

Claims:

1. An RNAi agent for inhibiting expression of a Receptor for Advanced Glycation End-products gene, comprising:
 - an antisense strand comprising at least 17 contiguous nucleotides differing by 0 or 1 nucleotides from any one of the sequences provided in Table 2 or Table 3; and
 - a sense strand comprising a nucleotide sequence that is at least partially complementary to the antisense strand.
2. The RNAi agent of claim 1, wherein the antisense strand comprises nucleotides 2-18 of any one of the sequences provided in Table 2 or Table 3.
3. The RNAi agent of claim 1 or claim 2, wherein the sense strand comprises a nucleotide sequence of at least 17 contiguous nucleotides differing by 0 or 1 nucleotides from any one of the sequences provided in Table 2 or Table 4, and wherein the sense strand has a region of at least 85% complementarity over the 17 contiguous nucleotides to the antisense strand.
4. The RNAi agent of any one of claims 1-3, wherein at least one nucleotide of the RNAi agent is a modified nucleotide or includes a modified internucleoside linkage.
5. The RNAi agent of any one of claims 1-4, wherein all or substantially all of the nucleotides are modified nucleotides.
6. The RNAi agent of any one of claims 4-5, wherein the modified nucleotide is selected from the group consisting of: 2'-O-methyl nucleotide, 2'-fluoro nucleotide, 2'-deoxy nucleotide, 2',3'-seco nucleotide mimic, locked nucleotide, 2'-F-arabino nucleotide, 2'-methoxyethyl nucleotide, abasic nucleotide, ribitol, inverted nucleotide, inverted 2'-O-methyl nucleotide, inverted 2'-deoxy nucleotide, 2'-amino-modified nucleotide, 2'-alkyl-modified nucleotide, morpholino nucleotide, vinyl phosphonate-containing nucleotide, cyclopropyl phosphonate-containing nucleotide, and 3'-O-methyl nucleotide.
7. The RNAi agent of claim 5, wherein all or substantially all of the nucleotides are modified with 2'-O-methyl nucleotides, 2'-fluoro nucleotides, or combinations thereof.
8. The RNAi agent of any one of claims 1-7, wherein the antisense strand comprises the nucleotide sequence of any one of the modified sequences provided in Table 3.
9. The RNAi agent of any one of claims 1-8, wherein the sense strand comprises the nucleotide sequence of any one of the modified sequences provided in Table 4.

10. The RNAi agent of claim 1, wherein the antisense strand comprises the nucleotide sequence of any one of the modified sequences provided in Table 3 and the sense strand comprises the nucleotide sequence of any one of the modified sequences provided in Table 4.
11. The RNAi agent of any one of claims 1-10, wherein the sense strand is between 18 and 30 nucleotides in length, and the antisense strand is between 18 and 30 nucleotides in length.
12. The RNAi agent of claim 11, wherein the sense strand and the antisense strand are each 21 nucleotides in length.
13. The RNAi agent of claim 12, wherein the RNAi agent has two blunt ends.
14. The RNAi agent of any one of claims 1-13, wherein the sense strand comprises one or two terminal caps.
15. The RNAi agent of any one of claims 1-14, wherein the sense strand comprises one or two inverted abasic residues.
16. The RNAi agent of claim 1, wherein the RNAi agent is comprised of a sense strand and an antisense strand that form a duplex having the structure of any one of the duplexes in Table 7A, Table 7B, Table 8, Table 9A, Table 9B, or Table 10.
17. The RNAi agent of claim 16, wherein all or substantially all of the nucleotides are modified nucleotides.
18. The RNAi agent of claim 1, comprising an antisense strand that consists of, consists essentially of, or comprises a nucleotide sequence that differs by 0 or 1 nucleotides from one of the following nucleotide sequences (5' → 3'):
 - UUGUGUUCAGUUCCAUC (SEQ ID NO:55);
 - UGAUGUUUUGAGCACCUAC (SEQ ID NO:65);
 - UCCAUAUCCUGUUCUUGC (SEQ ID NO:73);
 - UUGUGUUCAGUUCCAUCCG (SEQ ID NO:7);
 - UGAUGUUUUGAGCACCUACUC (SEQ ID NO:9); or
 - UCCAUAUCCUGUUCUUGCCU (SEQ ID NO:8).
19. The RNAi agent of claim 18, wherein the sense strand consists of, consists essentially of, or comprises a nucleotide sequence that differs by 0 or 1 nucleotides from one of the following nucleotide sequences (5' → 3'):
 - GAAUGGAAACUGAACACAA (SEQ ID NO:298);

GUAGGUGCUCAAAACAUC (SEQ ID NO:308);
GCAAUGAACAGGAAUIGAA (SEQ ID NO:316);
CGGAAUGGAAACUGAACACAA (SEQ ID NO:19);
GAGUAGGUGCUCAAAACAUC (SEQ ID NO:20); or
AGGCAAUGAACAGGAAUIGAA (SEQ ID NO:21).

20. The RNAi agent of claim 18 or 19, wherein all or substantially all of the nucleotides are modified nucleotides.

21. The RNAi agent of claim 1, comprising an antisense strand that comprises, consists of, or consists essentially of a modified nucleotide sequence that differs by 0 or 1 nucleotides from one of the following nucleotide sequences (5' → 3'):

usUfsgsUfgUfuCfaGfuUfuCfcAfuUfcCfsg (SEQ ID NO:2);
cPrpusUfsgsUfgUfuCfaGfuUfuCfcAfuUfcCfsg (SEQ ID NO:3);
usGfsasuguuugaGfcAfcCfuacusc (SEQ ID NO:5);
cPrpusGfsasuguuugaGfcAfcCfuacusc (SEQ ID NO:6);
usUfscsCfaUfuCfcUfgUfuCfaUfuGfcCfsu (SEQ ID NO:4);

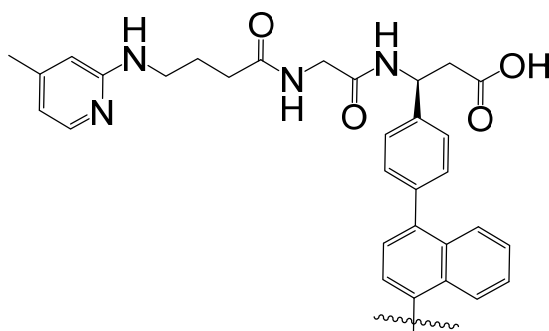
wherein a represents 2'-O-methyl adenosine, c represents 2'-O-methyl cytidine, g represents 2'-O-methyl guanosine, u represents 2'-O-methyl uridine; Af represents 2'-fluoro adenosine, Cf represents 2'-fluoro cytidine, Gf represents 2'-fluoro guanosine, Uf represents 2'-fluoro uridine; cPrpu represents 5'-cyclopropyl phosphonate-2'-O-methyl uridine; s represents a phosphorothioate linkage; and wherein all or substantially all of the nucleotides on the sense strand are modified nucleotides.

22. The RNAi agent of claim 1, wherein the sense strand comprises, consists of, or consists essentially of a modified nucleotide sequence that differs by 0 or 1 nucleotides from one of the following nucleotide sequences (5' → 3'):

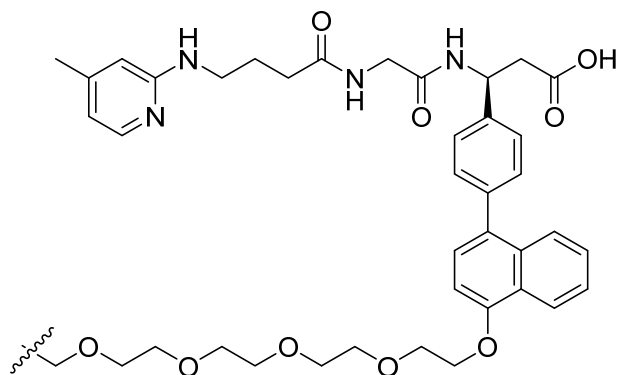
gsaguagGfuGfcUfcaaaacauca (SEQ ID NO:14);
asggcaaugAfAfCfaggaaugaa (SEQ ID NO:15);
csggauggAfAfAfcugaacacaa (SEQ ID NO:13);

wherein a represents 2'-O-methyl adenosine, c represents 2'-O-methyl cytidine, g represents 2'-O-methyl guanosine, i represents 2'-O-methyl inosine, u represents 2'-O-methyl uridine; Af represents 2'-fluoro adenosine, Cf represents 2'-fluoro cytidine, Gf represents 2'-fluoro guanosine, Uf represents 2'-fluoro uridine; and s represents a phosphorothioate linkage; and wherein all or substantially all of the nucleotides on the antisense strand are modified nucleotides.

23. The RNAi agent of any one of claims 18-22, wherein the sense strand further includes inverted abasic residues at the 3' terminal end of the nucleotide sequence, at the 5' end of the nucleotide sequence, or at both.
24. The RNAi agent of any one of claims 1-23, wherein the RNAi agent is linked to a targeting ligand.
25. The RNAi agent of claim 24, wherein the targeting ligand comprises the structure:



or a pharmaceutically acceptable salt thereof, or



or a pharmaceutically acceptable salt

thereof,

wherein indicates the point of connection to the RNAi agent.

- [illegible]

27. The RNAi agent of any one of claims 24-26, wherein the targeting ligand is conjugated to the sense strand.
28. The RNAi agent of claim 27, wherein the targeting ligand is conjugated to the 5' terminal end of the sense strand.
29. The RNAi agent of any of the preceding claims, wherein the RNAi agent is conjugated to a targeting ligand and has the duplex structure of AC000292, AC001266, AC001267, or AC001268.
30. A composition comprising the RNAi agent of any one of claims 1-29, wherein the composition further comprises a pharmaceutically acceptable excipient.
31. The composition of claim 30, further comprising a second RNAi agent capable of inhibiting the expression of Receptor for Advanced Glycation End-products gene expression.
32. The composition of any one of claims 30-31, further comprising one or more additional therapeutics.
33. The composition of any of claims 30-32, wherein the RNAi agent is a sodium salt.
34. The composition of any of claims 30-33, wherein the pharmaceutically acceptable excipient is a buffered saline solution.
35. Use of the composition according to any one of claims 30-34, for the manufacture of a medicament for treatment of a disease, disorder, or symptom that is mediated at least in part by Receptor for Advanced Glycation End-products receptor activity and/or Receptor for Advanced Glycation End-products gene expression.
36. The use of claim 35, wherein the disease is pulmonary inflammation.