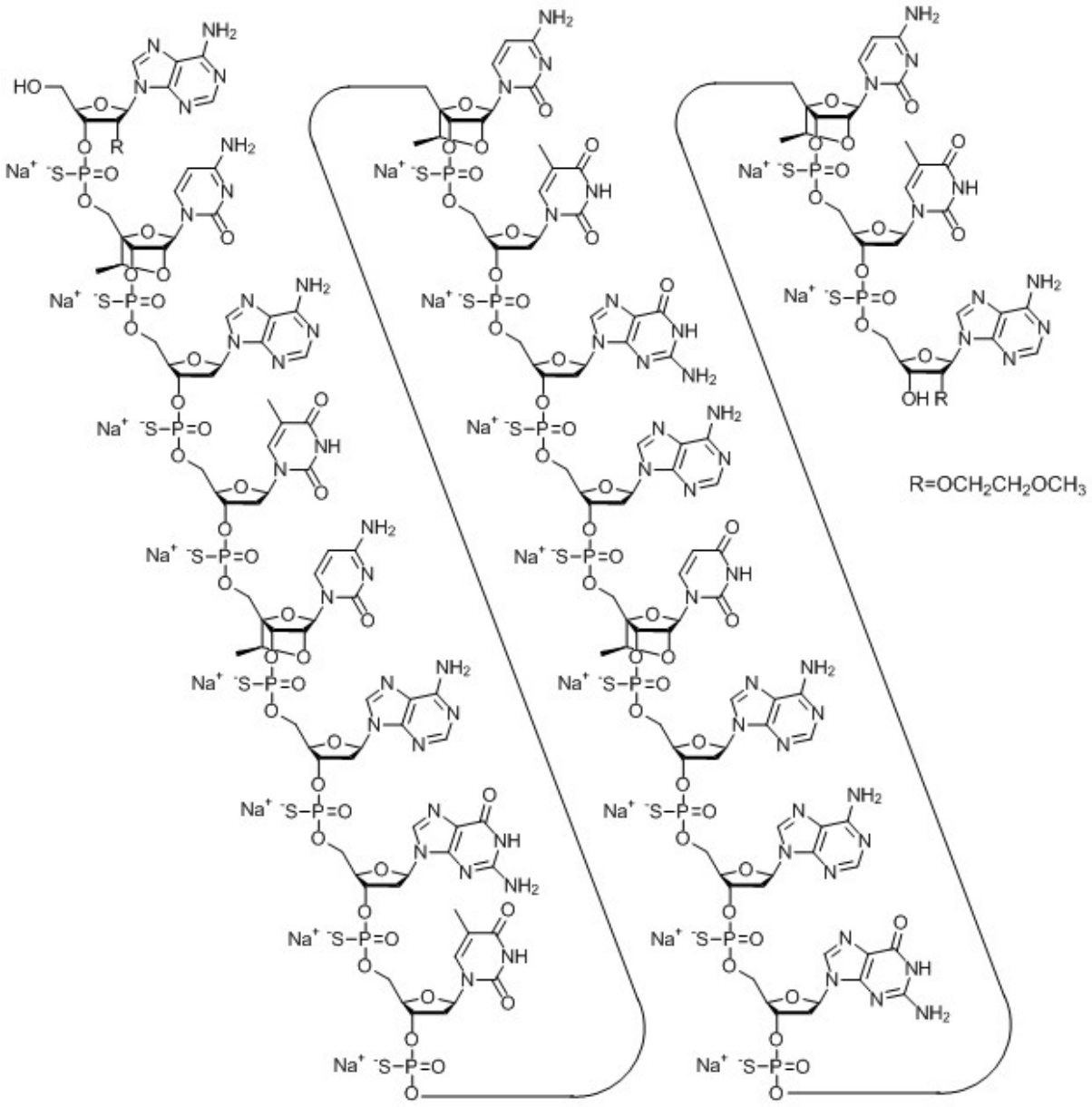


(SEQ ID NO: 3); or a pharmaceutically acceptable salt thereof.

28. The use of claim 27, wherein the modified oligonucleotide is present as a pharmaceutically acceptable salt of the structure.

29. The use of claim 28, wherein the modified oligonucleotide is present as a sodium salt of the structure.

30. The use of any one of claims 1 to 29, wherein the modified oligonucleotide has the structure:



(SEQ ID NO: 3).

31. The use of any one of claims 10 to 30, wherein the estimated glomerular filtration rate is calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation.

32. The use of any one of claims 10 to 30, wherein the estimated glomerular filtration rate is calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine-cystatin C equation.