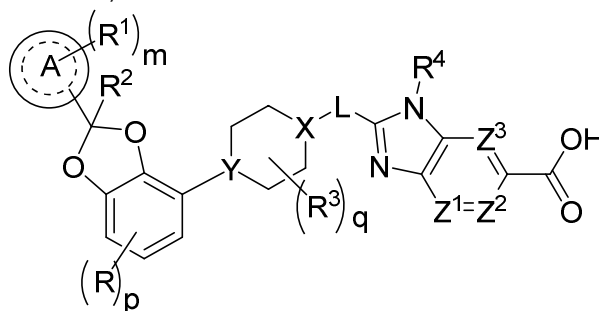


CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula I,



I

or a pharmaceutically acceptable salt thereof, wherein

R is F, Cl, or -CN;

p is 0 or 1;

Ring A is phenyl or a 6-membered heteroaryl;

m is 0, 1, 2, or 3;

each R¹ is independently selected from halogen, -CN, -C₁₋₃alkyl, or -OC₁₋₃alkyl, wherein the alkyl of C₁₋₃alkyl and OC₁₋₃alkyl is substituted with 0 to 3 F atoms;

R² is H or -C₁₋₃alkyl, wherein alkyl is substituted with 0 to 1 OH;

each R³ is independently F, -OH, -CN, -C₁₋₃alkyl, -OC₁₋₃alkyl, or -C₃₋₄cycloalkyl, or 2

R³s may together cyclize to form -C₃₋₄spirocycloalkyl, wherein the alkyl of C₁₋₃alkyl and OC₁₋₃alkyl, cycloalkyl, or spirocycloalkyl may be substituted as valency allows with 0 to 3 F atoms and with 0 to 1 -OH;

q is 0, 1, or 2;

X-L is N-CH₂, CHCH₂, or cyclopropyl;

Y is CH or N;

R⁴ is -C₁₋₃alkyl, -C₀₋₃alkylene-C₃₋₆cycloalkyl, -C₀₋₃alkylene-R⁵, or -C₁₋₃alkylene-R⁶, wherein said alkyl may be substituted as valency allows with 0 to 3 substituents independently selected from 0 to 3 F atoms and 0 to 1 substituent selected from -C₀₋₁alkylene-CN, -C₀₋₁alkylene-OR^O, -SO₂-N(R^N)₂, -C(O)-N(R^N)₂, -N(C=O)(R^N), and -N(R^N)₂, and

wherein said alkylene and cycloalkyl may be independently substituted as valency allows with 0 to 2 substituents independently selected from 0 to 2 F atoms and 0 to 1 substituent selected from -C₀₋₁alkylene-CN, -C₀₋₁alkylene-OR^O, and -N(R^N)₂;

R⁵ is a 4- to 6-membered heterocycloalkyl, wherein said heterocycloalkyl may be substituted with 0 to 2 substituents as valency allows independently selected from:

0 to 1 oxo (=O),

0 to 1 –CN,

0 to 2 F atoms, and

0 to 2 substituents independently selected from –C₁₋₃alkyl and –OC₁₋₃alkyl, wherein the alkyl of C₁₋₃alkyl and OC₁₋₃alkyl may be substituted with 0 to 3 substituents as valency allows independently selected from:

0 to 3 F atoms,

0 to 1 –CN, and

0 to 1 –OR^o;

R⁶ is a 5- to 6-membered heteroaryl, wherein said heteroaryl may be substituted with 0 to 2 substituents as valency allows independently selected from:

0 to 2 halogens,

0 to 1 substituent selected from –OR^o and –N(R^N)₂, and

0 to 2 –C₁₋₃alkyl, wherein the alkyl may be substituted with 0 to 3 substituents as valency allows independently selected from:

0 to 3 F atoms, and

0 to 1 –OR^o;

each R^o is independently H, or –C₁₋₃alkyl, wherein C₁₋₃alkyl may be substituted with 0 to 3 F atoms;

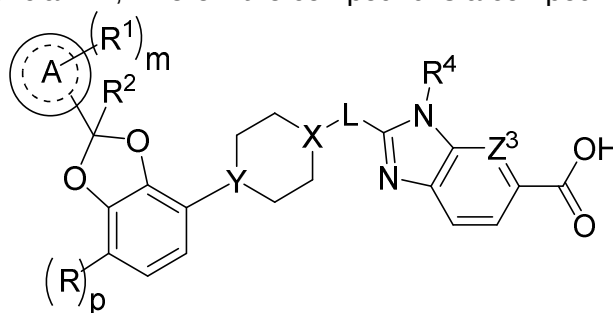
each R^N is independently H, or –C₁₋₃alkyl;

Z¹, Z², and Z³ are each –CR^Z, or

one of Z¹, Z², and Z³ is N and the other two are –CR^Z; and

each R^Z is independently H, F, Cl, or –CH₃.

2. The compound of claim 1, wherein the compound is a compound of Formula II



II

or a pharmaceutically acceptable salt thereof, wherein

R is F;

p is 0 or 1;

Ring A is phenyl or pyridinyl;

m is 0, 1, or 2;

each R^1 is independently selected from halogen, $-\text{CN}$, $-\text{C}_{1-3}\text{alkyl}$, or $-\text{OC}_{1-3}\text{alkyl}$, wherein the alkyl of $\text{C}_{1-3}\text{alkyl}$ and $\text{OC}_{1-3}\text{alkyl}$ is substituted with 0 to 3 F atoms;

R^2 is H or CH_3 ;

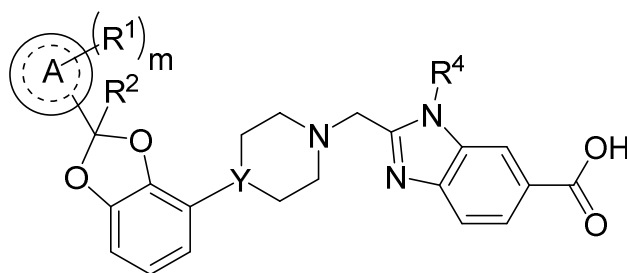
X-L is N-CH_2 , or cyclopropyl;

Y is CH or N;

Z^3 is $-\text{CR}^Z$ or N; and

R^Z is H, F, Cl, or $-\text{CH}_3$.

3. The compound of either claim 1 or claim 2, wherein the compound is a compound of Formula III



III

or a pharmaceutically acceptable salt thereof, wherein

Ring A is phenyl or pyridinyl;

m is 0, 1, or 2;

each R^1 is independently selected from F, Cl, or $-\text{CN}$;

R^2 is H or CH_3 ; and

Y is CH or N.

4. The compound of any of claims 1 to 3, wherein R_4 is $-\text{CH}_2-\text{R}^5$, wherein R^5 is the 4- to 5-membered heterocycloalkyl, wherein said heterocycloalkyl may be substituted with 0 to 2 substituents as valency allows independently selected from:

0 to 2 F atoms, and

0 to 1 substituent selected from $-\text{OCH}_3$ and $-\text{CH}_2\text{OCH}_3$;

or a pharmaceutically acceptable salt thereof.

5. The compound of any of claims 1 to 3, wherein R_4 is $-\text{CH}_2-\text{R}^6$, wherein R^6 is the 5-membered heteroaryl, wherein said heteroaryl may be substituted with 0 to 2 substituents as valency allows independently selected from:

0 to 2 halogens, wherein the halogen is independently selected from F and Cl,

0 to 1 $-\text{OCH}_3$, and

0 to 1 $-\text{CH}_3$, $-\text{CH}_2\text{CH}_3$, $-\text{CF}_3$, or $-\text{CH}_2\text{CH}_2\text{OCH}_3$;

or a pharmaceutically acceptable salt thereof.

6. The compound of any of claims 1 to 5, wherein R^2 is H, or a pharmaceutically acceptable salt thereof.

7. The compound of claim 6, wherein the compound is
2-({4-[2-(4-chloro-2-fluorophenyl)-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid; or

5 2-({4-[2-(4-chloro-2-fluorophenyl)-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-7-fluoro-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid,
or a pharmaceutically acceptable salt thereof.

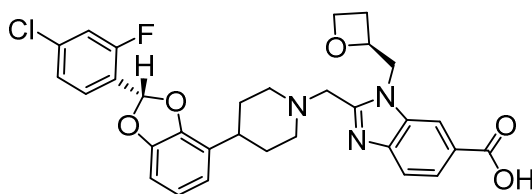
8. The compound of claim 6, wherein the compound is
2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-
10 [(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, or

2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-7-fluoro-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid,
or a pharmaceutically acceptable salt thereof.

9. A compound that is 2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, or a
15 pharmaceutically acceptable salt thereof, wherein the salt is a tris salt.

10. A compound that is 2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, as a
free acid.

20 11. A compound that is



or a pharmaceutically acceptable salt thereof.

12. The compound of any of claims 1 to 5, wherein R² is CH₃, or a pharmaceutically acceptable salt thereof.

25 13. The compound of claim 12, wherein the compound is
2-({4-[2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

2-({4-[2-(4-Cyano-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

30 2-({4-[2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

2-({4-[2-(4-Chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-3-(1,3-oxazol-2-ylmethyl)-3H-imidazo[4,5-b]pyridine-5-carboxylic acid;

2-({4-[2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(1-ethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazole-6-carboxylic acid;

2-({4-[2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-(1,3-oxazol-4-ylmethyl)-1H-benzimidazole-6-carboxylic acid;

5 2-({4-[2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-(pyridin-3-ylmethyl)-1H-benzimidazole-6-carboxylic acid;

2-({4-[2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-(1,3-oxazol-5-ylmethyl)-1H-benzimidazole-6-carboxylic acid;

10 2-({4-[2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(1-ethyl-1H-1,2,3-triazol-5-yl)methyl]-1H-benzimidazole-6-carboxylic acid;

2-({4-[2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-(1,3-oxazol-2-ylmethyl)-1H-benzimidazole-6-carboxylic acid;

2-({4-[2-(4-chloro-2-fluorophenyl)-7-fluoro-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

15 2-({4-[2-(4-cyano-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-(1,3-oxazol-2-ylmethyl)-1H-benzimidazole-6-carboxylic acid; or

2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-7-fluoro-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;
or a pharmaceutically acceptable salt thereof.

20 14. The compound of claim 12, wherein the compound is

2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid; or

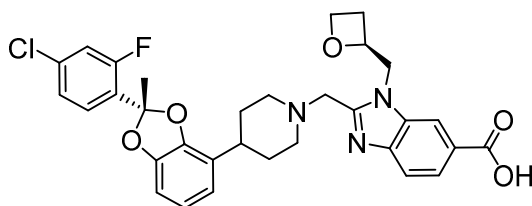
2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-7-fluoro-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

25 or a pharmaceutically acceptable salt thereof.

15. A compound that is 2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, or a pharmaceutically acceptable salt, wherein the salt is a tris salt.

30 16. A compound that is 2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl}methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, as a free acid.

17. A compound that is



or a pharmaceutically acceptable salt thereof.

18. The compound of claim 12, wherein the compound is

2-({4-[(2S)-2-(4-Cyano-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

2-({4-[(2S)-2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid; or

2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(1-ethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazole-6-carboxylic acid;

or a pharmaceutically acceptable salt thereof

19. The compound of claim 12, wherein the compound is

2-({4-[(2R)-2-(4-Cyano-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

2-({4-[(2R)-2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid; or

2-({4-[(2R)-2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(1-ethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazole-6-carboxylic acid,

or a pharmaceutically acceptable salt thereof.

20. A compound that is

2-({4-[2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

2-({4-[(2S)-2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid; or

2-({4-[(2R)-2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid,

as the free acid.

21. A compound that is

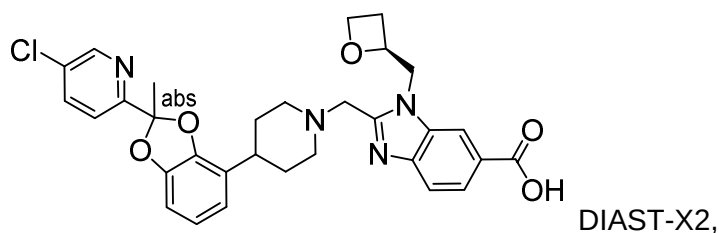
2-({4-[2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid;

2-({4-[(2S)-2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid; or

2-({4-[(2R)-2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid; or a pharmaceutically acceptable salt thereof, wherein the salt is a tris salt.

22. A compound that is 2-({4-[2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-

yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, DIAST-X2:



or pharmaceutically acceptable salt thereof.

23. A crystal form (Form I) of anhydrous 1,3-dihydroxy-2-(hydroxymethyl)propan-2-aminium salt of 2-({4-[(2S)-2-(4-chloro-2-fluorophenyl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid having a powder X-ray diffraction pattern (CuK α radiation) comprising at least two characteristic peaks, in terms of 2θ , selected from at $3.7 \pm 0.2^\circ$; $7.3 \pm 0.2^\circ$; $8.5 \pm 0.2^\circ$; $10.1 \pm 0.2^\circ$; $14.7 \pm 0.2^\circ$; and $16.9 \pm 0.2^\circ$.

24. The crystal form of claim 23 having a powder X-ray diffraction pattern comprising peaks, at least three characteristic peaks, in terms of 2θ , selected from at $3.7 \pm 0.2^\circ$; $7.3 \pm 0.2^\circ$; $8.5 \pm 0.2^\circ$; $10.1 \pm 0.2^\circ$; $14.7 \pm 0.2^\circ$; and $16.9 \pm 0.2^\circ$.

25. The crystal form of claim 23 having a powder X-ray diffraction pattern comprising peaks, at least four characteristic peaks, in terms of 2θ , selected from at $3.7 \pm 0.2^\circ$; $7.3 \pm 0.2^\circ$; $8.5 \pm 0.2^\circ$; $10.1 \pm 0.2^\circ$; $14.7 \pm 0.2^\circ$; and $16.9 \pm 0.2^\circ$.

26. The crystal form of claim 23 having a powder X-ray diffraction pattern comprising peaks, at least five characteristic peaks, in terms of 2θ , selected from at $3.7 \pm 0.2^\circ$; $7.3 \pm 0.2^\circ$; $8.5 \pm 0.2^\circ$; $10.1 \pm 0.2^\circ$; $14.7 \pm 0.2^\circ$; and $16.9 \pm 0.2^\circ$.

27. The crystal form of claim 23 having a powder X-ray diffraction pattern comprising characteristic peaks, in terms of 2θ , at $3.7 \pm 0.2^\circ$ and $7.3 \pm 0.2^\circ$.

28. The crystal form of claim 23 having a powder X-ray diffraction pattern comprising peaks, in terms of 2θ , at $3.7 \pm 0.2^\circ$; $7.3 \pm 0.2^\circ$; and $14.7 \pm 0.2^\circ$.

29. The crystal form of claim 27 or 28, wherein the X-ray powder diffraction pattern further comprises at least one peak, in terms of 2θ , selected from at $8.5 \pm 0.2^\circ$; $10.1 \pm 0.2^\circ$; and $16.9 \pm 0.2^\circ$.

30. The crystal form of claim 29 having a powder X-ray diffraction pattern comprising peaks, in terms of 2θ , at $3.7 \pm 0.2^\circ$; $7.3 \pm 0.2^\circ$; $14.7 \pm 0.2^\circ$; and $16.9 \pm 0.2^\circ$.

31. The crystal form of claim 30 having a powder X-ray diffraction pattern comprising peaks, in terms of 2θ , at $3.7 \pm 0.2^\circ$; $7.3 \pm 0.2^\circ$; $8.5 \pm 0.2^\circ$; $10.1 \pm 0.2^\circ$; $14.7 \pm 0.2^\circ$; and $16.9 \pm 0.2^\circ$.

32. The crystal form of any one of claims 23 to 31 having a powder X-ray diffraction pattern substantially as shown in Figure 1.

33. A crystal form (Form A) of anhydrous 1,3-dihydroxy-2-(hydroxymethyl)propan-2-aminium salt of 2-({4-[2-(5-Chloropyridin-2-yl)-2-methyl-1,3-benzodioxol-4-yl]piperidin-1-yl)methyl)-1-[(2S)-oxetan-2-ylmethyl]-1H-benzimidazole-6-carboxylic acid, DIAST-X2 having a powder X-ray diffraction pattern (CuK α radiation) comprising at least two characteristic peaks, in terms of 2 θ , selected from at 7.7 $\pm$ 0.2 $^\circ$; 15.2 $\pm$ 0.2 $^\circ$; 15.7 $\pm$ 0.2 $^\circ$; and 17.6 $\pm$ 0.2 $^\circ$.

34. The crystal form of claim 33 having a powder X-ray diffraction pattern comprising at least three characteristic peaks, in terms of 2 θ , selected from at 7.7 $\pm$ 0.2 $^\circ$; 15.2 $\pm$ 0.2 $^\circ$; 15.7 $\pm$ 0.2 $^\circ$; and 17.6 $\pm$ 0.2 $^\circ$.

35. The crystal form of claim 33 having a powder X-ray diffraction pattern comprising characteristic peaks, in terms of 2 θ , at 7.7 $\pm$ 0.2 $^\circ$ and 17.6 $\pm$ 0.2 $^\circ$.

36. The crystal form of claim 33 having a powder X-ray diffraction pattern comprising peaks, in terms of 2 θ , at 7.7 $\pm$ 0.2 $^\circ$; 15.2 $\pm$ 0.2 $^\circ$; and 17.6 $\pm$ 0.2 $^\circ$.

37. The crystal form of claim 33 having a powder X-ray diffraction pattern comprising peaks, in terms of 2 θ , at 7.7 $\pm$ 0.2 $^\circ$; 15.2 $\pm$ 0.2 $^\circ$; and 15.7 $\pm$ 0.2 $^\circ$.

38. The crystal form of claim 33 having a powder X-ray diffraction pattern comprising peaks, in terms of 2 θ , at 7.7 $\pm$ 0.2 $^\circ$; 15.2 $\pm$ 0.2 $^\circ$; 15.7 $\pm$ 0.2 $^\circ$; and 17.6 $\pm$ 0.2 $^\circ$.

39. The crystal form of any one of claims 33 to 38 having a powder X-ray diffraction pattern substantially as shown in Figure 2.

40. A pharmaceutical composition comprising the compound of any of claims 1 to 22, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

41. Use of the compound of any of claims 1 to 22, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of ~~A method for treating~~ a cardiometabolic and associated disease or disorder for which an agonist of GLP-1R is indicated, wherein comprising administering to a mammal in need of such treatment a therapeutically effective amount of the medicament is to be administered to a mammal in need thereof, and ~~compound of any of claims 1 to 22, or a pharmaceutically acceptable salt thereof,~~ wherein the disease or disorder is selected from the group consisting of T1D, T2DM, pre-diabetes, idiopathic T1D, LADA, EOD, YOAD, MODY, malnutrition-related diabetes, gestational diabetes, hyperglycemia, insulin resistance, hepatic insulin resistance, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, kidney disease, diabetic retinopathy, adipocyte dysfunction, visceral adipose deposition, sleep apnea, obesity, eating disorders, weight gain from use of other agents, excessive sugar craving, dyslipidemia, hyperinsulinemia, NAFLD, NASH, fibrosis, cirrhosis, hepatocellular carcinoma, cardiovascular disease, atherosclerosis, coronary artery disease, peripheral vascular disease, hypertension, endothelial dysfunction, impaired vascular compliance, congestive heart failure, myocardial infarction, stroke, hemorrhagic stroke, ischemic stroke, traumatic brain injury, pulmonary hypertension, restenosis after angioplasty, intermittent claudication, post-prandial lipemia, metabolic acidosis, ketosis, arthritis, osteoporosis, Parkinson's Disease, left ventricular hypertrophy, peripheral arterial

disease, macular degeneration, cataract, glomerulosclerosis, chronic renal failure, metabolic syndrome, syndrome X, premenstrual syndrome, angina pectoris, thrombosis, atherosclerosis, transient ischemic attacks, vascular restenosis, impaired glucose metabolism, conditions of impaired fasting plasma glucose, hyperuricemia, gout, erectile dysfunction, skin and connective tissue disorders, psoriasis, foot ulcerations, ulcerative colitis, hyper apo B lipoproteinemia, Alzheimer's Disease, schizophrenia, impaired cognition, inflammatory bowel disease, short bowel syndrome, Crohn's disease, colitis, irritable bowel syndrome, prevention or treatment of Polycystic Ovary Syndrome and treatment of addiction.

42. A pharmaceutical composition comprising the crystal form of any of claims 23 to 39 and a pharmaceutically acceptable excipient.

43. Use of the crystal form of any of claims 23 to 39 in the manufacture of a medicament for the treatment of ~~A method for treating~~ a cardiometabolic and associated disease or disorder for which an agonist of GLP-1R is indicated, ~~wherein comprising administering to a mammal in need of such treatment~~ a therapeutically effective amount of the medicament is to be administered to a mammal in need thereof, and the crystal form of any of claims 23 to 39, wherein the disease or disorder is selected from the group consisting of T1D, T2DM, pre-diabetes, idiopathic T1D, LADA, EOD, YOAD, MODY, malnutrition-related diabetes, gestational diabetes, hyperglycemia, insulin resistance, hepatic insulin resistance, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, kidney disease, diabetic retinopathy, adipocyte dysfunction, visceral adipose deposition, sleep apnea, obesity, eating disorders, weight gain from use of other agents, excessive sugar craving, dyslipidemia, hyperinsulinemia, NAFLD, NASH, fibrosis, cirrhosis, hepatocellular carcinoma, cardiovascular disease, atherosclerosis, coronary artery disease, peripheral vascular disease, hypertension, endothelial dysfunction, impaired vascular compliance, congestive heart failure, myocardial infarction, stroke, hemorrhagic stroke, ischemic stroke, traumatic brain injury, pulmonary hypertension, restenosis after angioplasty, intermittent claudication, post-prandial lipemia, metabolic acidosis, ketosis, arthritis, osteoporosis, Parkinson's Disease, left ventricular hypertrophy, peripheral arterial disease, macular degeneration, cataract, glomerulosclerosis, chronic renal failure, metabolic syndrome, syndrome X, premenstrual syndrome, angina pectoris, thrombosis, atherosclerosis, transient ischemic attacks, vascular restenosis, impaired glucose metabolism, conditions of impaired fasting plasma glucose, hyperuricemia, gout, erectile dysfunction, skin and connective tissue disorders, psoriasis, foot ulcerations, ulcerative colitis, hyper apo B lipoproteinemia, Alzheimer's Disease, schizophrenia, impaired cognition, inflammatory bowel disease, short bowel syndrome, Crohn's disease, colitis, irritable bowel syndrome, prevention or treatment of Polycystic Ovary Syndrome and treatment of addiction.

44. The compound of any of claims 1 to 22, or a pharmaceutically acceptable salt thereof, for use in the treatment of a cardiometabolic and associated disease or disorder for which an agonist of GLP-1R is indicated, wherein the disease or disorder is selected from the group consisting of T1D, T2DM, pre-diabetes, idiopathic T1D, LADA, EOD, YOAD, MODY, malnutrition-related diabetes, gestational diabetes, hyperglycemia, insulin resistance, hepatic insulin resistance, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, kidney disease, diabetic retinopathy, adipocyte dysfunction, visceral adipose deposition, sleep apnea, obesity, eating disorders, weight gain from use of other agents, excessive sugar craving, dyslipidemia, hyperinsulinemia, NAFLD, NASH, fibrosis, cirrhosis, hepatocellular carcinoma, cardiovascular disease, atherosclerosis, coronary artery disease, peripheral vascular disease, hypertension, endothelial dysfunction, impaired vascular compliance, congestive heart failure, myocardial infarction, stroke, hemorrhagic stroke, ischemic stroke, traumatic brain injury, pulmonary hypertension, restenosis after angioplasty, intermittent claudication, post-prandial lipemia, metabolic acidosis, ketosis, arthritis, osteoporosis, Parkinson's Disease, left ventricular hypertrophy, peripheral arterial disease, macular degeneration, cataract, glomerulosclerosis, chronic renal failure, metabolic syndrome, syndrome X, premenstrual syndrome, angina pectoris, thrombosis, atherosclerosis, transient ischemic attacks, vascular restenosis, impaired glucose metabolism, conditions of impaired fasting plasma glucose, hyperuricemia, gout, erectile dysfunction, skin and connective tissue disorders, psoriasis, foot ulcerations, ulcerative colitis, hyper apo B lipoproteinemia, Alzheimer's Disease, schizophrenia, impaired cognition, inflammatory bowel disease, short bowel syndrome, Crohn's disease, colitis, irritable bowel syndrome, prevention or treatment of Polycystic Ovary Syndrome and treatment of addiction.

45. The crystal form of any of claims 23 to 39 for use in the treatment of a cardiometabolic and associated disease or disorder for which an agonist of GLP-1R is indicated, wherein the disease or disorder is selected from the group consisting of T1D, T2DM, pre-diabetes, idiopathic T1D, LADA, EOD, YOAD, MODY, malnutrition-related diabetes, gestational diabetes, hyperglycemia, insulin resistance, hepatic insulin resistance, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, kidney disease, diabetic retinopathy, adipocyte dysfunction, visceral adipose deposition, sleep apnea, obesity, eating disorders, weight gain from use of other agents, excessive sugar craving, dyslipidemia, hyperinsulinemia, NAFLD, NASH, fibrosis, cirrhosis, hepatocellular carcinoma, cardiovascular disease, atherosclerosis, coronary artery disease, peripheral vascular disease, hypertension, endothelial dysfunction, impaired vascular compliance, congestive heart failure, myocardial infarction, stroke, hemorrhagic stroke, ischemic stroke, traumatic brain injury, pulmonary hypertension, restenosis after angioplasty, intermittent claudication, post-prandial lipemia, metabolic acidosis, ketosis, arthritis, osteoporosis, Parkinson's Disease, left ventricular hypertrophy, peripheral arterial disease, macular

degeneration, cataract, glomerulosclerosis, chronic renal failure, metabolic syndrome, syndrome X, premenstrual syndrome, angina pectoris, thrombosis, atherosclerosis, transient ischemic attacks, vascular restenosis, impaired glucose metabolism, conditions of impaired fasting plasma glucose, hyperuricemia, gout, erectile dysfunction, skin and connective tissue disorders, psoriasis, foot ulcerations, ulcerative colitis, hyper apo B lipoproteinemia, Alzheimer's Disease, schizophrenia, impaired cognition, inflammatory bowel disease, short bowel syndrome, Crohn's disease, colitis, irritable bowel syndrome, prevention or treatment of Polycystic Ovary Syndrome and treatment of addiction.