CLAIMS

1. A compound comprising a first modified oligonucleotide 14 to 23 linked nucleosides in length having a nucleobase sequence comprising at least 14 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 11-20 and a second modified oligonucleotide 14 to 23 linked nucleosides in length having a region of complementarity to the first modified oligonucleotide.

2. The compound of claim 1, wherein the first modified oligonucleotide has at least 80% complementarity over the length of the first modified oligonucleotide to a region of the nucleobase sequence of SEQ ID NO: 1 or 3.

3. The compound of claim 1 or 2, wherein the first modified oligonucleotide has at least 1 mismatch to a region of SEQ ID NO: 1 or 3 that is the same length as the first modified oligonucleotide.

4. The compound of any one of the preceding claims, wherein the region of complementarity between the first modified oligonucleotide and the second modified oligonucleotide is 14 to 23 linked nucleosides in length.

5. The compound of any one of the preceding claims, wherein the first modified oligonucleotide is fully complementary to the second modified oligonucleotide.

6. The compound of any one of the preceding claims, wherein at least one of the first and second modified oligonucleotides comprises a modified internucleoside linkage, and wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage or a methylphosphonate internucleoside linkage.

7. The compound of any one of the preceding claims, wherein each nucleoside of the first and second modified oligonucleotide comprises a modified sugar.

8. The compound of claim 7, wherein the modified sugar comprises a modification selected from group consisting of LNA, cEt, 2'-MOE, 2'-F, 2'-OMe, and 2'-deoxy, or a combination thereof.

9. The compound of claim 8, wherein the first modified oligonucleotide comprises no more than ten 2'-F sugar modifications, and wherein the second modified oligonucleotide comprises no more than five 2'-F sugar modifications.

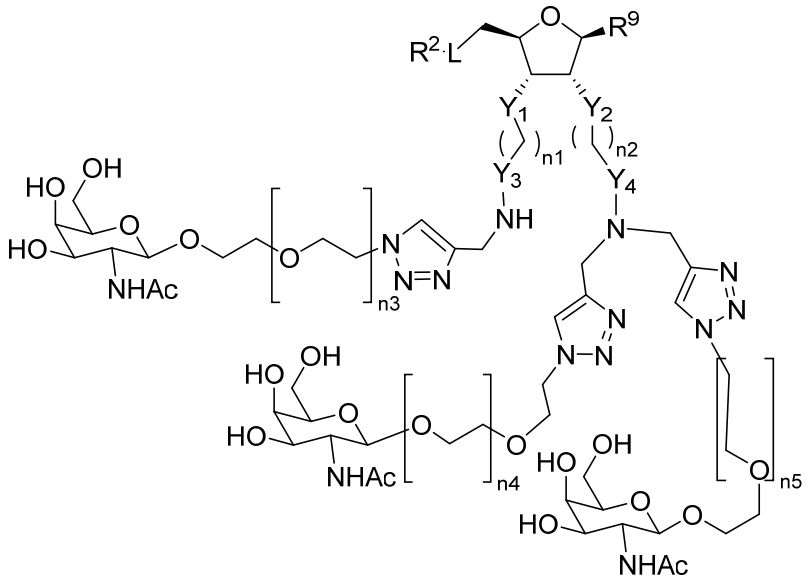
10. The compound of any preceding claim, further comprising a conjugate group.

11. The compound of claim 10, wherein the conjugate group is attached to the 5’ end of the second modified oligonucleotide.

12. The compound of claim 11, wherein the conjugate group comprises one or more GalNAc.

13. The compound of claim 12, wherein the one or more GalNAc are attached to the 2’ and/or 3’ position of the ribosyl ring of the 5’ nucleoside of the second modified oligonucleotide.

14. The compound of claim 13, wherein the 5’ nucleoside is of the following formula:



Formula X,

wherein:

R^9 is H, adenine, guanine, thymine, cytosine, or uracil, or adenine, guanine, thymine, cytosine, or uracil, each comprising a protecting group, a modified nucleobase, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, or a nucleobase isostere;

L is a bond, a phosphodiester bond, a phosphorothioate bond, a triazole, a tetrazole, an amide, a reverse-amide, a carbamate, a carbonate, urea, alkyl, or heteroalkyl;

R^2 is the remainder of the second modified oligonucleotide;

Y_1 is O, CH_2, CH_2O, or optionally substituted NH;

Y_2 is O, CH_2, CH_2O, or optionally substituted NH;

Y_3 is CO, SO_2, P(O)O, CH_2-O-C(O), CH_2-NH-C(O), CH_2-NH-SO_2, or CH_2;

Y_4 is CO, SO_2, P(O)O, CH_2-O-C(O), CH_2-NH-C(O), CH_2-NH-SO_2, or CH_2;

n_2 is 0, 1, 2, 3, 4, 5, or 6; and

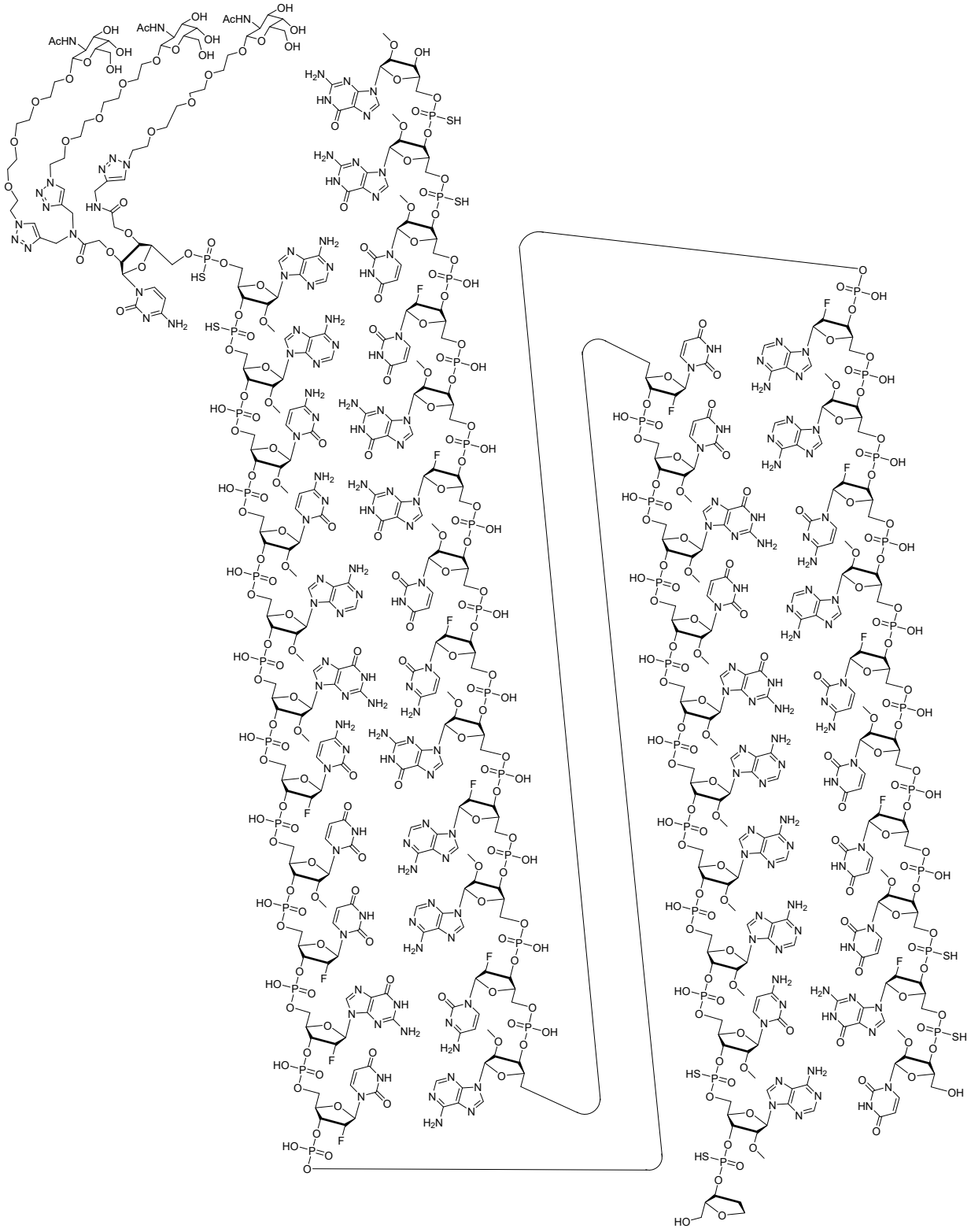
each n_1, n_3, n_4 and n_5 is independently 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

15. The compound of claim 13, wherein the 5' nucleoside is selected from any one of Formulae I-VIII and wherein R' is S or O, and R is the portion of the modified oligonucleotide other than the 5' nucleoside.

16. A compound comprising a first modified oligonucleotide selected from the group consisting of any one of Ref ID NOs: IA0500, IA1019, IA1022-1024, IA1027, IA1093-1095, and IA1103, and a second modified oligonucleotide 14 to 21 linked nucleosides in length fully complementary to the first modified oligonucleotide.

17. A compound comprising a first modified oligonucleotide selected from the group consisting of Ref ID NOs: IA0500, IA1019, IA1022-1024, IA1027, IA1093-1095, and IA1103 and a second modified oligonucleotide selected from the group consisting of Ref ID NOs: IS1255, IS1258, IS1259, IS1260, IS1279, IS1280, IS1372-1375, IS1381, and IS1382.

18. A compound according to the following chemical structure:



or a pharmaceutically acceptable salt or stereoisomer thereof.

19. The compound of any preceding claim, wherein the compound is in a pharmaceutically acceptable salt form, and wherein the pharmaceutically acceptable salt is a sodium salt or a potassium salt.

20. A composition comprising the compound of any preceding claim and a pharmaceutically acceptable carrier.

21. Use of the compound of any one of claims 1-19 or composition of claim 20 in the manufacture of a medicament for treating, preventing, or ameliorating a disease, disorder or condition associated with AGT.

22. The use of claim 21, wherein the disease is a RAAS related disease, disorder or condition or a symptom thereof, hypertension, resistant hypertension, fibrosis, kidney disease, chronic kidney disease, cardiovascular disease, coronary heart disease, heart failure, stroke, myocardial infarction, atrial fibrillation, aneurysm and peripheral artery disease, organ damage, heart damage, liver damage, kidney damage, inflammatory bowel disease, and/or cognitive impairment.