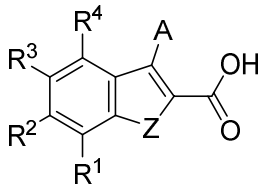
CLAIMS

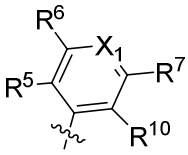
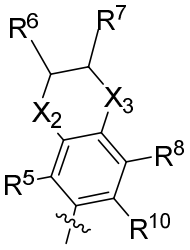
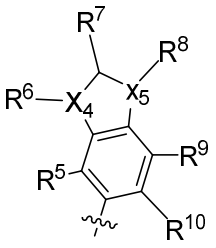
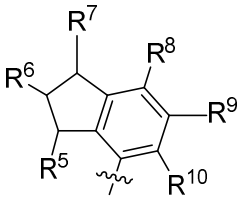
1. A compound of Formula I



Formula I

wherein

Z is O or S;

A is , , , or ;

X_1 is CR^{11} or N;

each of X_2 and X_3 are independently CR^{11} or O, wherein if X_2 is O then X_3 is CR^{11};

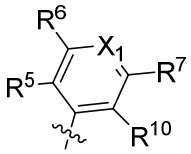
each of X_4 and X_5 are both C or one of X_4 and X_5 is C and the other is O; wherein, if X_4 is O, then R^6 is absent and if X_5 is O, then R^8 is absent;

each of R^1, R^3 and R^4 are independently selected from H and fluoro;

R^2 is H, fluoro or chloro;

each of R^5, R^6, R^7, R^8, R^9 and R^{11} are independently selected from H, halo, hydroxyl, amino, cyano, (C_1-C_4)alkyl, (C_3-C_6)cycloalkyl, (C_1-C_4)alkoxy, (C_1-C_4)fluoroalkyl, (C_3-C_6)fluorocycloalkyl, (C_1-C_4)fluoroalkoxy, or (C_1-C_4)alkyl-(C_1-C_4)alkoxy; and

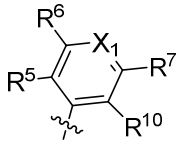
R^{10} is H, hydroxy, fluoro, chloro, cyano, or (C_1-C_4)alkyl;

wherein when A is  and X_1 is CR^{11},

i) at least one of R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10} and R^{11} is halo and at least one other of R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10} and R^{11} is other than H; or

ii) Z is S and R^2 is halo;

or a pharmaceutically acceptable salt of said compound.

2. The compound as recited in claim 1, wherein Z is S; A is  ; R^2 is fluoro or chloro; and X_1 is CR^{11}; or a pharmaceutically acceptable salt thereof.

3. The compound as recited in claim 2, wherein R^1, R^3 and R^4 are each H, and R^2 is fluoro; or a pharmaceutically acceptable salt thereof.

4. The compound as recited in claim 3, wherein R^5 is fluoro, chloro, cyano or $(C_1 –C_4)$alkyl and R^{10} is H, fluoro or chloro; or a pharmaceutically acceptable salt thereof.

5. The compound as recited in claim 4, wherein R^6 and R^7 are each independently selected from H, fluoro, chloro, cyano, $(C_1 –C_4)$alkyl, and $(C_1 –C_4)$alkoxy; or a pharmaceutically acceptable salt thereof.

6. The compound as recited in claim 5, wherein R^{11} is H, fluoro, chloro, cyano, $(C_1 –C_4)$alkyl, or $(C_1 –C_4)$alkoxy; or a pharmaceutically acceptable salt thereof.

7. A compound, wherein the compound is:

6-fluoro-3-(2,4,6-trifluoro-3-methoxyphenyl)-1-benzothiophene-2-carboxylic acid;

6-fluoro-3-(2,4,5-trifluoro-3-methoxyphenyl)-1-benzothiophene-2-carboxylic acid;

6-chloro-3-(2,4,5-trifluoro-3-methylphenyl)-1-benzothiophene-2-carboxylic acid;

6-chloro-3-(2,4-difluoro-3-methoxyphenyl)-1-benzothiophene-2-carboxylic acid;

3-(6-chloro-2,4-difluoro-3-methoxyphenyl)-6-fluoro-1-benzothiophene-2-carboxylic acid;

3-(6-chloro-2,4-difluoro-3-methoxyphenyl)-6-fluoro-1-benzothiophene-2-carboxylic acid, ATROP-2;

3-(3-chloro-2,4,5-trifluorophenyl)-6-fluoro-1-benzothiophene-2-carboxylic acid;

3-(4-chloro-2,6-difluoro-3-methoxyphenyl)-6-fluoro-1-benzothiophene-2-carboxylic acid;

6-chloro-3-(2,4,6-trifluoro-3-methoxyphenyl)-1-benzothiophene-2-carboxylic acid;

6-chloro-3-(3-ethyl-2,4,5-trifluorophenyl)-1-benzothiophene-2-carboxylic acid; or

ammonium 3-(3-ethyl-2,4,5-trifluorophenyl)-6-fluoro-1-benzothiophene-2-carboxylate;

or a pharmaceutically acceptable salt thereof.

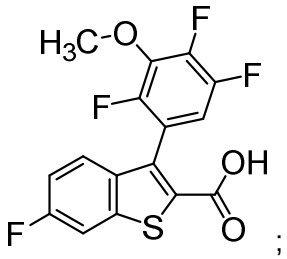
8. A compound, wherein the compound is:

6-fluoro-3-(2,4,5-trifluoro-3-methoxyphenyl)-1-benzothiophene-2-carboxylic acid; or

3-(6-chloro-2,4-difluoro-3-methoxyphenyl)-6-fluoro-1-benzothiophene-2-carboxylic acid, ATROP-2;

or a pharmaceutically acceptable salt thereof.

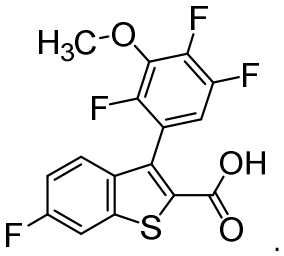
9. A compound, wherein the compound is:



;

or a pharmaceutically acceptable salt thereof.

10. A compound, wherein the compound is



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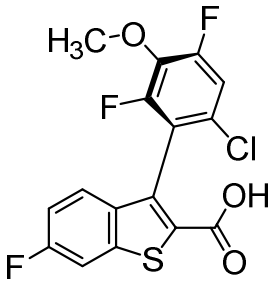
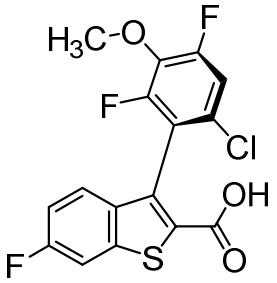
11. A compound, wherein the compound is:



or

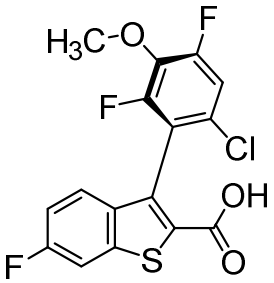


;

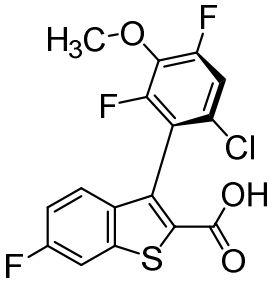
or a mixture thereof;

or a pharmaceutically acceptable salt of said compound or mixture of compounds.

12. A compound, wherein the compound is



or



;

or a mixture thereof.

13. Use of a compound of any one of claims 1-12, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a condition selected from the group

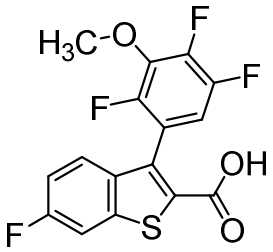
consisting of: fatty liver, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, nonalcoholic steatohepatitis with liver fibrosis, nonalcoholic steatohepotitis with cirrhosis, nonalcoholic steatohepatitis with cirrhosis and hepatocellular carcinoma, heart failure, cardiovascular death, congestive heart failure, heart failure with New York Heart Association Class I-IV symptoms, heart failure with reduced left ventricular function (HF-rEF), heart failure with preserved left ventricular function (HF-pEF), heart failure with midrange ejection fraction (HF-mrEF), cardiovascular death, heart failure in patients with Type II diabetes mellitus, coronary heart disease, unstable angina, peripheral arterial disease peripheral vascular disease, renovascular disease, pulmonary hypertension, vasculitis, acute coronary syndrome, Type I diabetes, Type II diabetes mellitus, idiopathic Type I 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, kidney disease, end-stage kidney disease, chronic kidney disease at risk of progression, and maple syrup urine disease.

14. The use of claim 13, wherein the condition is heart failure.

15. The use of claim 13, wherein the condition is kidney disease.

16. A pharmaceutical composition which comprises a therapeutically effective amount of a compound of any of claims 1 to 12 or a pharmaceutically acceptable salt of said compound and a pharmaceutically acceptable carrier, vehicle or diluent.

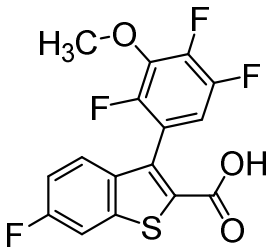
17. A crystal comprising a compound having the structure:



or a pharmaceutically acceptable salt thereof.

18. The crystal of claim 17, having a powder x-ray diffraction pattern comprising 2-theta values of (CuKα radiation, wavelength of 1.54056 Å) 7.6 ± 0.2, 14.6 ± 0.2, and 27.9 ± 0.2.

19. An amorphous form of a compound having the structure:



or a pharmaceutically acceptable salt thereof.

20. A compound of any one of claims 1-12, or a pharmaceutically acceptable salt thereof, for use in therapy.