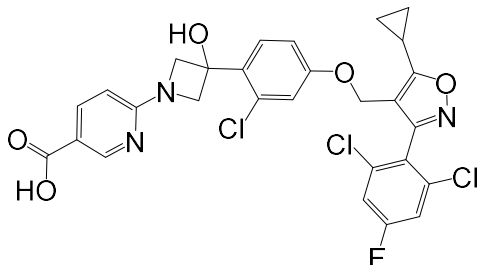


CLAIMS

1. A compound having the following Formula (I):



or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1 or pharmaceutically acceptable salt thereof for use in the treatment of a Farnesoid X Receptor (FXR) mediated condition.

3. The compound according to claim 2 or pharmaceutically acceptable salt thereof wherein the FXR mediated condition is a liver disease.

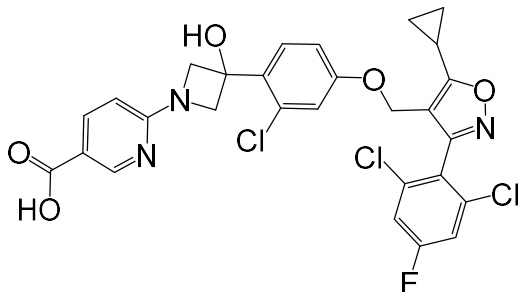
4. The compound according to ~~any of claims 2 to 3~~ or pharmaceutically acceptable salt thereof, wherein the FXR mediated condition is Non-Alcoholic Steatohepatitis (NASH).

5. The compound according to ~~any of claims 2 to 3~~ or pharmaceutically acceptable salt thereof, wherein the FXR mediated condition is Primary Sclerosing Cholangitis (PSC).

6. The compound according to ~~any of claims 2 to 3~~ or pharmaceutically acceptable salt thereof, wherein the FXR mediated condition is Primary Biliary Cholangitis (PBC).

7. The compound according to ~~any of claims 2 to 3~~ or pharmaceutically acceptable salt thereof, wherein the FXR mediated condition is liver fibrosis.

8. A pharmaceutical composition comprising a compound having the following Formula (I):



or a pharmaceutically acceptable salt thereof.

9. The pharmaceutical composition of claim 8, further comprising a pharmaceutically acceptable carrier.

10. ~~The use of a compound or pharmaceutically acceptable salt of claim 1, or a pharmaceutical composition of claim 8 or 9 in the manufacture of a medicament for treating a patient having a Farnesoid X Receptor (FXR) mediated condition comprising administering a compound or pharmaceutically acceptable salt of claim 1 or a pharmaceutical composition of claim 8 to a patient in need thereof.~~

11. ~~The method of claim 10,~~ wherein the FXR mediated condition is selected from the group consisting of:

a chronic intrahepatic or extrahepatic cholestatic condition;

liver fibrosis;

a chronic or obstructive inflammatory disorder of the liver;

liver cirrhosis;

liver steatosis or an associated syndrome;

a cholestatic or fibrotic effect that is associated with alcohol-induced cirrhosis or with a viral-borne form of hepatitis;

acute or chronic liver failure;

liver ischemia after major liver resection;

chemotherapy associated steatohepatitis (CASH);

Primary Biliary Cirrhosis (PBC);

Primary Sclerosing Cholangitis (PSC);

a neoplastic disease of the gastrointestinal tract or liver; and

an Inflammatory Bowel Disease (IBD);

a lipid disorder or lipoprotein disorder;

Type I Diabetes;

Type II Diabetes;

clinical complications of Type I and Type II Diabetes selected from the group consisting of diabetic nephropathy, diabetic neuropathy, diabetic retinopathy and other observed effects of clinically manifest long term Diabetes;

Non-Alcoholic Fatty Liver Disease (NAFLD);

Non-Alcoholic Steatohepatitis (NASH);

obesity;

a metabolic syndrome selected from the group consisting of combined conditions of dyslipidemia, diabetes and abnormally high body-mass index;

acute myocardial infarction;

acute stroke; and

thrombosis that occurs as an endpoint of chronic obstructive atherosclerosis;

a non-malignant hyperproliferative disorder;

a malignant hyperproliferative disorder selected from the group consisting of hepatocellular carcinoma, colon adenoma, and polyposis;

colon adenocarcinoma;

breast cancer;

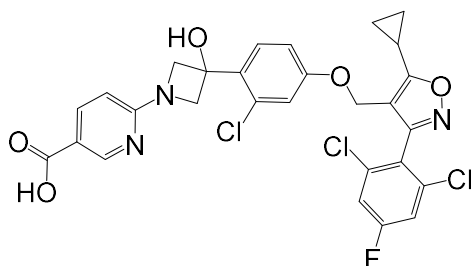
pancreas adenocarcinoma; and

Barrett's esophagus.

~~12. Use of a compound or pharmaceutically acceptable salt thereof of claim 1 for the manufacture of a medicament for the treatment of a Farnesoid X Receptor (FXR) mediated condition.~~

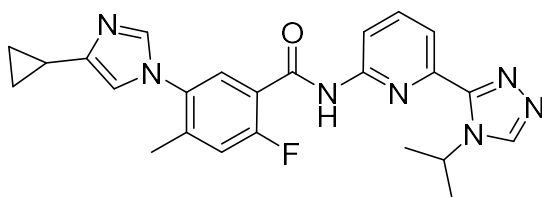
11. The use of a therapeutically effective amount of an Apoptosis Signal-Regulating Kinase 1 (ASK1) inhibitor in combination with a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, in the manufacture of a medicament for the treatment/prevention of a liver disease in a patient in need thereof

~~13. wherein the FXR agonist is a compound of Formula (I); method of treating and/or preventing a liver disease in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of an Apoptosis Signal-Regulating Kinase 1 (ASK1) inhibitor in combination with a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, wherein the FXR agonist is a compound of Formula (I):~~



or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment/prevention of a liver disease in a patient in need thereof.

~~14.12. The use~~method of claim 11~~13~~, wherein the ASK1 inhibitor is a compound of Formula (II):



or a pharmaceutically acceptable salt, a stereoisomer, a mixture of stereoisomers, or a tautomer thereof.

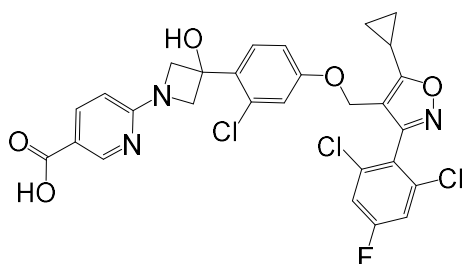
~~15.13.~~ The ~~method use of any one of claims 1113 to 1214~~, wherein FXR agonist and the ASK1 inhibitor are to be administered separately.

~~16.14.~~ The ~~method use of any one of claims 1113 to 1315~~, wherein the liver disease is non-alcoholic steatohepatitis (NASH).

~~17.15.~~ The ~~method use of any one of claims 1113 to 1315~~, wherein the liver disease is Primary Sclerosing Cholangitis (PSC).

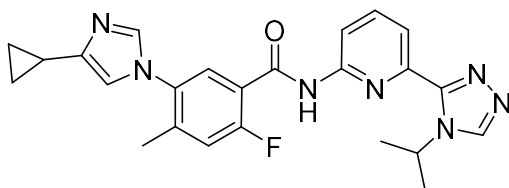
~~18.16.~~ The ~~method use of any one of claims 1113 to 1315~~, wherein the liver disease is Primary Biliary Cirrhosis (PBC).

~~19.17.~~ A pharmaceutical composition comprising a therapeutically effective amount of an Apoptosis Signal-Regulating Kinase 1 (ASK1) inhibitor and a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, wherein the FXR agonist is a compound of Formula (I):



or a pharmaceutically acceptable salt thereof.

~~20.18.~~ The pharmaceutical composition of claim ~~1719~~, wherein the ASK1 inhibitor is a compound of Formula (II):

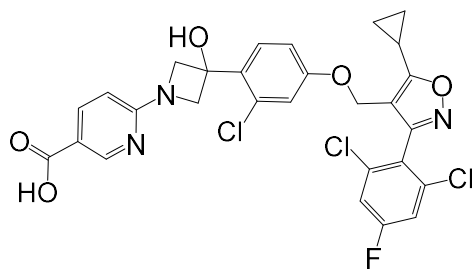


or a pharmaceutically acceptable salt, a stereoisomer, a mixture of stereoisomers, or a tautomer thereof.

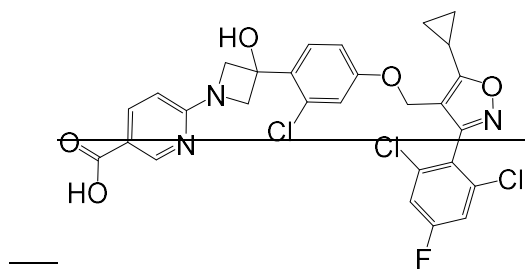
~~21.~~19. The pharmaceutical composition of ~~any of claims 17-19 to or~~ 17-19, further comprising a pharmaceutically acceptable carrier.

~~20.~~ A method ~~The use of a therapeutically effective amount of an Acetyl CoA Carboxylase (ACC) inhibitor in combination with a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, in the manufacture of a medicament for treating and/or preventing a liver disease in a patient in need thereof~~

~~22.~~ wherein the FXR agonist is a compound of Formula (I):

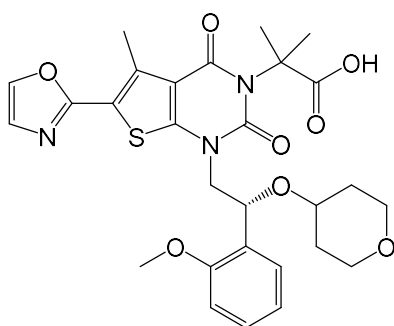


~~or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating and/or preventing a liver disease in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of an Acetyl CoA Carboxylase (ACC) inhibitor in combination with a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, wherein the FXR agonist is a compound of Formula (I):~~



~~or a pharmaceutically acceptable salt thereof.~~

~~23.~~ 21. ~~The method use~~ The method use of claim 20~~2~~, wherein the ACC inhibitor is a compound of Formula (III):



or a pharmaceutically acceptable salt, a stereoisomer, a mixture of stereoisomers, or a tautomer thereof.

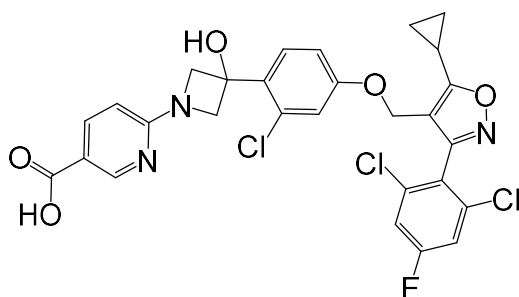
~~24.22.~~ The ~~method use of any one of claims 202 to or 213,~~ wherein the ACC inhibitor and the FXR agonist are administered separately.

~~25.23.~~ The ~~method use of any one of claims 202 to 224,~~ wherein the liver disease is non-alcoholic steatohepatitis (NASH).

~~26.24.~~ The ~~method use of any one of claims 202 to 224,~~ wherein the liver disease is Primary Sclerosing Cholangitis (PSC).

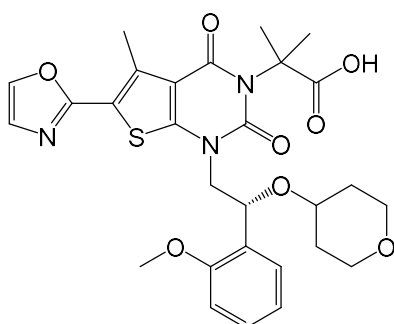
~~27.25.~~ The ~~method use of any one of claims 202 to 224,~~ wherein the liver disease is Primary Biliary Cirrhosis (PBC).

~~28.26.~~ A pharmaceutical composition comprising a therapeutically effective amount of an Acetyl CoA Carboxylase (ACC) inhibitor and a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, wherein the FXR agonist is a compound of Formula (I):



or a pharmaceutically acceptable salt thereof.

~~29.27.~~ The pharmaceutical composition of claim ~~268,~~ wherein the ACC inhibitor is a compound of Formula (III):

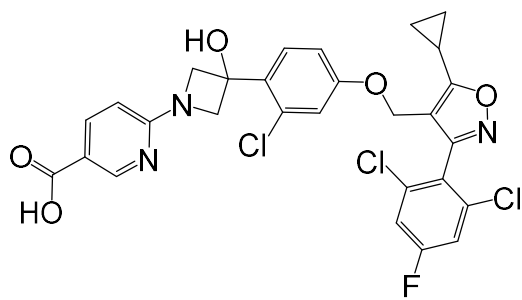


or a pharmaceutically acceptable salt, a stereoisomer, a mixture of stereoisomers, or a tautomer thereof.

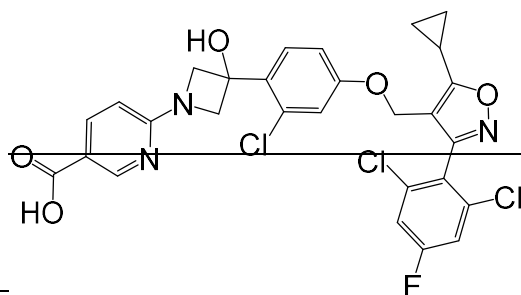
~~30-28.~~ The pharmaceutical composition of ~~any of claims 268 to or 279~~, further comprising a pharmaceutically acceptable carrier.

29. A method~~The use of~~ a therapeutically effective amount of a Thyroid Hormone Receptor (THR) β agonist in combination with a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, in the manufacture of a medicament for treating and/or preventing a liver disease in a patient in need thereof,

wherein the FXR agonist is a compound of Formula (I):

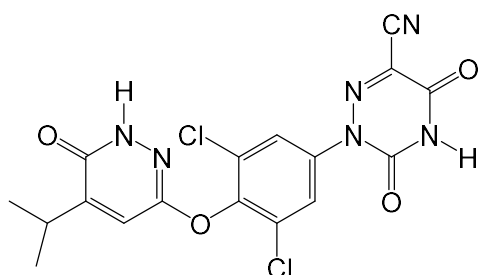


~~31. — or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating and/or preventing a liver disease in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a Thyroid Hormone Receptor (THR) β agonist in combination with a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, wherein the FXR agonist is a compound of Formula (I):~~



~~or a pharmaceutically acceptable salt thereof.~~

~~32.30.~~ The ~~method use~~ of claim ~~2931~~, wherein the THR β agonist is a compound of Formula (IV):



or a pharmaceutically acceptable salt, a stereoisomer, a mixture of stereoisomers, or a tautomer thereof.

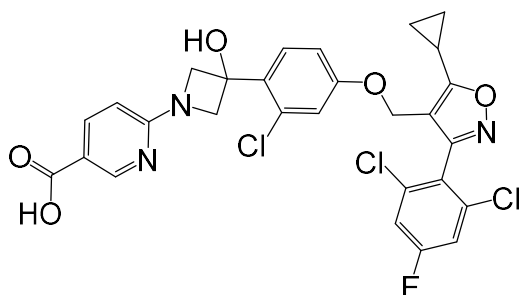
~~33.31.~~ The ~~method use~~ of ~~any one of~~ claims ~~2931 to or 3032~~, wherein the THR β agonist and the FXR agonist are administered separately.

~~34.32.~~ The ~~method use~~ of any one of claims ~~2931~~ to ~~3133~~, wherein the liver disease is non-alcoholic steatohepatitis (NASH).

~~35.33.~~ The ~~method use~~ of any one of claims ~~2931~~ to ~~3133~~, wherein the liver disease is Primary Sclerosing Cholangitis (PSC).

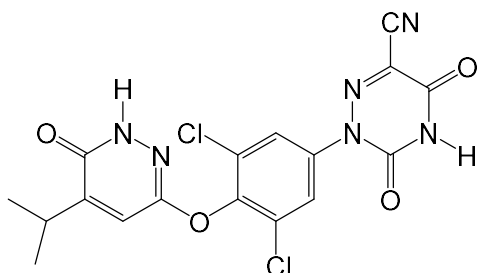
~~36.34.~~ The ~~method use~~ of any one of claims ~~2931~~ to ~~3133~~, wherein the liver disease is Primary Biliary Cirrhosis (PBC).

~~37.35.~~ A pharmaceutical composition comprising a therapeutically effective amount of a Thyroid Hormone Receptor (THR) β and a therapeutically effective amount of a Farnesoid X Receptor (FXR) agonist, wherein the FXR agonist is a compound of Formula (I):



or a pharmaceutically acceptable salt thereof.

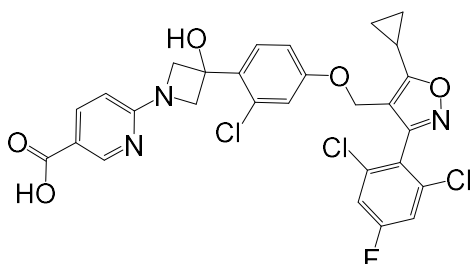
~~38.36.~~ The pharmaceutical composition of claim ~~35~~7, wherein the THR β agonist is a compound of Formula (IV):



or a pharmaceutically acceptable salt, a stereoisomer, a mixture of stereoisomers, or a tautomer thereof.

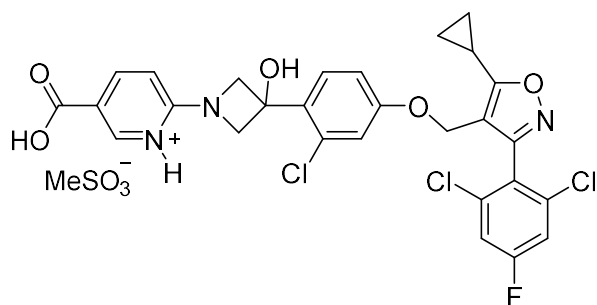
~~39.37.~~ The pharmaceutical composition of ~~any of claims 357 to or 368~~, further comprising a pharmaceutically acceptable carrier.

~~40.38. A method~~The use of inhibiting UGT1A1 in a patient having a liver disease,
~~comprising administering to the patient~~ a therapeutically effective amount of a compound of Formula (I):



or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for inhibiting UGT1A1 in a patient having a liver disease.

~~41.39.~~ A crystalline form of a compound of the following formula:



~~42.40.~~ The crystalline form of claim ~~39~~41, wherein the crystalline form is Form I.

43.41. The crystalline form of claim 40~~42~~, characterized by an X-ray diffraction pattern having 2 θ -reflections at 9.6, 19.3, and 22.6 degrees 2 θ , plus or minus 0.2 degrees 2 θ .

44.42. The crystalline form of ~~any of claims 40- or 41~~42-43, characterized by an X-ray diffraction pattern further comprising 2 θ -reflections at 3.2, 6.4, and 12.8 degrees 2 θ , plus or minus 0.2 degrees 2 θ .

45.43. The crystalline form of any of claims 40~~2-4~~24, characterized by an X-ray diffraction pattern further comprising 2 θ -reflections at 22.1, 25.8, 29.1 degrees 2 θ , plus or minus 0.2 degrees 2 θ .

46.44. The crystalline form of any of claims 40~~2-4~~35, having an X-ray diffraction pattern substantially as shown in Figure 4.

47.45. The crystalline form of any of claims 40~~2-4~~46, having a differential scanning calorimetry thermogram comprising an endothermic with onset at about 221 °C.

48.46. The crystalline form of any of claims 40~~2-4~~57, having a differential scanning calorimetry thermogram substantially as shown in Figure 5.

49.47. The crystalline form of any of claims 40~~2-4~~68, having a thermogravimetric analysis substantially as shown in Figure 6.