Claims

1. A pharmaceutical composition comprising (S)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide, or a pharmaceutically acceptable salt thereof, in combination with at least 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospir[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid, or a pharmaceutically acceptable salt thereof, each present in therapeutically effective amounts, in admixture with a pharmaceutically acceptable excipient.

2. A pharmaceutical composition comprising (S)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3 yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

3. The composition of claim 1 or claim 2, further comprising at least one additional pharmaceutical agent selected from the group consisting of an anti-inflammatory agent, an anti-diabetic agent, and a cholesterol/lipid modulating agent.

4. Use of a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a disease or condition selected from fatty liver, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic steatohepatitis with cirrhosis, and nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma or with a metabolic-related disease.

5. The use of claim 4, wherein the medicament is to be used in combination with at least a therapeutically effective amount of 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof.

6. Use of a therapeutically effective amount of 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydro spiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a disease or condition selected from fatty liver, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic

steatohepatitis with cirrhosis, and nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma or with a metabolic-related disease.

7. The use of claim 6, wherein the medicament is to be used in combination with at least a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof.

8. Use of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl) pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, and 4-(4-(1-iso propyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxy pyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a disease or condition selected from fatty liver, non-alcoholic fatty liver disease, nonalcoholic steatohepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic steatohepatitis with cirrhosis, and nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma or with a metabolic-related disease.

9. The use of any one of claims 4 to 8, wherein the disease or condition is fatty liver.

10. The use of any one of claims 4 to 8, wherein the disease or condition is nonalcoholic fatty liver disease.

11. The use of any one of claims 4 to 8, wherein the disease or condition is nonalcoholic steatohepatitis.

12. The use of any one of claims 4 to 8, wherein the disease or condition is nonalcoholic steatohepatitis with liver fibrosis.

13. The use of any one of claims 4 to 8, wherein the disease or condition is nonalcoholic steatohepatitis with cirrhosis.

14. The use of claim 13, wherein the disease or condition is nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma.

15. The use of claim 13, wherein the disease or condition is nonalcoholic steatohepatitis with cirrhosis and with a metabolic-related disease.

16. The use of any one of claims 4 to 8, wherein
a therapeutically effective amount of at least one other pharmaceutical agent selected from the group is to be administered, the group consisting of an acetyl-CoA carboxylase- (ACC) inhibitor, a diacylglycerol *O*-acyltransferase 1 (DGAT-1) inhibitor, monoacylglycerol O-acyltransferase inhibitors, a phosphodiesterase (PDE)-10 inhibitor, an AMPK activator, a sulfonylurea, a meglitinide, an α-amylase inhibitor, an α-glucoside hydrolase inhibitor, an α-glucosidase inhibitor, a PPARγ agonist, a PPAR α/γ agonist, a biguanide, a glucagon-like peptide 1 (GLP-1) modulator, liraglutide, albiglutide, exenatide, albiglutide, lixisenatide, dulaglutide, semaglutide, a protein tyrosine phosphatase-1B (PTP-1B) inhibitor, SIRT-1 activator, a dipeptidyl peptidase IV (DPP-IV) inhibitor, an insulin secreatagogue, a fatty acid oxidation inhibitor, an A2 antagonist, a c-jun amino-terminal kinase (JNK) inhibitor, glucokinase activators (GKa), insulin, an insulin mimetic, a glycogen phosphorylase inhibitor, a VPAC2 receptor agonist, SGLT2 inhibitors, a glucagon receptor modulator, GPR119 modulators, FGF21 derivatives or analogs, TGR5 receptor modulators, GPBAR1 receptor modulators, GPR40 agonists, GPR120 modulators, high affinity nicotinic acid receptor (HM74A) activators, SGLT1 inhibitors, inhibitors or modulators of carnitine palmitoyl transferase enzymes, inhibitors of fructose 1,6-diphosphatase, inhibitors of aldose reductase, mineralocorticoid receptor inhibitors, inhibitors of TORC2, inhibitors of CCR2 and/or CCR5, inhibitors of PKC isoforms (e.g. PKCα, PKCβ, PKCγ), inhibitors of fatty acid synthetase, inhibitors of serine palmitoyl transferase, modulators of GPR81, GPR39, GPR43, GPR41, GPR105, Kv1.3, retinol binding protein 4, glucocorticoid receptor, somatostatin receptors, inhibitors or modulators of PDHK2 or PDHK4, inhibitors of MAP4K4, modulators of IL1 family including IL1beta, HMG-CoA reductase inhibitors, squalene synthetase inhibitors, fibrates, bile acid sequestrants, ACAT inhibitors, MTP inhibitors, lipooxygenase inhibitors, cholesterol absorption inhibitors, PCSK9 modulators, cholesteryl ester transfer protein inhibitors and modulators of RXRalpha.

17. The use of any one of claims 4 to 16, wherein the medicament is for the treatment

of nonalcoholic fatty liver disease or nonalcoholic steatohepatitis, nonalcoholic steatohepatitis activity, nonalcoholic steatohepatitis disease or nonalcoholic steatohepatitis

18. The use of any one of claims 4 to 17, wherein

a therapeutically effective amount of a further agent comprising a pharmaceutical agent selected from the group consisting of an anti-inflammatory agent, an anti-diabetic agent, an anti-fibrotic agent, an anti-steatiotic agent, a cholesterol/lipid modulating agent and an anti-diabetic agent is also to be administered.

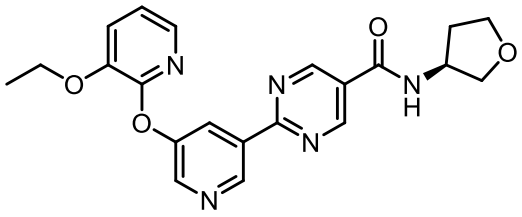
19. The use of any one of claims 4 to 17, wherein a therapeutically effective amount of three agents in the manufacture of a medicament for the treatment of fatty liver, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic steatohepatitis with cirrhosis, or nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma, wherein:

i. the first agent comprises (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetra hydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof;

ii. the second agent comprises 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro [indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl) benzoic acid or a pharmaceutically acceptable salt thereof; and

iii. the third agent comprises a pharmaceutical agent selected from the group consisting of an anti-inflammatory agent, an anti-diabetic agent, an anti-fibrotic agent, an anti-steatiotic agent, a cholesterol/lipid modulating agent and an anti-diabetic agent.

20. The use according to any of claims 4 to 8, 17 to 19, wherein (*S*)-2-(5-((3 ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carbox amide is a crystalline solid of structure:



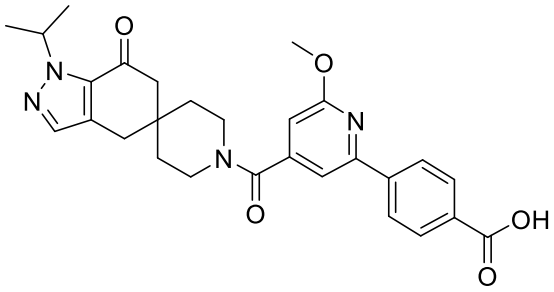
or a pharmaceutically acceptable salt thereof.

21. The use of claim 20, wherein the crystalline solid has a powder x-ray

diffraction pattern comprising 2-theta values of (CuKα radiation, wavelength of 1. 54056 Å) 5.3 ± 0.2, ± 0.2, and 15.4 ± 0.2.

22. The use of claim 20, wherein the crystalline solid has a powder x-ray diffraction pattern comprising 2-theta values of (CuKα radiation, wavelength of 1. 54056Å) 6.5 ± 0.2, ± 0.2, and 13.6 ± 0.2.

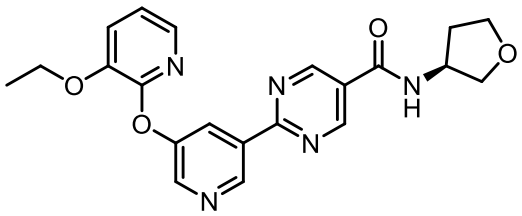
23. The use according to any of claims 4 to 8, 17 to 19, wherein 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid is a crystalline solid of structure:



or a pharmaceutically acceptable salt thereof.

24. The use of claim 23, wherein the crystalline solid is 2-amino-2-(hydroxy methyl)propane-1,3-diol salt of 4-(4-(1-isopropyl-7-oxo-1,4,6,7-tetrahydro spiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid.

25. The pharmaceutical composition of claim 1 or claim 2, wherein (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide is a crystalline solid of structure:

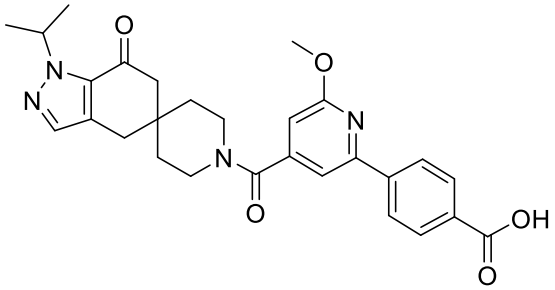


or a pharmaceutically acceptable salt thereof.

26. The pharmaceutical composition of claim 25, wherein the crystalline solid has a powder x-ray diffraction pattern comprising 2-theta values of (CuKα radiation, wavelength of 1. 54056 Å) 5.3 ± 0.2, 7.7 ± 0.2, and 15.4 ± 0.2.

27. The pharmaceutical composition of claim 25, wherein the crystalline solid has a powder x-ray diffraction pattern comprising 2-theta values of (CuKα radiation, wavelength of 1. 54056Å) 6.5 ± 0.2, 9.3 ± 0.2, and 13.6 ± 0.2.

28. The pharmaceutical composition of claim 1 or claim 2, wherein 4-(4-(1-isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxy pyridin-2-yl)benzoic acid is a crystalline solid of structure:



or a pharmaceutically acceptable salt thereof.

29. The pharmaceutical composition of claim 28, wherein the crystalline solid is 2-amino-2-(hydroxymethyl)propane-1,3-diol salt of 4-(4-(1-isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid.

30. The pharmaceutical composition of claim 2, wherein the additional pharmaceutical agent is selected from the group consisting of [(1R,5S,6R)-3-{2-[(2S)-2-methylazetidin-1-yl]-6-(trifluoromethyl)pyrimidin-4-yl}-3-azabicyclo[3.1.0]hex-6-yl]acetic acid; 2-[(1R,3R,5S)-3-({5-cyclopropyl-3-[2-(trifluoromethoxy)phenyl]-1,2-oxazol-4-yl}methoxy)-8-azabicyclo[3.2.1]octan-8-yl]-4-fluoro-1,3-benzothiazole-6-carboxylic acid; or 2-[(4-{6-[(4-cyano-2-fluorobenzyl)oxy] pyridin-2-yl}piperidin-1-yl)methyl]-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, or a pharmaceutically acceptable salt thereof.

31. The use of any one of claims 17 to 19, wherein at least one other pharmaceutical agent is to be used and is selected from the group consisting of [(1R, 5S,6R)-3-{2-[(2S)-2-methylazetidin-1-yl]-6-(trifluoromethyl)pyrimidin-4-yl}-3-azabicyclo[3.1.0] hex-6-yl]acetic acid; 2-[(1R,3R,5S)-3-({5-cyclopropyl-3-[2-(trifluoromethoxy)phenyl]-1,2-oxa zol-4-yl}methoxy)-8-azabicyclo[3.2.1]octan-8-yl]-4-fluoro-1,3-benzothiazole-6-carboxylic acid; or 2-[(4-{6-[(4-cyano-2-fluorobenzyl)oxy]pyridin-2-yl}piperidin-1-yl)methyl]-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, or a pharmaceutically acceptable salt thereof.

32. Use of a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5- carboxamide or a pharmaceutically acceptable salt thereof, and 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of heart failure, congestive heart failure, coronary heart disease, peripheral vascular disease, renovascular disease, pulmonary hypertension, vasculitis, acute coronary syndromes and modification of cardiovascular risk.

33. Use of a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of heart failure, congestive heart failure, coronary heart disease, peripheral vascular disease, renovascular disease, pulmonary hypertension, vasculitis, acute coronary syndromes and modification of cardio vascular risk.

34. The use of claim 33, wherein the medicament is to be used in combination with at least a therapeutically effective amount of 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro [indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof.

35. Use of a therapeutically effective amount of 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydro spiro [indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid, in the manufacture of a medicament for the treatment of heart failure, congestive heart failure, coronary heart disease, peripheral vascular disease, renovascular disease, pulmonary hypertension, vasculitis, acute coronary syndromes and modification of cardio vascular risk.

36. The use of claim 35, wherein the medicament is to be used in combination with at least a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetra hydro furan-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof.

37. Use of a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy) pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, and 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable

salt thereof in the manufacture of a medicament for the treatment of obesity, Type I diabetes, Type II diabetes mellitus, idiopathic TypeI diabetes (Type Ib), latent autoimmune diabetes in adults (LADA), early-onset Type 2 diabetes (EOD), youth-onset atypical diabetes (YOAD), maturity onset diabetes of the young (MODY), malnutrition- related diabetes, gestational diabetes, coronary heart disease, ischemic stroke, restenosis after angioplasty, peripheral vascular disease, intermittent claudication, myocardial infarction, dyslipidemia, post-prandial lipemia, conditions of impaired glucose tolerance (IGT), conditions of impaired fasting plasma glucose, metabolic acidosis, ketosis, arthritis, diabetic retinopathy, macular degeneration, cataract, diabetic nephropathy, glomerulosclerosis, chronic renal failure, diabetic neuropathy, metabolic syndrome, syndrome X, hyperglycemia, hyperinsulinemia, hypertriglyceridemia, insulin resistance, impaired glucose metabolism, skin and connective tissue disorders, foot ulcerations and ulcerative colitis, endothelial dysfunction and impaired vascular compliance, hyper apo B lipoproteinemia, and maple syrup urine disease.

38. Use of a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy) pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of obesity, Type I diabetes, Type II diabetes mellitus, idiopathic TypeI diabetes (Type Ib), latent autoimmune diabetes in adults (LADA), early-onset Type 2 diabetes (EOD), youth-onset atypical diabetes (YOAD), maturity onset diabetes of the young (MODY), malnutrition-related diabetes, gestational diabetes, coronary heart disease, ischemic stroke, restenosis after angioplasty, peripheral vascular disease, intermittent claudication, myocardial infarction, dyslipidemia, post-prandial lipemia, conditions of impaired glucose tolerance (IGT), conditions of impaired fasting plasma glucose, metabolic acidosis, ketosis, arthritis, diabetic retinopathy, macular degeneration, cataract, diabetic nephropathy, glomerulo-sclerosis, chronic renal failure, diabetic neuropathy, metabolic syndrome, syndrome X, hyperglycemia, hyperinsulinemia, hypertriglyceridemia, insulin resistance, impaired glucose metabolism, skin and connective tissue disorders, foot ulcerations and ulcerative colitis, endothelial dysfunction and impaired vascular compliance, hyper apo B lipoproteinemia, and maple syrup urine disease.

39. The use of claim 38, wherein the medicament is to be used in combination with at least a therapeutically effective amount of 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro [indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharma-ceutically acceptable salt thereof.

40. Use of a therapeutically effective amount of 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydro spiro [indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of obesity, Type I diabetes, Type II diabetes mellitus, idiopathic TypeI diabetes (Type Ib), latent autoimmune diabetes in adults (LADA), early-onset Type 2 diabetes (EOD), youth-onset atypical diabetes (YOAD), maturity onset diabetes of the young (MODY), malnutrition-related diabetes, gestational diabetes, coronary heart disease, ischemic stroke, restenosis after angioplasty, peripheral vascular disease, intermittent claudication, myocardial infarction, dyslipidemia, post-prandial lipemia, conditions of impaired glucose tolerance (IGT), conditions of impaired fasting plasma glucose, metabolic acidosis, ketosis, arthritis, diabetic retinopathy, macular degeneration, cataract, diabetic nephropathy, glomerulosclerosis, chronic renal failure, diabetic neuropathy, metabolic syndrome, syndrome X, hyperglycemia, hyperinsulinemia, hypertriglyceridemia, insulin resistance, impaired glucose metabolism, skin and connective tissue disorders, foot ulcerations and ulcerative colitis, endothelial dysfunction and impaired vascular compliance, hyper apo B lipoproteinemia, and maple syrup urine disease.

41. The use of claim 40, wherein the medicament is to be used in combination with at least a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetra hydro furan-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof.

42. The use of any one of claims 38 to 41, wherein the treatment is for Type II diabetes mellitus.

43. Use of a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy) pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, and 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of hepatocellular carcinoma, kidney renal clear cell carcinoma, head and neck squamous cell carcinoma, colorectal adenocarcinoma, mesothelioma, stomach adenocarcinoma, adrenocortical carcinoma, kidney papillary cell carcinoma, cervical and endocervical carcinoma, bladder urothelial carcinoma and lung adenocarcinoma.

44. Use of a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy) pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of heapto-cellular carcinoma, kidney renal clear cell carcinoma, head and neck squamous cell carcinoma, colorectal adenocarcinoma, mesothelioma, stomach adenocarcinoma, adrenocortical carcinoma, kidney papillary cell carcinoma, cervical and endocervical carcinoma, bladder urothelial carcinoma and lung adenocarcinoma.

45. The use of claim 44, wherein the medicament is to be used in combination with at least a therapeutically effective amount of 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro [indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof.

46. Use of a therapeutically effective amount of 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydro spiro [indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of heaptocellular carcinoma, kidney renal clear cell carcinoma, head and neck squamous cell carcinoma, colorectal adenocarcinoma, mesothelioma, stomach adenocarcinoma, adrenocortical carcinoma, kidney papillary cell carcinoma, cervical and endocervical carcinoma, bladder urothelial carcinoma and lung adenocarcinoma.

47. The use of claim 46, wherein the medicament is to be used in combination with at least a therapeutically effective amount of (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydro furan-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof.

48. The use of any one of claims 44 to 47, wherein the treatment is for hepatocellular carcinoma.

49. Use of the composition according to claim 2 in the manufacture of a medicament for the treatment of a disease or condition selected from fatty liver, non alcoholic fatty liver disease, nonalcoholic steatohepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic steatohepatitis with cirrhosis, and nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma or with a metabolic-related disease.

50. (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease or condition selected from fatty liver, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic steatohepatitis with cirrhosis, and nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma or with a metabolic-related disease.

51. 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof for use in the treatment of a disease or condition selected from fatty liver, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic steatohepatitis with cirrhosis, and nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma or with a metabolic-related disease.

52. (*S*)-2-(5-((3-ethoxypyridin-2-yl)oxy)pyridin-3-yl)-N-(tetrahydrofuran-3-yl)pyrimidine-5-carboxamide or a pharmaceutically acceptable salt thereof, and 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof for use as a medicament.

53. 4-(4-(1-Isopropyl-7-oxo-1,4,6,7-tetrahydrospiro[indazole-5,4'-piperidine]-1'-carbonyl)-6-methoxypyridin-2-yl)benzoic acid or a pharmaceutically acceptable salt thereof for use as a medicament.

54. The composition according to claim 2 for use in the treatment of a disease or condition selected from fatty liver, nonalcoholic fatty liver disease, nonalcoholic steato-hepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic steatohepatitis with cirrhosis, and nonalcoholic steatohepatitis with cirrhosis and with hepatocellular carcinoma or with a metabolic-related disease.