fructose by KHK is associated with diseases, disorders or conditions such as liver disease (*e.g.*, fatty liver, steatohepatitis), dyslipidemia (*e.g.*, hyperlipidemia, high LDL cholesterol, low HDL cholesterol, hypertriglyceridemia, postprandial hypertriglyceridemia), disorders of glycemic control (*e.g.*, insulin resistance, type 2 diabetes), cardiovascular disease (*e.g.,* hypertension, endothelial cell dysfunction), kidney disease (*e.g.*, acute kidney disorder, tubular dysfunction, proinflammatory changes to the proximal tubules, chronic kidney disease), metabolic syndrome, adipocyte dysfunction, visceral adipose deposition, obesity, hyperuricemia, gout, eating disorders, and excessive sugar craving.

Accordingly, there is a need in the art for compositions and methods for treating diseases, disorders, and conditions associated with KHK activity.

Summary of the Invention

In one aspect, provided herein is a double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of ketohexokinase (KHK) in a cell, or a pharmaceutically acceptable salt thereof,

a) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand comprises at least 20 contiguous nucleotides from the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or at least 20 contiguous nucleotides from the nucleotide sequence 5'- ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand;

b) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand comprises the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or the nucleotide sequence 5'-ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand;

c) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand consists of the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or the nucleotide sequence 5'-ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand;

d) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand comprises the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or the nucleotide sequence 5'-ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, and the sense strand comprises the nucleotide sequence 5'-GCAGGAAGCACUGAGAUUCGU-3' of SEQ ID NO:104, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand; or

e) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand consists of the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or the nucleotide sequence 5'-ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, and the sense strand consists of the nucleotide sequence 5'-GCAGGAAGCACUGAGAUUCGU-3' of SEQ ID NO:104, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand.

In another aspect, provided herein is a cell, or a pharmaceutically acceptable salt thereof, containing the dsRNA agent as described herein.

In another aspect, provided herein is a pharmaceutical composition for inhibiting expression of a gene encoding ketohexokinase (KHK) comprising the dsRNA agent, or a pharmaceutically acceptable salt thereof, as described herein.

In another aspect, provided herein is an *in vitro* method of inhibiting expression of a ketohexokinase (KHK) gene in a cell, the method comprising contacting the cell with the dsRNA agent, or a pharmaceutically acceptable salt thereof, as described herein, or the pharmaceutical composition as described herein, thereby inhibiting expression of the KHK gene in the cell.

In another aspect, provided herein is use of the dsRNA agent, or a pharmaceutically acceptable salt thereof, as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating a subject having a ketohexokinase-associated disorder, wherein a therapeutically effective amount of the dsRNA agent, or a pharmaceutically acceptable salt thereof, as described herein, or the pharmaceutical composition as described herein is to be administered to the subject, thereby treating the subject having the ketohexokinase-associated disorder, wherein the ketohexokinase-associated disorder is selected from the group consisting of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), dyslipidemia, abnormal lipid deposition or dysfunction, insulin resistance not related to immune response to insulin, type 2

diabetes, glucose intolerance, acute kidney disorder, tubular dysfunction, proinflammatory changes to the proximal tubules, chronic kidney disease and cardiovascular disease.

In another aspect, provided herein is use of the dsRNA agent, or a pharmaceutically acceptable salt thereof, as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for preventing at least one symptom of a ketohexokinase-associated disorder in a subject having the disorder, wherein a prophylactically effective amount of the dsRNA agent, or a pharmaceutically acceptable salt thereof, as described herein, or the pharmaceutical composition as described herein is to be administered to the subject, thereby preventing at least one symptom in the subject having the disorder, wherein the ketohexokinase-associated disorder is selected from the group consisting of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), dyslipidemia, abnormal lipid deposition or dysfunction, insulin resistance not related to immune response to insulin, type 2 diabetes, glucose intolerance, acute kidney disorder, tubular dysfunction, proinflammatory changes to the proximal tubules, chronic kidney disease and cardiovascular disease.

In another aspect, provided herein is a kit comprising the dsRNA agent as described herein or the pharmaceutical composition as described herein.

In another aspect, provided herein is a vial comprising the dsRNA agent as described herein or the pharmaceutical composition as described herein.

In yet another aspect, provided herein is a syringe comprising the dsRNA agent as described herein or the pharmaceutical composition as described herein.

The present invention provides iRNA compositions which affect the RNA-induced silencing complex (RISC)-mediated cleavage of RNA transcripts of a gene encoding ketohexokinase (KHK). The ketohexokinase (KHK) may be within a cell, *e.g.,* a cell within a subject, such as a human subject.

In an aspect, the invention provides a double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of ketohexokinase in a cell, wherein the dsRNA 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 0, 1, 2, or 3 nucleotides from the nucleotide sequence of SEQ ID NO:1 and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of SEQ ID NO:2.

In another aspect, the present invention provides a double stranded ribonucleic acid (dsRNA) for inhibiting expression of ketohexokinase in a cell, wherein said dsRNA comprises a sense strand and an antisense strand forming a double stranded region, wherein the antisense strand comprises a region of complementarity to an mRNA encoding ketohexokinase, and wherein the region of complementarity comprises at least 15 contiguous nucleotides differing by no more than 0, 1, 2, or 3 nucleotides from any one of the antisense nucleotide sequences in any one of Tables 2-5.

In one aspect, the present invention provides a double stranded ribonucleic acid (dsRNA) for inhibiting expression of ketohexokinase in a cell, wherein said dsRNA 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 0, 1, 2, or 3 nucleotides from any one of the nucleotide sequence of nucleotides 943-965; 788-810; 734-756; 1016-1038; 1013-1035; 1207-1229; 1149-1171; 574-596; 1207-1229 or 828-850 of the nucleotide sequence of SEQ ID NO:1, and the antisense strand comprises at least 19 contiguous nucleotides from the corresponding nucleotide sequence of SEQ ID NO:2.

In one embodiment, the antisense strand comprises at least 15 contiguous nucleotides differing by nor more than 0, 1, 2, or 3 nucleotides from any one of the antisense strand nucleotide

We claim:

1. A double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of ketohexokinase (KHK) in a cell, or a pharmaceutically acceptable salt thereof,

a) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand comprises at least 20 contiguous nucleotides from the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or at least 20 contiguous nucleotides from the nucleotide sequence 5'- ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand;

b) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand comprises the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or the nucleotide sequence 5'-ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand;

c) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand consists of the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or the nucleotide sequence 5'-ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand;

d) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand comprises the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or the nucleotide sequence 5'-ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, and the sense strand comprises the nucleotide sequence 5'-GCAGGAAGCACUGAGAUUCGU-3' of SEQ ID NO:104, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand; or

e) wherein the dsRNA agent, or the pharmaceutically acceptable salt thereof, comprises a sense strand and an antisense strand forming a double stranded region,

wherein the antisense strand consists of the nucleotide sequence 5'-ACGAAUCUCAGTGCUUCCUGCAC-3' of SEQ ID NO:463 or the nucleotide sequence 5'-ACGAAUCUCAGUGCUUCCUGCAC-3' of SEQ ID NO: 173, and the sense strand consists of the nucleotide sequence 5'-GCAGGAAGCACUGAGAUUCGU-3' of SEQ ID NO:104, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification, and wherein a ligand is conjugated to at least one strand

.

2. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 1, wherein at least one of the nucleotide modifications is selected from the group consisting of a deoxy-nucleotide modification, a 3'-terminal deoxythymidine (dT) nucleotide modification, a 2'-O-methyl nucleotide modification, a 2'-fluoro nucleotide modification, a 2'-deoxy nucleotide modification, a locked nucleotide modification, an unlocked nucleotide modification, a conformationally restricted nucleotide modification, a constrained ethyl nucleotide modification, an abasic nucleotide modification, a 2'-amino nucleotide modification, a 2'-O-allyl nucleotide modification, 2'-C-alkyl nucleotide modification, 2'-hydroxly nucleotide modification, a 2'-methoxyethyl nucleotide modification, a 2'-O-alkyl nucleotide modification, a morpholino nucleotide modification, a phosphoramidate modification, a non-natural base comprising nucleotide modification, a tetrahydropyran nucleotide modification, a 1,5-anhydrohexitol nucleotide modification, a cyclohexenyl nucleotide modification, a nucleotide comprising a phosphorothioate group modification, a nucleotide comprising a methylphosphonate group modification, a nucleotide comprising a 5'-phosphate modification, a nucleotide comprising a 5'-phosphate mimic modification, a thermally destabilizing nucleotide modification, a glycol modified nucleotide (GNA) modification, and a 2-O-(N-methylacetamide) nucleotide modification; and combinations thereof.

3. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 1 or 2, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a nucleotide modification selected from the group consisting of a 2'-O-methyl nucleotide modification, a 2'-fluoro nucleotide modification, a GNA modification, and a 2'-deoxy nucleotide modification.

4. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-3, wherein the double stranded region is 19-30 nucleotide pairs in length.

5. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 4, wherein the double stranded region is 19-25 nucleotide pairs in length.

6. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 4, wherein the double stranded region is 19-23 nucleotide pairs in length.

7. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 4, wherein the double stranded region is 21-23 nucleotide pairs in length.

8. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-7, wherein each strand is independently no more than 30 nucleotides in length.

9. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-8, wherein the sense strand is 21 nucleotides in length and the antisense strand is 23 nucleotides in length.

10. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-9, wherein at least one strand comprises a 3’ overhang of at least 1 nucleotide.

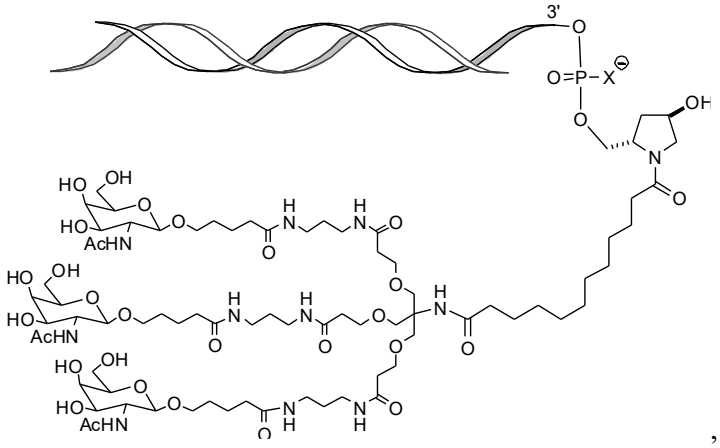
11. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-9, wherein at least one strand comprises a 3’ overhang of at least 2 nucleotides.

12. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-11, wherein the sense strand comprises the nucleotide sequence 5’-gscsaggaAfgCfAfCfugagauucgu-3’ of SEQ ID NO: 242 and the antisense strand comprises the nucleotide sequence 5’-asCfsgaau(Cgn)ucagugCfuUfccugcsasc-3’ of SEQ ID NO: 311, wherein a, g, c and u are 2′-O-methyl (2′-OMe) A, G, C, and U; Af, Cf and Uf are 2′-deoxy-2’-fluoro (2’-F) A, C and U; Cgn is C-glycol nucleic acid (GNA); and s is a phosphorothioate linkage.

13. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-11, wherein the sense strand consists of the nucleotide sequence 5’-gscsaggaAfgCfAfCfugagauucgu-3’ of SEQ ID NO: 242 and the antisense strand consists of the nucleotide sequence 5’-asCfsgaau(Cgn)ucagugCfuUfccugcsasc-3’ of SEQ ID NO: 311, wherein a, g, c and u are 2′-O-methyl (2′-OMe) A, G, C, and U; Af, Cf and Uf are 2′-deoxy-2’-fluoro (2’-F) A, C and U; Cgn is C-glycol nucleic acid (GNA); and s is a phosphorothioate linkage.

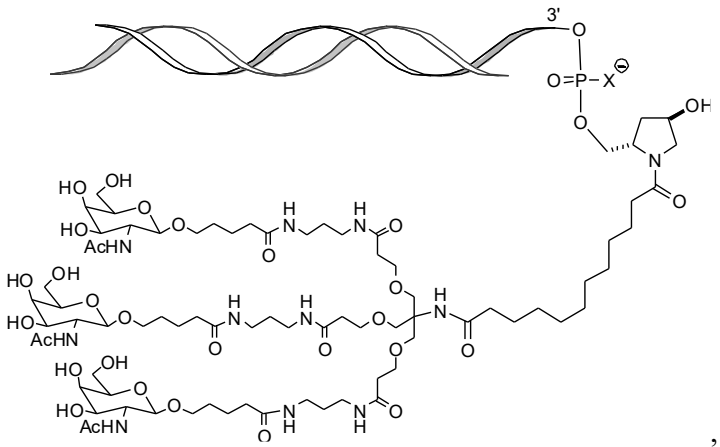
14. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-11, wherein the sense strand comprises the nucleotide sequence 5’-gscsaggaAfgCfAfCfugagauucgu-3’ of SEQ ID NO: 242 and the antisense strand comprises the nucleotide sequence 5’-asCfsgaau(Cgn)ucagugCfuUfccugcsasc-3’ of SEQ ID NO: 311, wherein a, g, c and u are 2′-O-methyl

(2′-OMe) A, G, C, and U; Af, Cf and Uf are 2′-deoxy-2’-fluoro (2’-F) A, C and U; Cgn is C-glycol nucleic acid (GNA); and s is a phosphorothioate linkage, and wherein the ligand is conjugated to the 3’-end of the sense strand as shown in the following schematic



, wherein X is O.

15. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-11, wherein the sense strand consists of the nucleotide sequence 5’-gscsaggaAfgCfAfCfugagauucgu-3’ of SEQ ID NO: 242 and the antisense strand consists of the nucleotide sequence 5’-asCfsgaau(Cgn)ucagugCfuUfccugcsasc-3’ of SEQ ID NO: 311, wherein a, g, c and u are 2′-O-methyl (2′-OMe) A, G, C, and U; Af, Cf and Uf are 2′-deoxy-2’-fluoro (2’-F) A, C and U; Cgn is C-glycol nucleic acid (GNA); and s is a phosphorothioate linkage, and wherein the ligand is conjugated to the 3’-end of the sense strand as shown in the following schematic



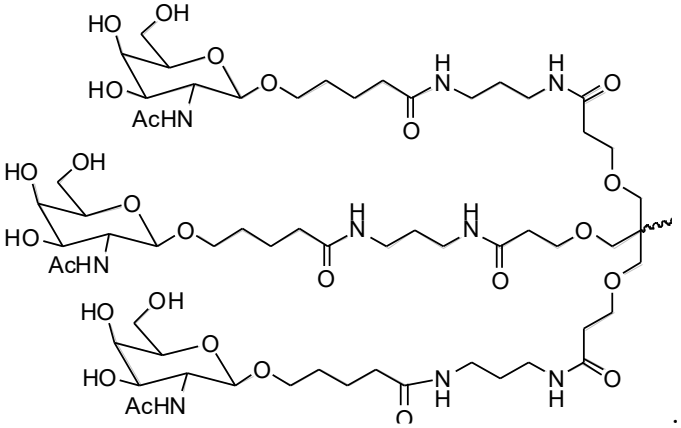
, wherein X is O.

16. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-11, wherein the ligand is conjugated to the 3’ end of the sense strand of the dsRNA agent.

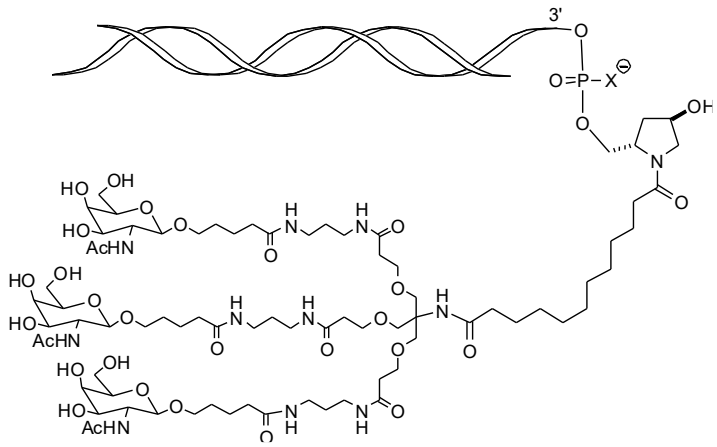
17. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-11 and 16, wherein the ligand is an N-acetylgalactosamine (GalNAc) derivative.

18. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-11 and 16, wherein the ligand is one or more GalNAc derivatives attached through a monovalent, bivalent, or trivalent branched linker.

19. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 17 or 18, wherein the ligand is



20. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 19, wherein the dsRNA agent, or a pharmaceutically acceptable salt thereof, is conjugated to the ligand as shown in the following schematic



and, wherein X is O or S.

21. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 20, wherein X is O.

22. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-11 and 16-21, wherein the dsRNA agent, or a pharmaceutically acceptable salt thereof, further comprises at least one phosphorothioate or methylphosphonate internucleotide linkage.

23. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 22, wherein the dsRNA agent comprises 6-8 phosphorothioate or methylphosphonate internucleotide linkages.

24. The dsRNA agent, or a pharmaceutically acceptable salt thereof, of claim 23, wherein the antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-end and two phosphorothioate internucleotide linkages at the 3'-end, and the sense strand comprises at least two phosphorothioate internucleotide linkages at the 5'-end.

25. A cell containing the dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-24.

26. A pharmaceutical composition for inhibiting expression of a gene encoding ketohexokinase (KHK) comprising the dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-24.

27. The pharmaceutical composition of claim 26, wherein the dsRNA agent, or a pharmaceutically acceptable salt thereof, is in an unbuffered solution.

28. The pharmaceutical composition of claim 27, wherein the unbuffered solution is saline or water.

29. The pharmaceutical composition of claim 26, wherein the dsRNA agent is in a buffer solution.

30. The pharmaceutical composition of claim 29, wherein the buffer solution comprises acetate, citrate, prolamine, carbonate, or phosphate or any combination thereof.

31. The pharmaceutical composition of claim 30, wherein the buffer solution is phosphate buffered saline (PBS).

32. An *in vitro* method of inhibiting expression of a ketohexokinase (KHK) gene in a cell, the method comprising contacting the cell with the dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-24, or the pharmaceutical composition of any one of claims 26-31, thereby inhibiting expression of the KHK gene in the cell.

33. The method of claim 32, wherein contacting the cell with the dsRNA agent, or a pharmaceutically acceptable salt thereof, inhibits the expression of ketohexokinase by at least 50%, 60%, 70%, 80%, 90%, or 95%.

34. Use of the dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-24, or the pharmaceutical composition of any one of claims 26-31 in the manufacture of a medicament for treating a subject having a ketohexokinase-associated disorder, wherein a therapeutically effective amount of the dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-24, or the pharmaceutical composition of any one of claims 26-31 is to be administered to the subject, thereby treating the subject having the ketohexokinase-associated disorder, wherein the ketohexokinase-associated disorder is selected from the group consisting of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), dyslipidemia, abnormal lipid deposition or dysfunction, insulin resistance not related to immune response to insulin, type 2 diabetes, glucose intolerance, acute kidney disorder, tubular dysfunction, proinflammatory changes to the proximal tubules, chronic kidney disease and cardiovascular disease.

35. Use of the dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-24, or the pharmaceutical composition of any one of claims 26-31 in the manufacture of a medicament for preventing at least one symptom of a ketohexokinase-associated disorder in a subject having the disorder, wherein a prophylactically effective amount of the dsRNA agent, or a pharmaceutically acceptable salt thereof, of any one of claims 1-24, or the pharmaceutical composition of any one of claims 26-31 is to be administered to the subject, thereby preventing at least one symptom in the subject having the disorder, wherein the ketohexokinase-associated disorder is selected from the group consisting of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), dyslipidemia, abnormal lipid deposition or dysfunction, insulin resistance not related to immune response to insulin, type 2 diabetes, glucose intolerance, acute kidney disorder, tubular dysfunction, proinflammatory changes to the proximal tubules, chronic kidney disease and cardiovascular disease .

36. The use of claim 34 or 35, wherein the dyslipidemia comprises one or more of hyperlipidemia, high LDL cholesterol, low HDL cholesterol, hypertriglyceridemia, postprandial hypertriglyceridemia, adipocyte dysfunction, visceral adipose deposition, obesity, and metabolic syndrome.

37. The use of claim 34 or 35, wherein the cardiovascular disease comprises at least one of hypertension and endothelial cell dysfunction.

38. The use of any one of claims 34-37, wherein the subject is human.

39. The use of claim 38, wherein the subject has or is prone to compromised renal function.

40. The use of any one of claims 34-39, wherein the dsRNA agent, or a pharmaceutically acceptable salt thereof, is to be administered to the subject subcutaneously.

41. The use of any one of claims 34-40, wherein an additional agent for the treatment of a KHK-associated disorder is to be administered.

42. The use of any one of claims 34-41, further comprising determining the level of ketohexokinase in a sample(s) from the subject.

43. The use of claim 42, wherein the level of ketohexokinase in the subject sample(s) is a ketohexokinase protein level in a blood or serum sample(s).

44. The use of any one of claims 34-43, further comprising measuring a level of fructose metabolism in the subject.

45. The use of any one of claims 34-44, further comprising measuring a uric acid level in the subject.

46. The use of any one of claims 34-45, further comprising measuring a serum lipid level in the subject..

47. A kit comprising the dsRNA agent of any one of claims 1-24 or the pharmaceutical composition of any one of claims 26-31.

48. A vial comprising the dsRNA agent of any one of claims 1-24 or the pharmaceutical composition of any one of claims 26-31.

49. A syringe comprising the dsRNA agent of any one of claims 1-24 or the pharmaceutical composition of any one of claims 26-31.