CLAIMS

What is claimed is:

1. A compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides having a nucleobase sequence comprising a portion of at least 8 contiguous nucleobases complementary to an equal length portion of nucleobases 2250 to 2337 of SEQ ID NO: 1, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to SEQ ID NO: 1.

2. A compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides having a nucleobase sequence comprising a portion of at least 8 contiguous nucleobases complementary to an equal length portion of nucleobases 2281 to 2300 of SEQ ID NO: 1, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to SEQ ID NO: 1.

3. The compound of claim 1 or 2, wherein the modified oligonucleotide consists of 15 to 30, 15 to 25, 15 to 24, 16 to 24, 17 to 24, 18 to 24, 19 to 24, 20 to 24, 19 to 22, 20 to 22, 16 to 20, 16 or 20 linked nucleosides.

4. The compound of claim 1 or 2, wherein the modified oligonucleotide comprises a nucleobase sequence comprising a portion of at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or at least 20 contiguous nucleobases complementary to an equal length portion of SEQ ID NO: 1

5. The compound of any preceding claim, wherein the nucleobase sequence of the modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to SEQ ID NO: 1

6. A compound comprising a modified oligonucleotide comprising 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of the nucleobase sequence of SEQ ID NOs: 14-2051.

7. A compound comprising a modified oligonucleotide comprising 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of the nucleobase sequence of SEQ ID NOs: 46, 53-54, 61, 68, 76, 83, 85, 93, 96-97, 109, 127, 129-130, 132, 134-15, 137-39, 142, 163-172, 180-184, 186, 189, 234, 236, 238-239, 267, 313, 411, 452, 463-470, 475-478, 480, 500-503, 512, 517-518, 524-526, 654, 689, 702, 725-726, 728, 738, 779, 786-787, 800, 808, 810-811, 825, 865, 868, 889, 894, 903,

905, 909, 954, 966, 1011, 1015, 1021, 1024, 1080, 1085, 1258-1259, 1261-1262, 1293-1294, 1299, 1325, 1470, 1472-1473, 1522, 1542, 1604, 1623-1624, 1667, 1670, 1682-1683, 1687, 1700, 1703-1704, 1708, 1714, 1716, 1719-1720, 1724-1726, 1729-1730, 1827, 1936, 1843-1844, 1846, 1886, 1893-1894, 1914, 1923, 1925, 1932, 1979, 1986, 1988, 1990, 2003, 2015, 2018, 2020, 2027-2028, 2035, 2037, 2039, 2044.

8. A compound comprising a modified oligonucleotide comprising 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of the nucleobase sequence of SEQ ID NOs: 238, 1714, 1719, 1893-1894, 1914, 1923, 1925, 2003.

9. A compound comprising a modified oligonucleotide comprising 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of the nucleobase sequence of SEQ ID NO: 1914.

10. The compound of any preceding claim, wherein the compound is single-stranded.

11. The compound of any preceding claim, wherein the compound is double-stranded.

12. The compound of any preceding claim, wherein at least one internucleoside linkage is a modified internucleoside linkage.

13. The compound of claim 12, wherein at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.

14. The compound of claim 12, wherein each modified internucleoside linkage is a phosphorothioate internucleoside linkage.

15. The compound of any preceding claim, wherein the modified oligonucleotide comprises at least one modified sugar.

16. The compound of claim 15, wherein at least one modified sugar is a bicyclic sugar.

17. The compound of claim 15, wherein at least one modified sugar comprises a 2'-O-methoxyethyl, a constrained ethyl (cEt), a 3'-fluoro-HNA or a 4'- $(CH_2)_n$-O-2' bridge, wherein n is 1 or 2.

18. The compound of any preceding claim, wherein at least one nucleoside comprises a modified nucleobase.

19. The compound of claim 18, wherein the modified nucleobase is a 5-methylcytosine.

20. The compound of any preceding claim, wherein the modified oligonucleotide consists of 12 to 30 linked nucleosides and comprises:

a. a gap segment consisting of linked deoxynucleosides;

b. a 5' wing segment consisting of linked nucleosides; and

c. a 3' wing segment consisting of linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar.

21. The compound of claim 20, wherein the modified oligonucleotide consists of 16 to 20 linked nucleobases.

22. The compound of claim 20, wherein the modified oligonucleotide further comprises at least one phosphorothioate internucleoside linkage.

23. The compound of claim 20, wherein the modified oligonucleotide further comprises a modified nucleobase.

24. The compound of claim 20, wherein the modified oligonucleotide consists of 16 to 20 linked nucleosides comprising:

a. a gap segment consisting of ten linked deoxynucleosides;

b. a 5' wing segment consisting of three to five linked nucleosides; and

c. a 3' wing segment consisting of three to five linked nucleosides;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment, wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar, wherein each internucleoside linkage is a phosphorothioate linkage and wherein each cytosine residue is a 5-methylcytosine.

25. A compound comprising a modified oligonucleotide according to the following formula: mCes Aes mCes Aes Aes Ads mCds Ads Ads Gds mCds Tds Gds Gds Tds mCes Ges Ges Tes Te (SEQ ID NO: 1914); wherein,

A = an adenine,

mC = a 5'-methylcytosine

G = a guanine,

T = a thymine,

e = a 2'-O-methoxyethyl modified nucleoside,

d = a 2'-deoxynucleoside, and

s = a phosphorothioate internucleoside linkage.

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

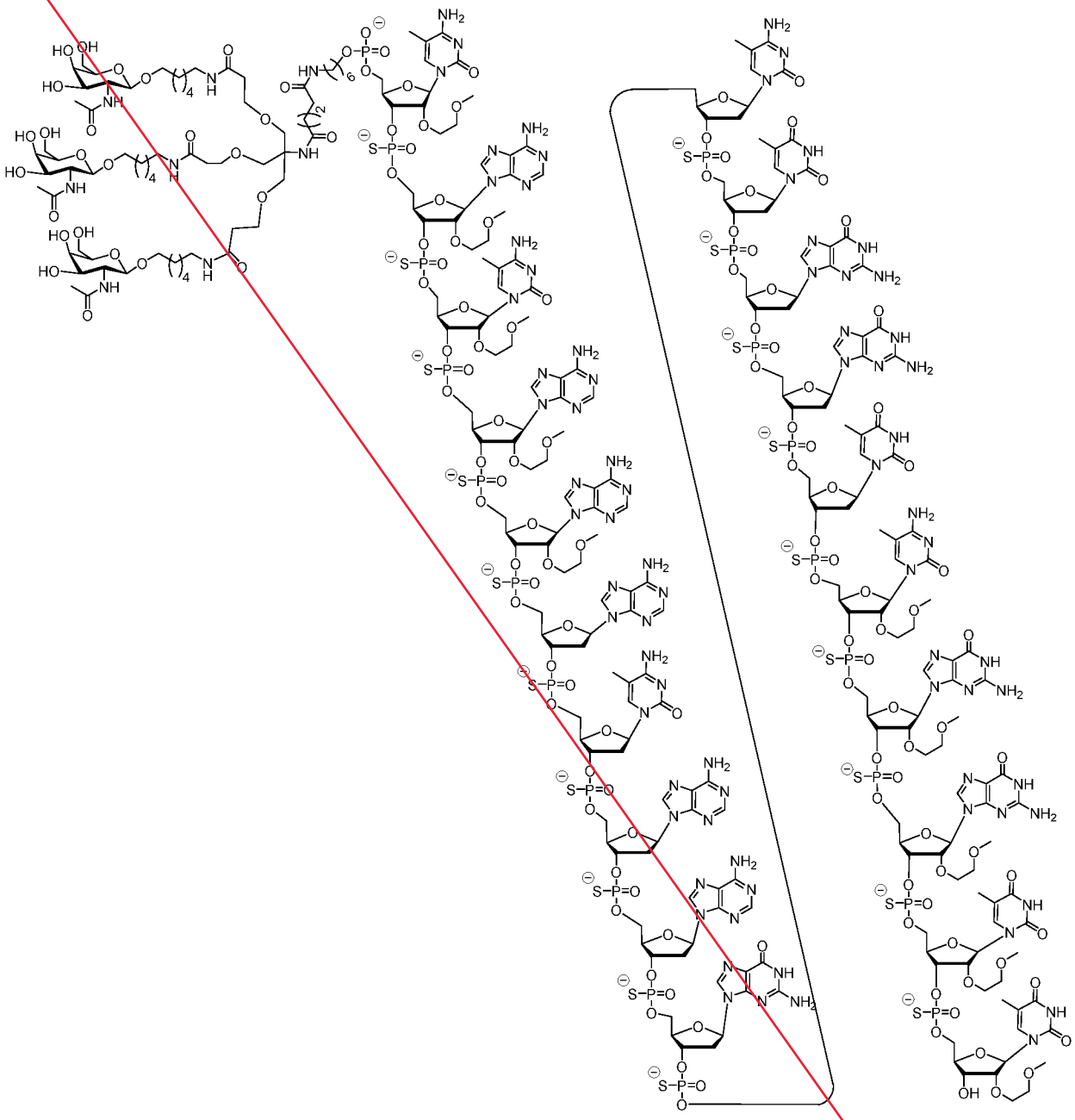
27. The compound of 26, wherein the conjugate group is a GalNAc moiety.

28. A compound comprising a modified oligonucleotide consisting of 20 linked nucleosides having a nucleobase sequence comprising at least 8 contiguous nucleobases of SEQ ID NO: 1914, wherein the modified oligonucleotide comprises:

a. a gap segment consisting of ten linked deoxynucleosides;
b. a 5' wing segment consisting of five linked nucleosides;
c. a 3' wing segment consisting of five linked nucleosides; and
d. a GalNAc conjugate;

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment, wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar, wherein each internucleoside linkage is a phosphorothioate linkage and wherein each cytosine residue is a 5-methylcytosine.

29. A modified oligonucleotide according to the following formula:



30. A composition comprising a compound or modified oligonucleotide of any preceding claim, or a salt thereof, and a pharmaceutically acceptable carrier or diluent.

31. A composition comprising a compound or modified oligonucleotide of any preceding claim, for use in therapy.

32. A composition comprising a compound or modified oligonucleotide of any preceding claim, for use in the preparation of a medicament.

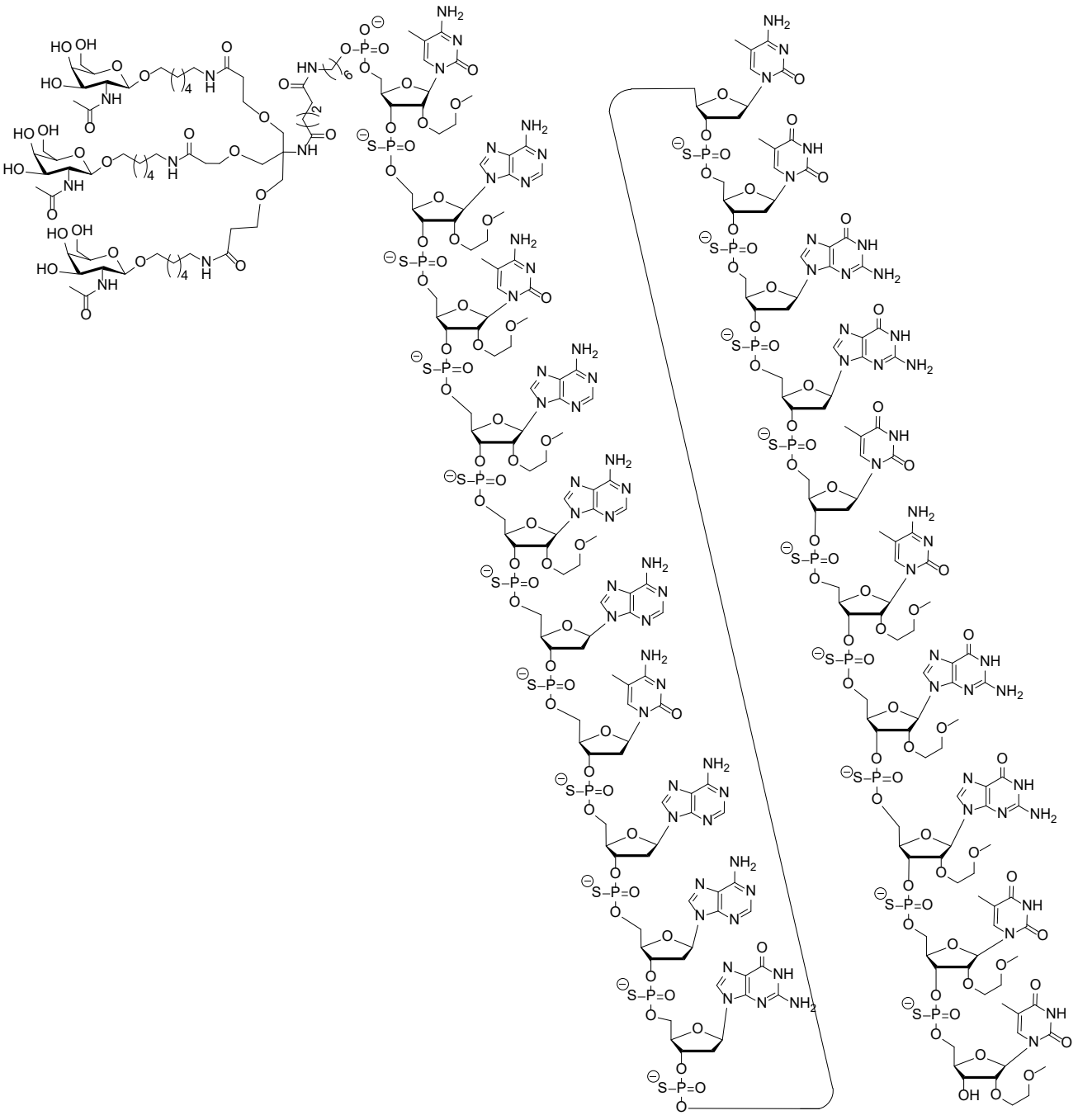
33. The compound or modified oligonucleotide of any preceding claim, for use in reducing AGT in a cell, tissue, organ or animal.

34. The compound or modified oligonucleotide of any preceding claim, for use in treating, preventing, ameliorating or slowing progression of a disease, disorder or condition related to a RAAS pathway related disease, disorder and/or condition in an animal.

35. The compound or modified oligonucleotide of claim 34, wherein the disease, disorder or condition is hypertension.

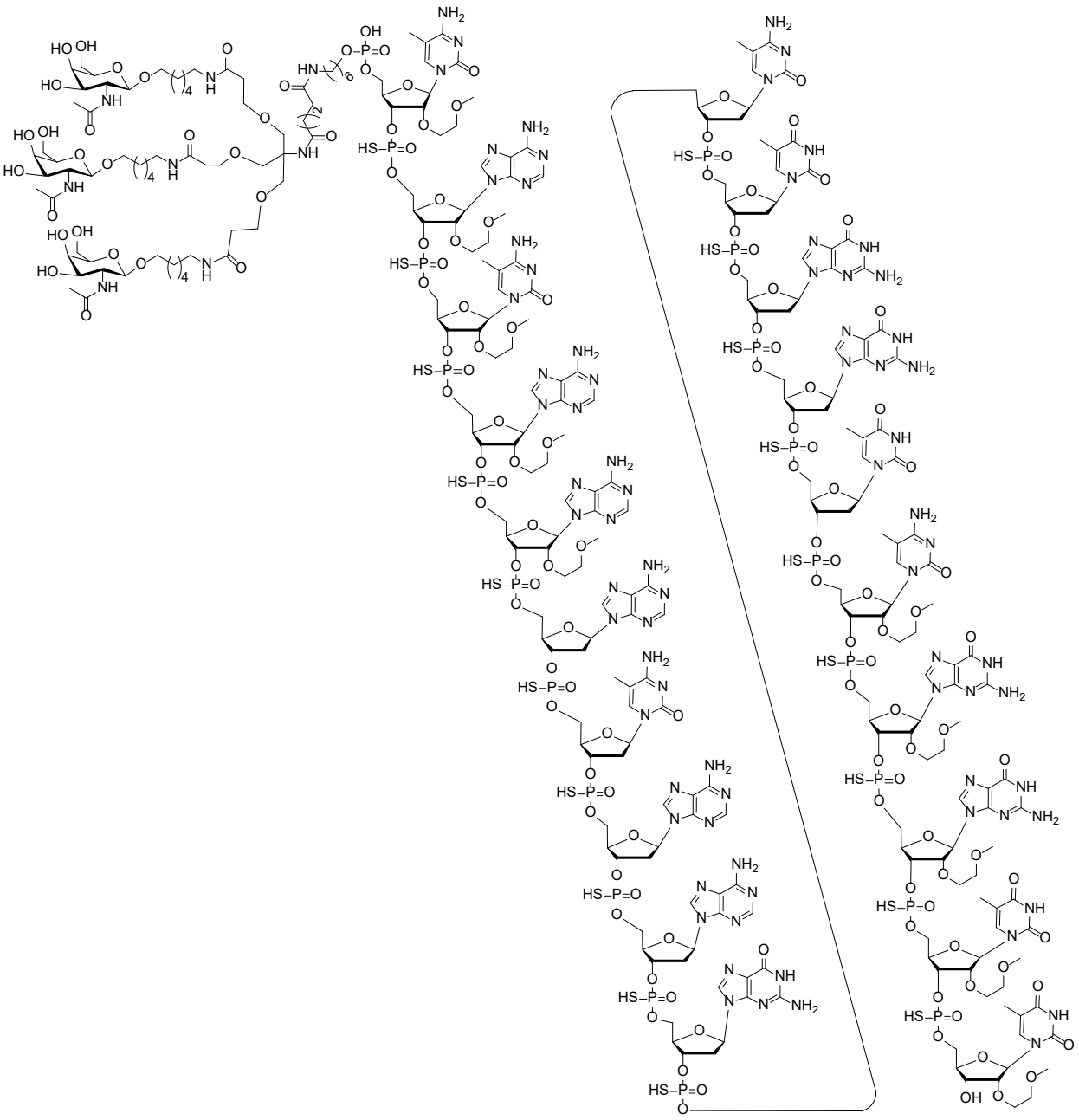
CLAIMS

1. A compound, wherein the anion form of the compound has the following chemical structure:



(SEQ ID NO: 1914).

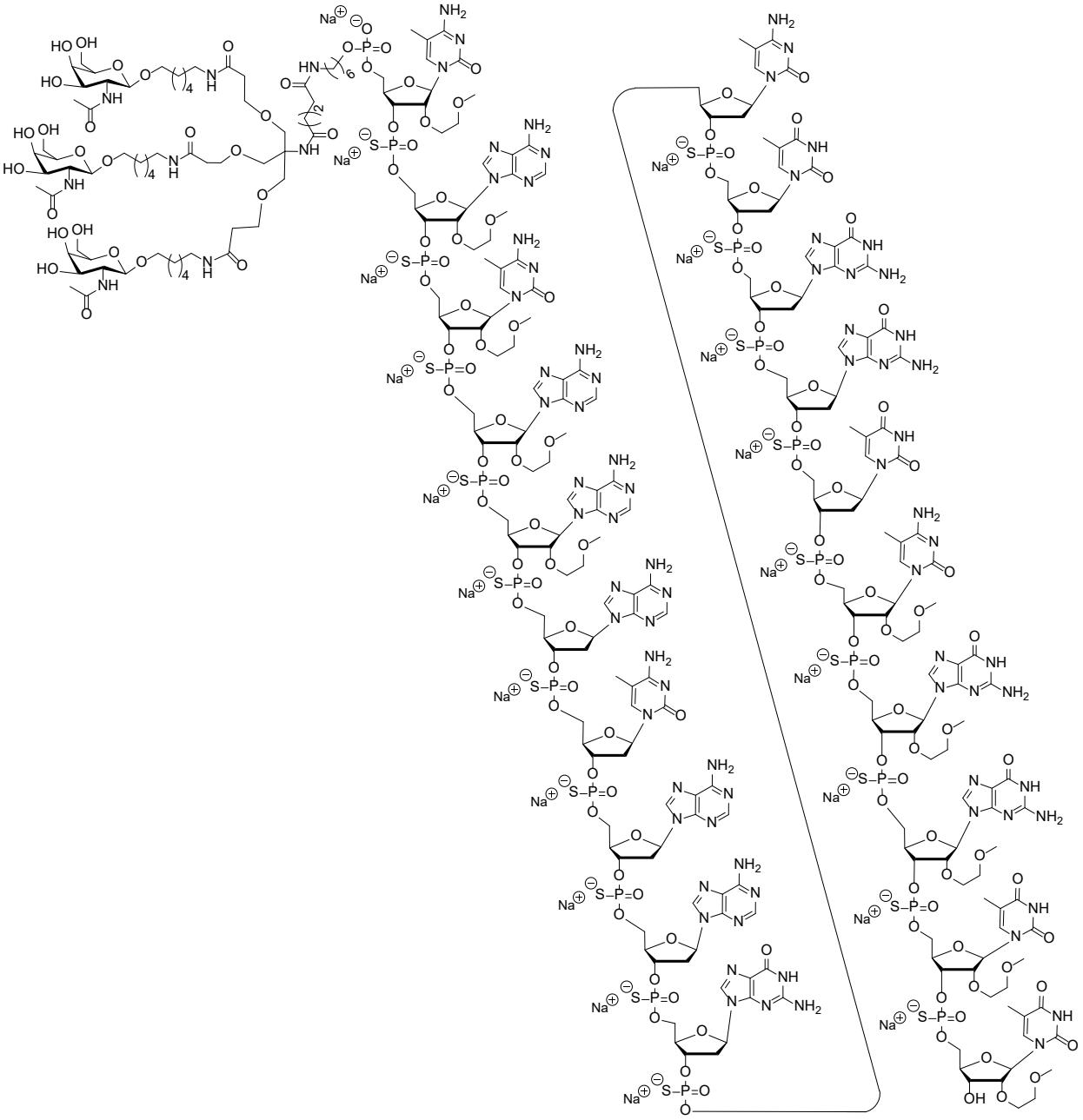
2. A compound according to the following chemical structure:



(SEQ ID NO: 1914), or a salt thereof.

3. The compound of claim 2, which is the sodium salt or the potassium salt.

4. A compound according to the following chemical structure:



(SEQ ID NO: 1914).

5. A compound comprising a modified oligonucleotide according to the following formula: mCes Aes mCes Aes Aes Ads mCds Ads Ads Gds mCds Tds Gds Gds Tds mCes Ges Ges Tes Te (SEQ ID NO: 1914); wherein,

A = an adenine nucleobase,

mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

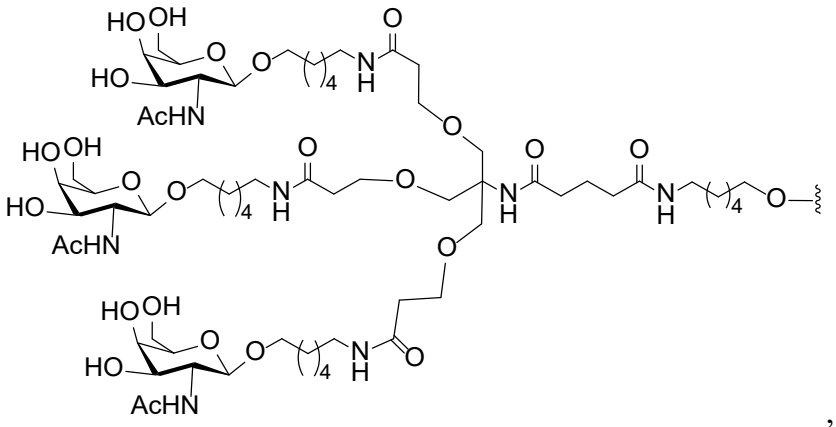
T = a thymine nucleobase,

e = a 2'-$O(CH_2)_2OCH_3$ ribosyl sugar moiety,

d = a 2'-deoxyribosyl sugar moiety, and

s = a phosphorothioate internucleoside linkage,

wherein the compound further comprises a 5'-Trishexylamino-(THA)-C6 $GalNAc_3$ conjugate where the point of attachment of the conjugate to the modified oligonucleotide is the 5' terminal nucleoside, wherein the 5'-Trishexylamino-(THA)-C6 $GalNAc_3$ conjugate has the formula:



,

wherein the modified oligonucleotide is linked to the 5'-Trishexylamino-(THA)-C6 $GalNAc_3$ conjugate by a cleavable moiety, and wherein the cleavable moiety is 5'-P(OH)(=O)-O-3'.

6. A pharmaceutical composition comprising a compound of any preceding claim, and a pharmaceutically acceptable carrier or diluent.

7. A pharmaceutical composition comprising a compound of any of claims 1-5, for use in therapy.

8. A compound of any of claims 1-5, for use in the preparation of a medicament.

9. Use of the compound of any one of claims 1-5 and 8, or the pharmaceutical composition of claim 6 , in the manufacture of a medicament for reducing AGT mRNA and/or AGT protein levels in a cell, tissue, organ or animal.

10. Use of the compound of any one of claims 1-5 and 8, or the pharmaceutical composition of claim 6 , in the manufacture of a medicament for treating, preventing, ameliorating or slowing progression of a RAAS pathway related disease, disorder and/or condition in an animal.

11. The use of claim 10, wherein:

(i) the RAAS pathway related disease, disorder and/or condition is hypertension,

(ii) the RAAS pathway related disease, disorder and/or condition is heart disease, or

(iii) the RAAS pathway related disease, disorder and/or condition is Marfan Syndrome.

12. The use of claim 11 wherein the hypertension is resistant hypertension.

13. The use of claim 11 wherein the heart disease is myocardial infarction, heart failure or valvular heart disease.