We claim:

1. A double stranded RNAi agent that inhibits expression of hydroxyacid oxidase (HAO1) in a cell,

wherein said double stranded RNAi agent comprises a sense strand and an antisense strand forming a double-stranded region,

wherein said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence 5'-UAUAUUUCCAGGAUGAAAGUCCA-3' (SEO ID NO: 706);

wherein all of the nucleotides of said sense strand and all of the nucleotides of said antisense strand comprise a nucleotide modification, and

wherein at least one strand is conjugated to a ligand.

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

3. The double stranded RNAi agent of claim 1, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand independently comprise a 2'-O-methyl nucleotide modification or a 2'-fluoro nucleotide modification.

4. The double stranded RNAi agent of any one of claims 1 to 3, wherein at least one strand comprises a 3' overhang of at least 1 nucleotide.

5. The double stranded RNAi agent of any one of claims 1 to 3, wherein at least one strand comprises a 3’ overhang of at least 2 nucleotides.

6. The double stranded RNAi agent of any one of claims 1 to 5, wherein said agent further comprises at least one phosphorothioate or methylphosphonate internucleotide linkage.

7. The double stranded RNAi agent of claim 6, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at the 3’-terminus of one strand.

8. The double stranded RNAi agent of claim 7, wherein said strand is the antisense strand.

9. The double stranded RNAi agent of claim 7, wherein said strand is the sense strand.

10. The double stranded RNAi agent of claim 6, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at the 5’-terminus of one strand.

11. The double stranded RNAi agent of claim 10, wherein said strand is the antisense strand.

12. The double stranded RNAi agent of claim 10, wherein said strand is the sense strand.

13. The double stranded RNAi agent of claim 6, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at both the 5’- and 3’-terminus of one strand.

14. The double stranded RNAi agent of claim 13, wherein said strand is the antisense strand.

15. The double stranded RNAi agent of claim 6, wherein said double stranded RNAi agent comprises 6-8 phosphorothioate internucleotide linkages.

16. The double stranded RNAi of claim 15, 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.

17. The double stranded RNAi agent of any one of claims 1 to 16, wherein the base pair at the 1 position of the 5′-end of the antisense strand of the duplex is an AU base pair.

18. A double stranded RNAi agent that inhibits expression of hydroxyacid oxidase (HAO1) in a cell,

wherein said double stranded RNAi agent comprises a sense strand and an antisense strand forming a double stranded region,

wherein said sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of GACUUUCAUCCUGGAAAUAUA (SEO ID NO: 589) and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706),

wherein all of the nucleotides of said sense strand independently comprise a modification selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification,

wherein said sense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus,

wherein all of the nucleotides of said antisense strand independently comprise a modification selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification,

wherein said antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus and two phosphorothioate internucleotide linkages at the 3'-terminus, and

wherein said sense strand is conjugated to a ligand which is one or more GalNAc derivatives.

19. The double stranded RNAi agent of any one of claims 1 to 18, wherein the double-stranded region is 15-30 nucleotide pairs in length.

20. The double stranded RNAi agent of any one of claims 1 to 19, wherein each strand is 15-30 nucleotides in length.

21. The double stranded RNAi agent of claim 20, wherein each strand is independently 19-30 nucleotides in length.

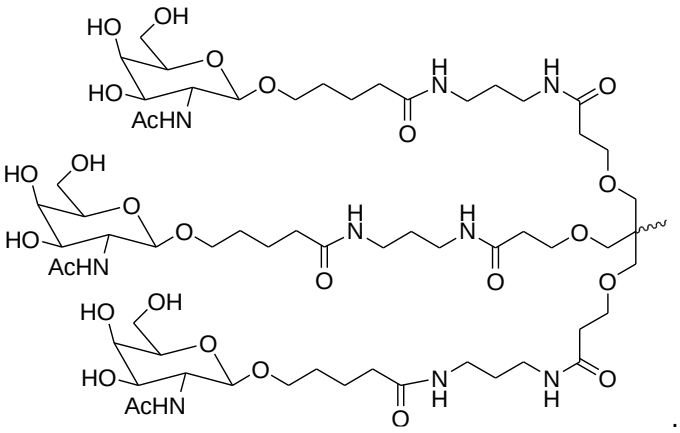
22. The double stranded RNAi agent of claim 20, wherein each strand is independently 19-25 nucleotides in length.

23. The double stranded RNAi agent of claim 20, wherein each strand is independently 19-23 nucleotides in length.

24. The double stranded RNAi agent of any one of claims 1 to 16, wherein the ligand is one or more GalNAc derivatives.

25. The double stranded RNAi agent of any one of claims 1 to 24, wherein the ligand is one or more GalNAc derivatives attached through a bivalent or trivalent branched linker.

26. The double stranded RNAi agent of claim 25, wherein the ligand is



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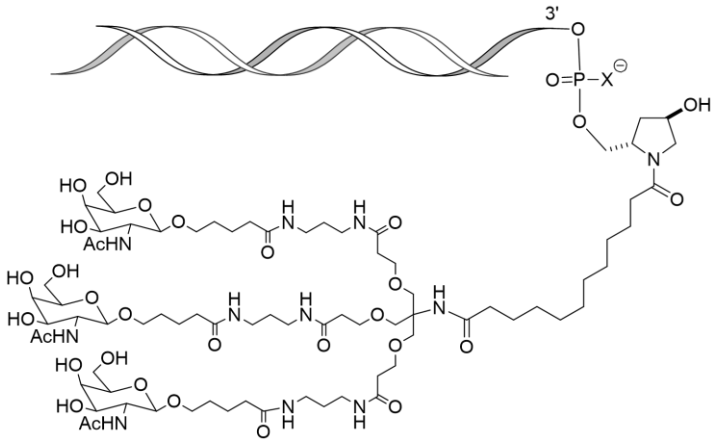
27. The double stranded RNAi agent of any one of claims 1 to 26, wherein the ligand is attached to the 3′ end of the sense strand.

28. The double stranded RNAi agent of claim 27, wherein the double stranded RNAi agent is conjugated to the ligand as shown in the following schematic



wherein X is O or S.

29. The double stranded RNAi agent of any one of claims 1 to 28, wherein the antisense strand comprises at least 17 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706).

30. The double stranded RNAi agent of any one of claims 1 to 29, wherein the sense strand comprises at least 17 contiguous nucleotides differing by no more

than 3 nucleotides from the nucleotide sequence of GACUUUCAUCCUGGAAAUAUA (SEO ID NO: 589) and the antisense strand comprises at least 17 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706).

31. The double stranded RNAi agent of any one of claims 1 to 30, wherein the antisense strand comprises at least 19 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706).

32. The double stranded RNAi agent of any one of claims 1 to 31, wherein the sense strand comprises at least 19 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of GACUUUCAUCCUGGAAAUAUA (SEO ID NO: 589) and the antisense strand comprises at least 19 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706).

33. The double stranded RNAi agent of any one of claims 1 to 32, wherein the antisense strand comprises the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706).

34. The double stranded RNAi agent of any one of claims 1 to 33, wherein the sense strand comprises the nucleotide sequence of GACUUUCAUCCUGGAAAUAUA (SEO ID NO: 589) and the antisense strand comprises the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706).

35. The double stranded RNAi agent of any one of claims 1 to 34, wherein the antisense strand consists of the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706).

36. The double stranded RNAi agent of any one of claims 1 to 35, wherein the sense strand consists of the nucleotide sequence of

GACUUUCAUCCUGGAAAUAUA (SEO ID NO: 589) and the antisense strand consists of the nucleotide sequence UAUAUUUCCAGGAUGAAAGUCCA (SEO ID NO: 706).

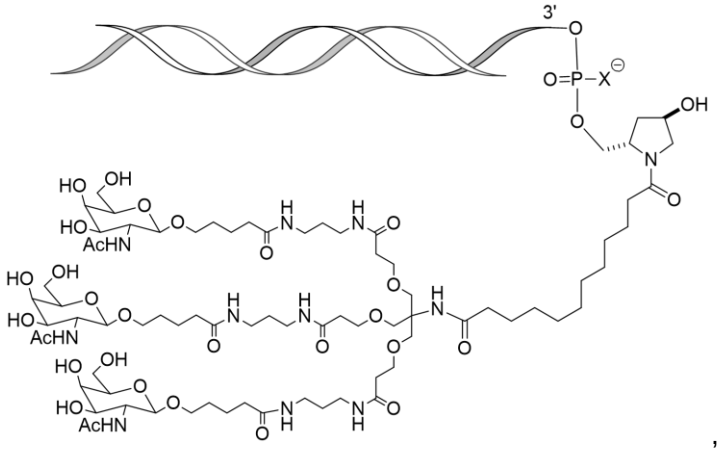
37. The double stranded RNAi agent of any one of claims 1 to 36, wherein the sense strand comprises the nucleotide sequence 5'-gsascuuuCfaUfCfCfuggaaauaua-3' (SEQ ID NO:213) and the antisense strand comprises the nucleotide sequence 5'-usAfsuauUfuCfCfaggaUfgAfaagucscsa-3' (SEQ ID NO:330),

wherein a, g, c, and u are 2'-O-methyl (2'-OMe) modified A, G, C, and U nucleotides, respectively; Af, Gf, Cf, and Uf are 2'fluoro A, G, C, and U modified nucleotides, respectively; and s is a phosphorothioate linkage.

38. The double stranded RNAi agent of any one of claims 1 to 37, wherein the sense strand comprises the nucleotide sequence of 5'-gsascuuuCfaUfCfCfuggaaauaua-3' (SEQ ID NO:213) and the antisense strand comprises the nucleotide sequence 5'-usAfsuauUfuCfCfaggaUfgAfaagucscsa-3' (SEQ ID NO:330),

wherein a, g, c, and u are 2'-O-methyl (2'-OMe) modified A, G, C, and U nucleotides, respectively; Af, Gf, Cf, and Uf are 2'fluoro A, G, C, and U modified nucleotides, respectively; and s is a phosphorothioate linkage,

wherein a ligand is conjugated to the 3' end of the sense strand as shown in the following schematic



, wherein X is O.

39. An isolated cell containing the double stranded RNAi agent of any one of claims 1 to 38.

40. A pharmaceutical composition comprising the double stranded RNAi agent of any one of claims 1 to 38.

41. The pharmaceutical composition of claim 40, wherein the double stranded RNAi agent is present in an unbuffered solution.

42. The pharmaceutical composition of claim 41, wherein the unbuffered solution is water.

43. The pharmaceutical composition of claim 41, wherein the unbuffered solution is saline.

44. The pharmaceutical composition of claim 40, wherein the double stranded RNAi agent is present in a buffer solution.

45. The pharmaceutical composition of claim 44, wherein the buffer solution comprises acetate, citrate, prolamine, carbonate, or phosphate or any combination thereof.

46. The pharmaceutical composition of claim 44, wherein the buffer solution is phosphate buffered saline (PBS).

47. An *in vitro* method of inhibiting HAO1 expression in a cell, the method comprising:

(a) contacting the cell with the double stranded RNAi agent of any one of claims 1 to 38, or the pharmaceutical composition of any one of claims 40 to 46; and

(b) maintaining the cell produced in step (a) for a time sufficient to obtain degradation of the mRNA transcript of a HAO1 gene, thereby inhibiting expression of the HAO1 gene in the cell.

48. Use of the double stranded RNAi agent of any one of claims 1 to 38 or the pharmaceutical composition of any one of claims 40 to 46 in the manufacture of a medicament for treating a subject having a HAO1-associated disorder.

49. The use of claim 48, wherein the subject has primary hyperoxaluria type 1 (PH1).

50. The use of claim 48 or 49, wherein the double stranded RNAi agent is to be administered at a dose of about 0.01 mg/kg to about 10 mg/kg or about 1 mg/kg to about 10 mg/kg.

51. The use of any one of claims 48 to 50, wherein the double stranded RNAi agent is to be subcutaneously administered.

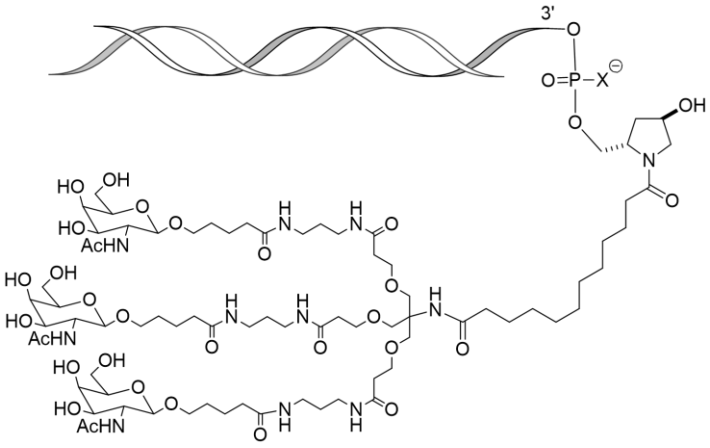
52. The use of any one of claims 48 to 51, wherein said double stranded RNAi agent is to be administered in two or more doses.

53. A double stranded RNAi agent, or salt thereof, that inhibits expression of hydroxyacid oxidase (HAO1) in a cell,

comprising a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises the nucleotide sequence of 5'-gsascuuuCfaUfCfCfuggaaauaua-3' (SEQ ID NO:213) and the antisense strand comprises the nucleotide sequence 5'-usAfsuauUfuCfCfaggaUfgAfaagucscsa-3' (SEQ ID NO:330),

wherein a, g, c, and u are 2'-O-methyl (2'-OMe) modified A, G, C, and U nucleotides, respectively; Af, Gf, Cf, and Uf are 2'fluoro A, G, C, and U modified nucleotides, respectively; and s is a phosphorothioate linkage,

wherein a ligand is conjugated to the 3' end of the sense strand as shown in the following schematic



, wherein X is O.

54. An isolated cell containing the double stranded RNAi agent of claim 53.

55. A pharmaceutical composition comprising the double stranded RNAi agent of claim 53.

56. The pharmaceutical composition of claim 55, wherein the double stranded RNAi agent is present in an unbuffered solution.

57. The pharmaceutical composition of claim 56, wherein the unbuffered solution is water.

58. The pharmaceutical composition of claim 56, wherein the unbuffered solution is saline.

59. The pharmaceutical composition of claim 55, wherein the double stranded RNAi agent is present in a buffer solution.

60. The pharmaceutical composition of claim 59 wherein the buffer solution comprises acetate, citrate, prolamine, carbonate, or phosphate or any combination thereof.

61. The pharmaceutical composition of claim 59, wherein the buffer solution is phosphate buffered saline (PBS).

62. Use of the double stranded RNAi agent of claim 53 or the pharmaceutical composition of any one of claims 55 to 61 in the manufacture of a medicament for treating a subject having an HAO1-associated disorder.

63. The use of claim 62, wherein the subject has primary hyperoxaluria type 1 (PH1).

64. The use of claim 62 or 63, wherein the double stranded RNAi agent is to be administered at a dose of about 0.01 mg/kg to about 10 mg/kg or about 1 mg/kg to about 10 mg/kg.

65. The use of any one of claims 62 to 64, wherein the double stranded RNAi agent is to be subcutaneously administered.

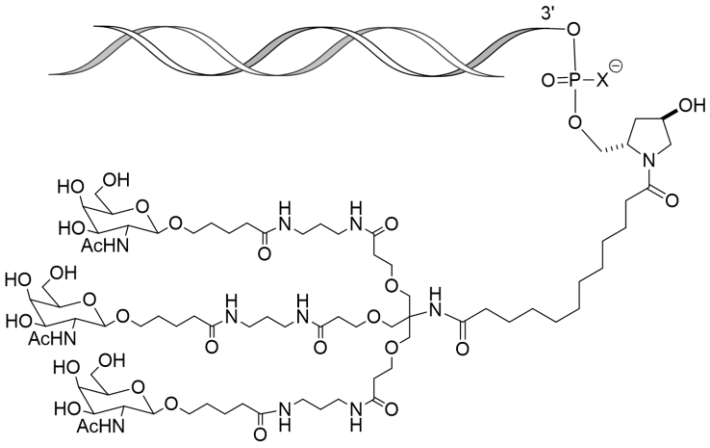
66. The use of any one of claims 62 to 65, wherein said double stranded RNAi agent is to be administered in two or more doses.

67. A double stranded RNAi agent, or salt thereof, that inhibits expression of hydroxyacid oxidase (HAO1) in a cell,

comprising a sense strand and an antisense strand forming a double stranded region, wherein the sense strand consists of the nucleotide sequence of 5'-gsascuuuCfaUfCfCfuggaaauaua-3' (SEQ ID NO:213) and the antisense strand consists of the nucleotide sequence 5'-usAfsuauUfuCfCfaggaUfgAfaagucscsa-3' (SEQ ID NO:330),

wherein a, g, c, and u are 2'-O-methyl (2'-OMe) modified A, G, C, and U nucleotides, respectively; Af, Gf, Cf, and Uf are 2'fluoro A, G, C, and U modified nucleotides, respectively; and s is a phosphorothioate linkage,

wherein a ligand is conjugated to the 3' end of the sense strand as shown in the following schematic



, wherein X is O.

68. An isolated cell containing the double stranded RNAi agent of claim 67.

69. A pharmaceutical composition comprising the double stranded RNAi agent of claim 67.

70. The pharmaceutical composition of claim 69, wherein the double stranded RNAi agent is present in an unbuffered solution.

71. The pharmaceutical composition of claim 70, wherein the unbuffered solution is water.

72. The pharmaceutical composition of claim 70, wherein the unbuffered solution is saline.

73. The pharmaceutical composition of claim 69, wherein the double stranded RNAi agent is present in a buffer solution.

74. The pharmaceutical composition of claim 73 wherein the buffer solution comprises acetate, citrate, prolamine, carbonate, or phosphate or any combination thereof.

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75. The pharmaceutical composition of claim 73, wherein the buffer solution is phosphate buffered saline (PBS).

76. Use of the double stranded RNAi agent of claim 67 or the pharmaceutical composition of any one of claims 69 to 75 in the manufacture of a medicament for treating a subject having an HAO1-associated disorder.

77. The use of claim 76, wherein the subject has primary hyperoxaluria type 1 (PH1).

78. The use of claim 76 or 77, wherein the double stranded RNAi agent is to be administered at a dose of about 0.01 mg/kg to about 10 mg/kg or about 1 mg/kg to about 10 mg/kg.

79. The use of any one of claims 76 to 78, wherein the double stranded RNAi agent is to be subcutaneously administered.

80. The use of any one of claims 76 to 79, wherein said double stranded RNAi agent is to be administered in two or more doses.

81. The double stranded RNAi agent of any one of claims 1 to 38, 53 or 67, or the pharmaceutical composition of any one of claims 40 to 46, 55 to 61 or 69 to 75 for use in therapy.