We claim:

1. A double stranded ribonucleic acid (RNAi) agent for inhibiting expression of angiotensinogen (AGT) in a cell, or a salt thereof, wherein the double stranded RNAi agent comprises a sense strand and an antisense strand forming a double stranded region,

wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from nucleotides 635-653 of SEQ ID NO:1, and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides at the corresponding position of the nucleotide sequence of SEQ ID NO:2,

wherein all of the nucleotides of said sense strand and all of the nucleotides of said antisense strand are modified nucleotides, and

wherein the sense strand is conjugated to a ligand attached at the 3'-terminus.

2. The double stranded RNAi agent of claim 1, or salt thereof, wherein at least one of the modified nucleotides is selected from the group consisting of a 3'-terminal deoxy-thymine (dT) nucleotide, a 2'-O-methyl modified nucleotide, a 2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked nucleotide, an unlocked nucleotide, a conformationally restricted nucleotide, a constrained ethyl nucleotide, an abasic nucleotide, a 2'-amino-modified nucleotide, a 2'-alkyl-modified nucleotide, a morpholino nucleotide, a phosphoramidate, a non-natural base comprising nucleotide, a nucleotide comprising a 5'-phosphorothioate group, and a terminal nucleotide linked to a cholesteryl derivative or a dodecanoic acid bisdecylamide group.

3. The double stranded RNAi agent of claim 1, or salt thereof, wherein at least one strand comprises a 3' overhang of at least 1 nucleotide; or at least one strand comprises a 3' overhang of at least 2 nucleotides.

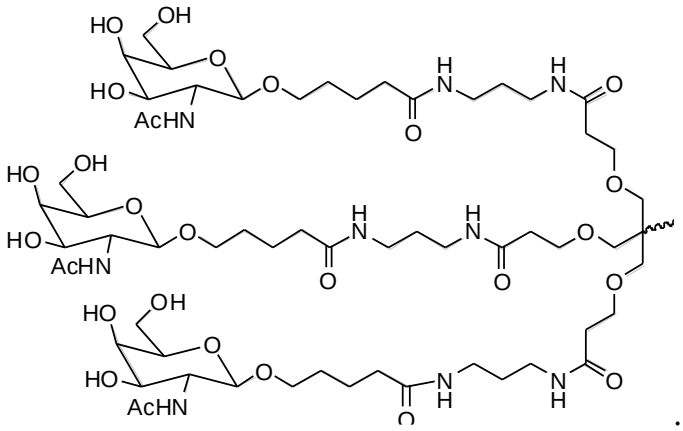
4. The double stranded RNAi agent of claim 1, or salt thereof, wherein the double stranded region is 15-30 nucleotide pairs in length; 17-23 nucleotide pairs in length; 17-25

nucleotide pairs in length; 23-27 nucleotide pairs in length; 19-21 nucleotide pairs in length; or 21-23 nucleotide pairs in length.

5. The double stranded RNAi agent of claim 1, or salt thereof, wherein each strand is independently 15-30 nucleotides in length; or 19-30 nucleotides in length.

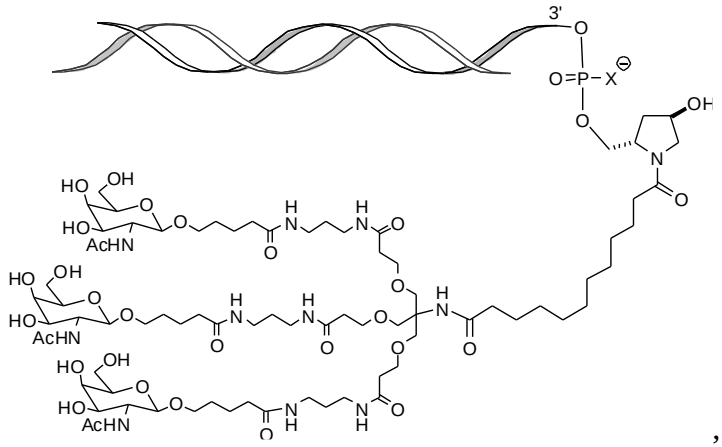
6. The double stranded RNAi agent of claim 1, or salt thereof, wherein the ligand is one or more GalNAc derivatives attached through a bivalent or trivalent branched linker.

7. The double stranded RNAi agent of claim 1, or salt thereof, wherein the ligand is



8. The double stranded RNAi agent of claim 1, or salt thereof, wherein the ligand is attached to the 3’ end of the sense strand.

9. The double stranded RNAi agent of claim 8, or salt thereof, wherein the RNAi agent is conjugated to the ligand as shown in the following schematic



,

wherein X is O or S.

10. The double stranded RNAi agent of claim 1, or salt thereof, wherein the RNAi agent further comprises at least one phosphorothioate or methylphosphonate internucleotide linkage.

11. The double stranded RNAi agent of claim 1, or salt thereof, wherein the sense strand is 21 nucleotides in length and the antisense strand is 23 nucleotides in length.

12. A double stranded ribonucleic acid (RNAi) agent for inhibiting expression of angiotensinogen (AGT) in a cell, or a salt thereof, wherein the double stranded RNAi agent comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of 5’-UUACUCUCAUUGUGGAUGA-3’ (SEQ ID NO:876),

wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand are modified nucleotides, and

wherein the sense strand is conjugated to a ligand attached at the 3’-terminus.

13. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the antisense strand comprises at least 17 contiguous nucleotides of 5’-UUACUCUCAUUGUGGAUGA-3’ (SEQ ID NO:876).

14. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the antisense strand comprises at least 19 contiguous nucleotides of 5’-UUACUCUCAUUGUGGAUGA-3’ (SEQ ID NO:876).

15. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the sense strand comprises at least 15 contiguous nucleotides of 5’-UCAUCCACAAUGAGAGUAA-3’ (SEQ ID NO: 679).

16. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the sense strand comprises at least 17 contiguous nucleotides of 5’-UCAUCCACAAUGAGAGUAA-3’ (SEQ ID NO: 679).

17. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the sense strand comprises at least 19 contiguous nucleotides of 5’-UCAUCCACAAUGAGAGUAA-3’ (SEQ ID NO: 679).

18. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the sense strand comprises at least 15 contiguous nucleotides of the nucleotide sequence 5’-UCAUCCACAAUGAGAGUAA-3’ (SEQ ID NO: 679) and the antisense strand comprises at least 15 contiguous nucleotides of the nucleotide sequence of 5’-UUACUCUCAUUGUGGAUGA-3’ (SEQ ID NO:876).

19. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the sense strand comprises the nucleotide sequence 5’-UCAUCCACAAUGAGAGUAA-3’ (SEQ ID

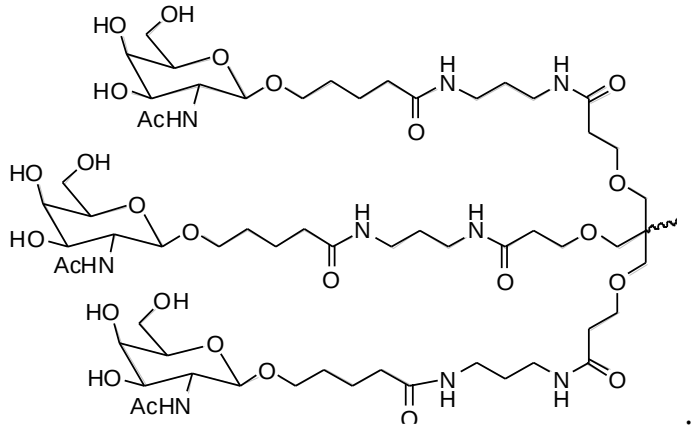
NO: 679) and the antisense strand comprises at least 17 contiguous nucleotides of the nucleotide sequence of 5'-UUACUCUCAUUGUGGAUGA-3' (SEQ ID NO:876).

20. The double stranded RNAi agent of claim 12, or a salt thereof, wherein at least one strand comprises a 3' overhang of at least 2 nucleotides.

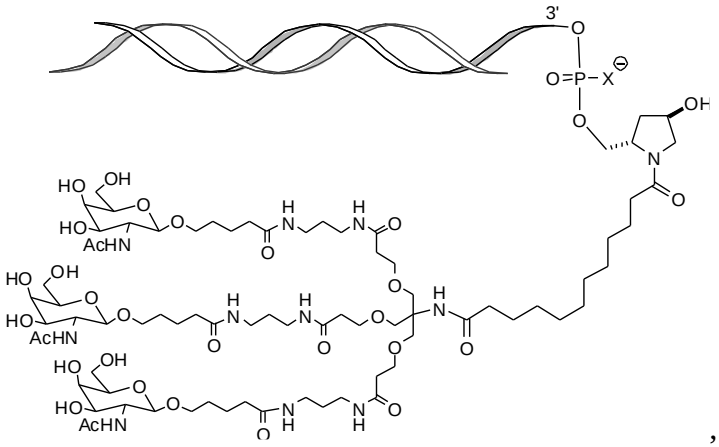
21. The double stranded RNAi agent of claim 12, or a salt thereof, wherein each strand is independently 19-30 nucleotides in length.

22. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the ligand is one or more GalNAc derivatives attached through a bivalent or trivalent branched linker.

23. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the ligand is:



24. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the double stranded RNAi agent is conjugated to the ligand as shown in the following schematic



, wherein X is O or S.

25. The double stranded RNAi agent of claim 12, or a salt thereof, wherein the double stranded RNAi agent further comprises at least one phosphorothioate or methylphosphonate internucleotide linkage.

26. The double stranded RNAi agent of claim 25, or a salt thereof, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at the 3'-terminus of one strand.

27. The double stranded RNAi agent of claim 26, or a salt thereof, wherein the strand is the antisense strand.

28. The double stranded RNAi agent of claim 26, or a salt thereof, wherein the strand is the sense strand.

29. The double stranded RNAi agent of claim 25, or a salt thereof, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at the 5'-terminus of one strand.

30. The double stranded RNAi agent of claim 29, or a salt thereof, wherein the strand is the antisense strand.

31. The double stranded RNAi agent of claim 29, or a salt thereof, wherein the strand is the sense strand.

32. The double stranded RNAi of claim 25, or a salt thereof, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at both the 5'- and 3'-terminus of one strand.

33. The double stranded RNAi of claim 32, or a salt thereof, wherein the one strand is the antisense strand.

34. The double stranded RNAi of claim 25, or a salt thereof, wherein the RNAi agent comprises 6-8 phosphorothioate internucleotide linkages.

35. The double stranded RNAi of claim 25, or a salt thereof, wherein the antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus and two phosphorothioate internucleotide linkages at the 3'-terminus, and the sense strand comprises at least two phosphorothioate internucleotide linkages at either the 5'-terminus or the 3'-terminus.

36. An isolated cell containing the double stranded RNAi agent, or salt thereof, of any one of claims 1-35.

37. A pharmaceutical composition comprising the double stranded RNAi agent, or salt thereof, of any one of claims 1-35.

38. A method of inhibiting angiotensinogen (AGT) expression in a cell, the method comprising:

(a) contacting the cell with the double stranded RNAi agent, or salt thereof, of any one of claims 1-35, or the pharmaceutical composition of claim 37; and

(b) maintaining the cell produced in step (a) for a time sufficient to obtain degradation of the mRNA transcript of a AGT gene, thereby inhibiting expression of the AGT gene in the cell.

39. Use of the double stranded RNAi agent, or salt thereof, of any one of claims 1-35, or the pharmaceutical composition of claim 37 in the manufacture of a medicament for treating a subject having an angiotensinogen (AGT)-associated disorder.

40. The use of claim 39, wherein the subject is a human.

41. The use of claim 39, wherein the angiotensinogen (AGT)-associated disease is selected from the group consisting of hypertension, borderline hypertension, primary hypertension, secondary hypertension, hypertensive emergency, hypertensive urgency, isolated systolic or diastolic hypertension, pregnancy-associated hypertension, diabetic hypertension, resistant hypertension, refractory hypertension, paroxysmal hypertension, renovascular hypertension, Goldblatt hypertension, ocular hypertension, glaucoma, pulmonary hypertension, portal hypertension, systemic venous hypertension, systolic hypertension, labile hypertension; hypertensive heart disease, hypertensive nephropathy, atherosclerosis, arteriosclerosis, vasculopathy, diabetic nephropathy, diabetic retinopathy, chronic heart failure, cardiomyopathy, diabetic cardiac myopathy,glomerulosclerosis, coarctation of the aorta, aortic aneurism, ventricular fibrosis, Cushing's syndrome, and other glucocorticoid excess states including chronic steroid therapy, pheochromocytoma, reninoma, secondary aldosteronism and other mineralocorticoid excess states, sleep apnea, thyroid/parathyroid disease, heart failure, myocardial infarction, angina, stroke, diabetes

mellitus, renal disease, renal failure, systemic sclerosis, intrauterine growth restriction (IUGR) , and fetal growth restriction.

42. The use of claim 39, wherein the angiotensinogen (AGT)-associated disease is hypertension.

43. The use of claim 42, wherein the hypertension is selected from the group consisting of borderline hypertension, primary hypertension, secondary hypertension, hypertensive emergency, hypertensive urgency, isolated systolic or diastolic hypertension, pregnancy-associated hypertension, diabetic hypertension, resistant hypertension, refractory hypertension, paroxysmal hypertension, renovascular hypertension, Goldblatt hypertension, ocular hypertension, glaucoma, pulmonary hypertension, portal hypertension, systemic venous hypertension, systolic hypertension, labile hypertension; hypertensive heart disease, and hypertensive nephropathy.

44. The use of claim 39, wherein the double stranded RNAi agent or a salt thereof, is to be subcutaneously administered to the subject.

45. The use of claim 39, wherein an additional therapeutic agent is to be further administered to the subject.

46. The use of claim 45, wherein the additional therapeutic agent is selected from the group consisting of a diuretic, an angiotensin converting enzyme (ACE) inhibitor, an angiotensin II receptor antagonist, a beta-blocker, a vasodilator, a calcium channel blocker, an aldosterone antagonist, an alpha2-agonist, a renin inhibitor, an alpha-blocker, a peripheral acting adrenergic agent, a selective D1 receptor partial agonist, a nonselective alpha-adrenergic antagonist, a synthetic, steroidal antimineralocorticoid agent, or a combination of

any of the foregoing, and a hypertension therapeutic agent formulated as a combination of agents.

47. The double stranded RNAi agent, or salt thereof, of any one of claims 1-35, or the pharmaceutical composition of claim 37 for use in therapy.