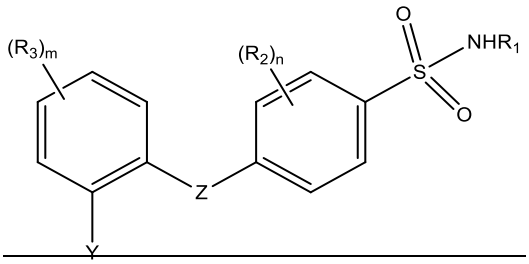
WHAT IS CLAIMED IS

1. A compound of Formula (**I**),



Formula (**I**)

or a pharmaceutically acceptable salt, or a stereoisomeric or tautomeric form thereof, wherein:

Z is -O- or -S-;

Y is -X-C(=O)NR_4R_5, -$(CH_2)_3$-NR_9R_{10}, or 4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrimidine-(2-yl or 3-yl);

X is (C_6-C_{10})aryl or 5- or 6-membered heteroaryl;

R_1 is a partially unsaturated or aromatic 5- or 6-membered heterocycle;

R_2 is independently at each occurrence -F, -Cl, -Br, -CH_3 or -CN;

R_3 is independently at each occurrence -H, -F, -Cl, -Br, -CF_3, -OCF_3, -CN, (C_1-C_{12})alkyl, or (C_1-C_{12})alkoxy;

R_4 and R_5 are each independently H, (C_1-C_9)alkyl, (C_4-C_{12})cycloalkyl, or R_4 and R_5 together form a 5- to 7-membered heterocycloalkyl ring; with the proviso that:

R_4 and R_5 are not both H; and

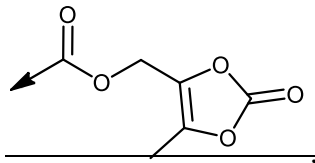
at least one of R_4 and R_5 independently or said heterocycloalkyl ring formed by R_4 and R_5 together is substituted with 1 or 2 substituents selected from the group consisting of -CO_2H, -CO_2R_6, -CN, -OH, -$CONR_7R_8$, and -NR_7R_8; wherein:

R_6 is (C_1-C_{12})alkyl;

R_7 and R_8 are each independently H, (C_1-C_{12})alkyl, or R_7 and R_8 together form a 4- to 7-membered heterocycloalkyl ring;

R_9 is (C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, pyrazolyl or pyridinyl; wherein R_9 is optionally further substituted with 1 or 2 substituents selected from the group consisting of -COOH, -$COOR_{11}$, -$CONR_{11}R_{12}$, -SO_2R_{11}, -$SO_2NR_{11}R_{12}$, -OH, -CN, -OR_{11}, and -$NR_{11}R_{12}$; wherein R_{11} and R_{12} may form a 6 membered heterocycloalkyl ring

R_{10} is R_{11}, $-COR_{11}$, $-COOR_{11}$, $-SO_2R_{11}$, 5-methyl-2-oxo-1,3-dioxol-4-yl,

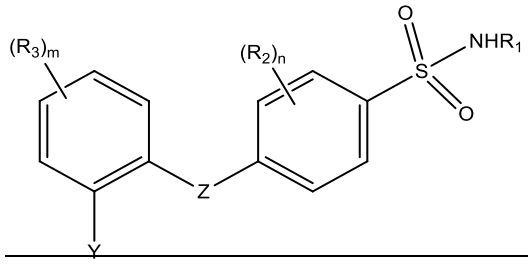


, $-COO-CH(CH_3)OCOCH(CH_3)_2$; or R_9 and R_{10} together form a piperazinone or a 4- to 8- membered heterocycloalkyl ring, wherein said heterocycloalkyl ring is substituted with 1 or 2 substituents selected from the group consisting of $-COOH$, $-COOR_{11}$, $-CH_2-COOR_{11}$, $-OH$, $-NH_2$, $-CN$, and (C_1-C_8)alkoxy;

R_{11} and R_{12} are independently H or (C_1-C_6)alkyl, optionally substituted with 4- to 8-membered heterocycloalkyl ring; and

m and n are each independently 1, 2, 3, or 4.

2. A compound of Formula (**I'**),



Formula (**I'**)

or a pharmaceutically acceptable salt, or a stereoisomeric or tautomeric form thereof, wherein:

Z is $-O-$ or $-S-$;

Y is $-X-C(=O)NR_4R_5$, $-(CH_2)_3-NR_9R_{10}$, or 4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrimidine-(2-yl or 3-yl);

X is (C_6-C_{10})aryl or 5- or 6-membered heteroaryl;

R_1 is a partially unsaturated or aromatic 5- or 6-membered heterocycle;

R_2 is independently at each occurrence $-F$, $-Cl$, $-Br$, $-CH_3$ or $-CN$;

R_3 is independently at each occurrence $-H$, $-F$, $-Cl$, $-Br$, $-CF_3$, $-OCF_3$, $-CN$, (C_1-C_{12})alkyl, or (C_1-C_{12})alkoxy;

R_4 and R_5 are each independently H, (C_1-C_9)alkyl, (C_4-C_{12})cycloalkyl, or R_4 and R_5 together form a 5- to 7-membered heterocycloalkyl ring; with the proviso that: R_4 and R_5 are not both H; and

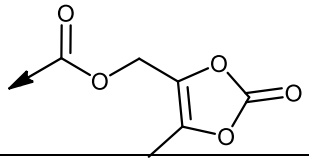
at least one of R_4 and R_5 independently or said heterocycloalkyl ring formed by R_4 and R_5 together is substituted with 1 or 2 substituents selected from the group consisting of $-CO_2H$, $-CO_2R_6$, -CN, -OH, $-CONR_7R_8$, and $-NR_7R_8$; wherein:

R_6 is (C_1-C_{12})alkyl;

R_7 and R_8 are each independently H, (C_1-C_{12})alkyl, or R_7 and R_8 together form a 4- to 7-membered heterocycloalkyl ring;

R_9 is (C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, pyrazolyl or pyridinyl; wherein R_9 is optionally further substituted with 1 or 2 substituents selected from the group consisting of -COOH, $-COOR_{11}$, $-CONR_{11}R_{12}$, $-SO_2R_{11}$, $-SO_2NR_{11}R_{12}$, -OH, -CN, $-OR_{11}$, and $-NR_{11}R_{12}$; wherein R_{11} and R_{12} may form a 6 membered heterocycloalkyl ring

R_{10} is R_{11}, (C_3-C_6)alkynyl, (C_3-C_6)alkenyl, $-COR_{11}$, $-COOR_{11}$, $-SO_2R_{11}$,



5-methyl-2-oxo-1,3-dioxol-4-yl,

, $-COO-CH(CH_3)OCOCH(CH_3)_2$; or R_9 and R_{10} together form a piperazinone or a 4-to 8- membered heterocycloalkyl ring, wherein said heterocycloalkyl ring is substituted with 1 or 2 substituents selected from the group consisting of -COOH, $-COOR_{11}$, $-CH_2-COOR_{11}$, -OH, $-NH_2$, -CN, and (C_1-C_8)alkoxy; or R_9 and R_{10} together form a unsubstituted 4- to 8-membered heterocycloalkyl ring, wherein said heterocycloalkyl ring is fused with a 5-membered heteroaryl; and

R_{11} and R_{12} are independently H or (C_1-C_6)alkyl, optionally substituted with 4- to 8-membered heterocycloalkyl ring; and

m and n are each independently 1, 2, 3, or 4.

3. The compound of any of claims 1 or 2, wherein Y is $-(CH_2)_3-NR_9R_{10}$.

4. The compound of claim 3, wherein R_1 is an aromatic 5- or 6-membered heterocycle, with 1-3 heteroatoms independently selected from the group consisting of N, O, and S.

5. The compound of any of claims 3 or 4, wherein R_1 is pyridyl or pyrimidinyl.

6. The compound of any of claims 3 or 4, wherein R_1 is an aromatic 5-membered heterocycle with 1 or 2 nitrogen atoms and optionally 1 or 2 sulphur atoms.

7. The compound of any of claims 3 or 4, or 6 wherein R_1 is thiazolyl, isothiazolyl, or thiadiazolyl.

8. The compound of any of claims 3, 4, 6, or 7, wherein R_1 is thiazolyl.

9. The compound of any of claims 3, 4, 6, 7, or 8, wherein R_1 is thiazol-4-yl.

10. The compound of any of claims 3, 4, 6, or 7, wherein R_1 is 1,2,4-thiadiazol-5-yl.

11. The compound of any of claims 3-10, wherein R_2 is independently at each occurrence -F or -Cl.

12. The compound of any of claims 3-11, wherein n is 1, 2, or 3.

13. The compound of any of claims 3-12, wherein n is 2.

14. The compound of any of claims 3-13, wherein Z is -O-.

15. The compound of any of claims 3-14, wherein R_3 is independently at each occurrence -H, -F, -Cl, or -Br.

16. The compound of any of claims 3-15, wherein R_3 is -H or -Cl.

17. The compound of any of claims 3-16, wherein R_3 is -Cl.

18. The compound of any of claims 3-17, wherein m is 1, 2, or 3.

19. The compound of any of claims 3-18, wherein m is 1.

20. The compound of any of claims 3-19, wherein R_9 is (C_1-C_6)alkyl; wherein R_9 is optionally further substituted with 1 or 2 substituents selected from the group consisting of -COOH, -COOMe, $-CONH_2$, and $-NH_2$.

21. The compound of any of claims 3-20, wherein R_9 is methyl or ethyl.

22. The compound of any of claims 3-21, wherein R_9 is further substituted with -COOH.

23. The compound of any of claims 3-22, wherein R_{10} is -H, -COMe, -COOEt.

24. The compound of any of claims 3-22, wherein R_{10} is -H or -COMe.

25. The compound of any of claims 3-24, wherein R_{10} is -H.

26. The compound of any of claims 3-19, wherein R_{10} is H and R_9 is $(C_1\text{-}C_6)$alkyl, wherein R_9 is further substituted with -$CONR_{11}R_{12}$, wherein R_{11} and R_{12} are independently H or $(C_1\text{-}C_6)$alkyl.

27. The compound of claim 26, wherein the R_9 is further substituted with -$CONH_2$.

28. The compound of claim 27, wherein the R_9 is methyl.

29. The compound of any of claims 3-19, wherein R_9 and R_{10} together form a 4 to 8 membered heterocycloalkyl ring, wherein said heterocycloalkyl ring is substituted with 1 or 2 groups selected from the group consisting of -COOH, -COOMe, -COOEt, -CH_2-COOH, and -NH_2.

30. The compound of any of claims 3-19, wherein R_9 and R_{10} together form a 4 to 8 membered heterocycloalkyl ring, wherein said heterocycloalkyl ring is substituted with 1 or 2 groups selected from the group consisting of -COOH, -CH_2-COOH, and -NH_2.

31. The compound of any of claims 3-19, wherein R_9 and R_{10} together form a piperidine substituted with 1 or 2 groups selected from the group consisting of -COOH, -COOMe, -COOEt, -CH_2-COOH, -CH_2-COOMe, -CH_2-COOEt, and -NH_2.

32. The compound of any of claims 3-19, wherein R_9 and R_{10} together form a piperidine substituted with 1 or 2 groups selected from the group consisting of -COOH, -CH_2-COOH, and -NH_2.

33. The compound of any of claims 1 or 2, wherein Y is -X-$C(=O)NR_4R_5$.

34. The compound of claim 33, wherein R_1 is an aromatic 5- or 6-membered heterocycle, with 1-3 heteroatoms independently selected from the group consisting of N, O, and S.

35. The compound of any of claims 33 or 34, wherein R_1 is pyridyl or pyrimidinyl.

36. The compound of any of claims 33 or 34, wherein R_1 is an aromatic 5-membered heterocycle with 1 or 2 nitrogen atoms and optionally 1 or 2 sulphur atoms.

37. The compound of any of claims 33, 34, or 36 wherein R_1 is thiazolyl, isothiazolyl, or thiadiazolyl.

38. The compound of any of claims 33, 34, 36, or 37, wherein R_1 is thiazolyl.

39. The compound of any of claims 33, 34, 36, or 37, wherein R_1 is 1,2,4-thiadiazol-5-yl.

40. The compound of any of claims 33-39, wherein R_2 is independently at each occurrence -F or -Cl.

41. The compound of any of claims 33-40, wherein n is 1, 2, or 3.

42. The compound of any of claims 33-41, wherein n is 2.

43. The compound of any of claims 33-42, wherein Z is -O-.

44. The compound of any of claims 33-43, wherein R_3 is independently at each occurrence
-H, -F, -Cl, or -Br.

45. The compound of any of claims 33-44, wherein R_3 is -H or -Cl.

46. The compound of any of claims 33-45, wherein R_3 is -Cl.

47. The compound of any of claims 33-46, wherein m is 1, 2, or 3.

48. The compound of any of claims 33-47, wherein m is 1.

49. The compound of any of claims 33-48, wherein X is 5- or 6-membered heteroaryl.

50. The compound of any of claims 33-49, wherein X is pyridyl or pyrimidinyl.

51. The compound of any of claims 33-50, wherein X is pyridyl.

52. The compound of any of claims 33-51, wherein R_4 is H and R_5 is (C_1-C_9)alkyl.

53. The compound of any of claims 33-52, wherein R_5 is methyl or ethyl, substituted with 1 or 2 substituents selected from the group consisting of -CO_2H, -CO_2R_6, and -$CONR_7R_8$.

54. The compound of any of claims 33-53, wherein R_6 is (C_1-C_6)alkyl.

55. The compound of any of claims 33-53, wherein R_5 is methyl or ethyl, substituted with -CO_2H.

56. The compound of any of claims 1 or 2, wherein Y is 4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrimidine-(2-yl or 3-yl).

57. The compound of claim 56, wherein Y is 4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrimidine-3-yl.

58. The compound of any of claims 56 or 57, wherein R_1 is an aromatic 5- or 6-membered heterocycle, with 1-3 heteroatoms independently selected from the group consisting of N, O, and S.

59. The compound of any of claims 56-58, wherein R_1 is pyridyl or pyrimidinyl.

60. The compound of any of claims 56-58, wherein R_1 is an aromatic 5-membered heterocycle with 1 or 2 nitrogen atoms and optionally 1 or 2 sulphur atoms.

61. The compound of any of claims 56-58, or 60 wherein R_1 is thiazolyl, isothiazolyl, or thiadiazolyl.

62. The compound of any of claims 56-58, 60, or 61, wherein R_1 is thiazolyl.

63. The compound of any of claims 56-58, 60, or 61, wherein R_1 is 1,2,4-thiadiazol-5-yl.

64. The compound of any of claims 56-63, wherein R_2 is independently at each occurrence -F or -Cl.

65. The compound of any of claims 56-64, wherein n is 1, 2, or 3.

66. The compound of any of claims 56-65, wherein n is 2.

67. The compound of any of claims 56-66, wherein Z is -O-.

68. The compound of any of claims 56-67, wherein R_3 is independently at each occurrence

-H, -F, -Cl, or -Br.

69. The compound of any of claims 56-68, wherein R_3 is -H or -Cl.

70. The compound of any of claims 56-69, wherein R_3 is -Cl.

71. The compound of any of claims 56-70, wherein m is 1, 2, or 3.

72. The compound of any of claims 56-71, wherein m is 1.

73. The compound of any of claims 1 or 2, wherein the compound is

3-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)propanoic acid,

2-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)acetic acid,

5-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)pentanoic acid,

4-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)butanoic acid,

2-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)propanoic acid,

(R)-2-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)propanoic acid,

2-(6-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)acetic acid,

(S)-2-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)propanoic acid,

3-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-cyanophenoxy)-5-chlorophenyl)picolinamido)propanoic acid,

3-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2,5-difluorophenoxy)-5-chlorophenyl)picolinamido)propanoic acid,

2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetic acid,

3-((3-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-

chlorophenyl)propyl)amino)propanoic acid,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetic acid,
1-(3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)piperidine-4-carboxylic acid,
3-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)propanoic acid,
4-amino-1-(3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)piperidine-4-carboxylic acid,
2-amino-4-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)butanoic acid,
2-((3-(5-chloro-2-(2,5-difluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetic acid,
1-(3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)piperidine-3-carboxylic acid,
2-((3-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)phenyl)propyl)amino)acetic acid,
2-((3-(5-chloro-2-(2,5-difluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetic acid,
3-((3-(5-chloro-2-(2,5-difluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)propanoic acid,
3-((3-(5-chloro-2-(2-cyano-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)propanoic acid,
methyl 2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetate,
3-((3-(2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)-5-fluorophenyl)propyl)amino)propanoic acid,
3-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)propanamide,
2-(N-(3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)acetamido)acetic acid,
2-(1-(3-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)propyl)piperidin-4-yl)acetic acid,
3-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-

yl)sulfamoyl)phenoxy)phenyl)propyl)amino)propanoic acid,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)-N-methylacetamide,
5-chloro-4-(4-chloro-2-(3-((2-(methylsulfonyl)ethyl)amino)propyl)phenoxy)-2-fluoro-N-(thiazol-4-yl)benzenesulfonamide,
1-(3-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)propyl)piperidine-4-carboxylic acid,
5-chloro-4-(4-chloro-2-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-3-yl)phenoxy)-2-fluoro-N-(thiazol-4-yl)benzenesulfonamide,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(ethoxycarbonyl)amino)acetic acid,
ethyl 2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetate,
4-(2-(3-((1H-pyrazol-4-yl)amino)propyl)-4-chlorophenoxy)-5-chloro-2-fluoro-N-(thiazol-2-yl)benzenesulfonamide,
3-((3-(5-chloro-2-(2,5-difluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)propanoic acid,
5-chloro-4-(4-chloro-2-(3-((2-(methylsulfonyl)ethyl)amino)propyl)phenoxy)-2-fluoro-N-(thiazol-4-yl)benzenesulfonamide,
4-(2-(3-((1H-pyrazol-3-yl)amino)propyl)-4-chlorophenoxy)-5-chloro-2-fluoro-N-(thiazol-4-yl)benzenesulfonamide,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)-N-methylacetamide,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)(methyl)amino)acetic acid,
5-chloro-4-(4-chloro-2-(3-(6,7-dihydro-1H-pyrazolo[4,3-c]pyridin-5(4H)-yl)propyl)phenoxy)-2-fluoro-N-(thiazol-4-yl)benzenesulfonamide,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetamide,
isopentyl 2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetate,
isopropyl 2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetate,
methyl 2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-

~~yl)sulfamoyl)phenoxy)phenyl)propyl)(methyl)amino)acetate,~~

~~2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)((pentyloxy)carbonyl)amino)acetic acid,~~

~~2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(prop-2-yn-1-yl)amino)acetic acid,~~

~~5-chloro-4-(4-chloro-2-(3-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)propyl)phenoxy)-2-fluoro-N-(thiazol-4-yl)benzenesulfonamide,~~

~~5-chloro-2-fluoro-4-(2-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-3-yl)phenoxy)-N-(thiazol-2-yl)benzenesulfonamide,~~

~~5-chloro-4-(4-chloro-2-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-3-yl)phenoxy)-2-fluoro-N-(thiazol-2-yl)benzenesulfonamide,~~

~~5-chloro-2-fluoro-4-(2-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-3-yl)phenoxy)-N-(thiazol-4-yl)benzenesulfonamide,~~

~~5-chloro-4-(4-chloro-2-(3-((2-(methylsulfonyl)ethyl)amino)propyl)phenoxy)-2-fluoro-N-(thiazol-2-yl)benzenesulfonamide,~~

~~2-((3-(2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetamide,~~

~~2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)(prop-2-yn-1-yl)amino)acetic acid,~~

~~2-(allyl(3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetic acid,~~

~~2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetamide,~~

~~2-(but-2-yn-1-yl(3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetic acid,~~

~~2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(propyl)amino)acetic acid,~~

~~3-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(prop-2-yn-1-yl)amino)propanoic acid,~~

~~2-((3-(5-chloro-2-(2,5-difluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(prop-2-yn-1-yl)amino)acetic acid,~~

~~ethyl 2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(methyl)amino)acetate, or~~

~~2-((3-(5-chloro-2-(2,5-difluoro-4-(N-(thiazol-4-~~

yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetamide;
or a pharmaceutically acceptable salt, or a stereoisomeric or tautomeric form thereof.

74. The compound of any of claims 1, 2, or 73, wherein the compound is
2-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)acetic acid,
3-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)propanoic acid,
2-(4-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)picolinamido)propanoic acid,
3-((3-(2-(4-(N-(1,2,4-thiadiazol-5-yl)sulfamoyl)-2-chloro-5-fluorophenoxy)-5-chlorophenyl)propyl)amino)propanoic acid,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetamide,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)((pentyloxy)carbonyl)amino)acetic acid, or
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(prop-2-yn-1-yl)amino)acetic acid;
or a pharmaceutically acceptable salt, or a stereoisomeric or tautomeric form thereof.

75. The compound of any of claims 1, 2, or 73, wherein the compound is
3-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)propanoic acid,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetamide,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(prop-2-yn-1-yl)amino)acetic acid,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)(prop-2-yn-1-yl)amino)acetic acid,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetamide,
2-((3-(5-chloro-2-(2-chloro-5-fluoro-4-(N-(thiazol-2-yl)sulfamoyl)phenoxy)phenyl)propyl)(propyl)amino)acetic acid,
2-((3-(5-chloro-2-(2,5-difluoro-4-(N-(thiazol-2-

yl)sulfamoyl)phenoxy)phenyl)propyl)(prop-2-yn-1-yl)amino)acetic acid, or 2-((3-(5-chloro-2-(2,5-difluoro-4-(N-(thiazol-4-yl)sulfamoyl)phenoxy)phenyl)propyl)amino)acetamide;
or a pharmaceutically acceptable salt, or a stereoisomeric or tautomeric form thereof.

76. A method for treating neuropathic pain comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) or a compound of Formula (I'), or a pharmaceutically acceptable salt, solvate or tautomeric form thereof.

77. A method for treating pain comprising use of a compound of Formula (I) or of a compound of Formula (I'), as a voltage-gated sodium channel inhibitor.

78. The method of claim 77, wherein the pain is neuropathic, nociceptive or inflammatory pain.

79. The method of claim 77, wherein the voltage-gated sodium channel is NaV1.7.

80. A pharmaceutical composition comprising a compound of any one of claims 1 to 75 and a pharmaceutically acceptable carrier.

81. The composition of claim 80, wherein the composition is suitable for topical, oral, subcutaneous, or intravenous administration.

82. A method for prevention or treatment of pain in a subject, wherein the method comprises administering to the subject in need of such prevention or treatment a therapeutically effective amount of a compound of any one of claims 1 to 75.

83. The method of claim 82, wherein the therapeutically effective amount is effective to alleviate pain in a subject, wherein the compound of any one of claims 1 to 75 shows a reduction in pain response in the Formalin Assay in phase 1 or phase 2, or both, at a dose between 0.1 mg/kg and 1,000 mg/kg, at a dose between 0.5 mg/kg and 100 mg/kg, or at a dose between 1 mg/kg to 50 mg/kg.

84. The method of claim 82, wherein the pain is nociceptive pain, such as that resulting from physical trauma (e.g., a cut or contusion of the skin; or a chemical or thermal burn), osteoarthritis, rheumatoid arthritis or tendonitis; myofascial pain; neuropathic

pain, such as that associated with stroke, diabetic neuropathy, luetic neuropathy, postherpetic neuralgia, trigeminal neuralgia, fibromyalgia, or painful neuropathy induced iatrogenically by drugs; or mixed pain (i.e., pain with both nociceptive and neuropathic components); visceral pain; headache pain (e.g., migraine headache pain); CRPS; CRPS type I; CRPS type II; RSD; reflex neurovascular dystrophy; reflex dystrophy; sympathetically maintained pain syndrome; causalgia; Sudeck atrophy of bone; algoneurodystrophy; shoulder hand syndrome; post-traumatic dystrophy; autonomic dysfunction; autoimmune-related pain; inflammation-related pain; cancer-related pain; phantom limb pain; chronic fatigue syndrome; post-operative pain; spinal cord injury pain; central post-stroke pain; radiculopathy; sensitivity to temperature, light touch or color change to the skin (allodynia); pain from hyperthermic or hypothermic conditions; and other painful conditions (e.g., diabetic neuropathy, luetic neuropathy, postherpetic neuralgia, trigeminal neuralgia); chronic pain; acute pain; pain from neuromas, pain or itch associated with channelopathies (e.g., small fiber neuralgia, IEM or Raynodes); or itch from various origins (e.g., allergic itch).

85. A method for modulating the activity of a voltage-gated sodium channel, wherein the method comprises contacting a cell that expresses the voltage-gated sodium channel with a compound of any one of claims 1 to 75.

86. The method of claim 85, wherein the voltage-gated sodium channel is NaV1.7.

87. The method of claim 85, wherein the method results in inhibition of the voltage-gated sodium channel.

88. A method for treating or preventing prediabetes comprising administering to a subject in need thereof a therapeutically effective amount of a compound of any one of claims 1 to 75, or a pharmaceutically acceptable salt, solvate or tautomeric form thereof.

89. A method for treating or preventing diabetes comprising administering to a subject in need thereof a therapeutically effective amount of a compound of any one of claims 1 to 75, or a pharmaceutically acceptable salt, solvate or tautomeric form thereof.

90. A method for maintaining or lowering blood or plasma glucose in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of

a compound of any one of claims 1 to 75, or a pharmaceutically acceptable salt, solvate or tautomeric form thereof.

91. A method for maintaining or lowering blood or plasma glycated hemoglobin in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of any one of claims 1 to 75, or a pharmaceutically acceptable salt, solvate or tautomeric form thereof.

92. The method of any one of claims 90 or 91, wherein the subject has prediabetes.

93. The method of any one of claims 90 or 91, wherein the subject has diabetes.

94. The method of any one of claims 89 or 93, wherein diabetes is gestational diabetes, type-1 diabetes, type-2 diabetes, or latent autoimmune diabetes of adults.

95. The method of claim 94, wherein diabetes is gestational diabetes.

96. The method of claim 94, wherein diabetes is type-1 diabetes.

97. The method of claim 94, wherein diabetes is type-2 diabetes.

98. The method of claim 97, wherein type-2 diabetes is hyperinsulinemic Type 2 diabetes.

99. The method of claim 94, wherein diabetes is latent autoimmune diabetes of adults.

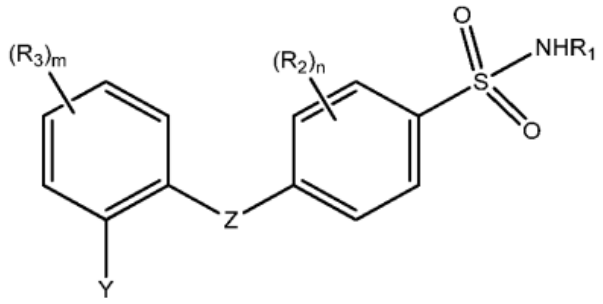
100. The method of any one of claims 88 or 92, wherein the prediabetes is caused by or accompanied by obesity.

101. The method of any one of claims 89 or, wherein the diabetes is caused by or accompanied by obesity.

102. The method of any one of claims 89 or 93, wherein the subject has not been previously treated for prediabetes.

103. The method of any one of claims 89 or 93, wherein the subject has not been previously treated for diabetes.

1. A compound of Formula (I'),



Formula (**I'**)

or a pharmaceutically acceptable salt, or a stereoisomeric or tautomeric form thereof, wherein:

Z is -O-;

Y is $-(CH_2)_3-NR_9R_{10}$;

R_1 is thiazolyl, isothiazolyl, or thiadiazolyl;

R_2 is independently at each occurrence -F, -Cl, or -CN;

R_3 is independently at each occurrence -H, -F, or -Cl;

R_9 is (C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, pyrazolyl or pyridinyl; wherein R_9 is optionally further substituted with 1 or 2 substituents selected from the group consisting of -COOH, $-COOR_{11}$, $-CONR_{11}R_{12}$, $-SO_2R_{11}$, $-SO_2NR_{11}R_{12}$, -OH, -CN, $-OR_{11}$, and $-NR_{11}R_{12}$; wherein R_{11} and R_{12} may form a 6 membered heterocycloalkyl ring;

R_{10} is (C_3-C_6)alkynyl, (C_3-C_6)alkenyl; or R_9 and R_{10} together form a unsubstituted 4- to 8-membered heterocycloalkyl ring, wherein said heterocycloalkyl ring is fused with a 5-membered heteroaryl; and

R_{11} and R_{12} are independently H or (C_1-C_6)alkyl, optionally substituted with 4- to 8-membered heterocycloalkyl ring; and

m and n are each independently 1, or 2.

2. The compound of claim 1, wherein R_2 is independently at each occurrence -F or -Cl.

3. The compound of claim 1, wherein n is 2.

4. The compound of claim 1, wherein R_3 is independently at each occurrence -F, or -Cl.

5. The compound of claim 1, wherein m is 1.

6. The compound of claim 1, wherein R_9 is (C1-C6) alkyl; wherein R_9 is optionally further substituted with 1 or 2 substituents selected from the group consisting of -COOH, -COOMe, -$CONH_2$, and -NH_2.

7. The compound of claim 1, wherein R_9 is (C1-C6) alkyl, wherein R_9 is further substituted with —$CONR_{11}R_{12}$, wherein R_{11} and R_{12} are independently H or (C_1 -C_6) alkyl.

8. A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt, or tautomeric form thereof and a pharmaceutically acceptable carrier.

9. The pharmaceutical composition of claim 8, wherein the pharmaceutical composition is suitable for topical, oral, subcutaneous, or intravenous administration.

10. Use of a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt, or tautomeric form thereof in the manufacture of a medicament for treating pain in a subject, wherein the medicament is to be administered to the subject.

11. The use of claim 10, wherein the therapeutically effective amount is effective to alleviate pain in a subject, wherein the compound of claim 1 shows a reduction in pain response in the Formalin Assay in phase 1 or phase 2, or both, at a dose between 0.1 mg/kg and 1,000 mg/kg, at a dose between 0.5 mg/kg and 100 mg/kg, or at a dose between 1 mg/kg to 50 mg/kg.

12. The use of claim 10, wherein the pain is nociceptive pain, such as that resulting from physical trauma includes a cut or contusion of the skin; or a chemical or thermal burn, osteoarthritis, rheumatoid arthritis or tendonitis; myofascial pain; neuropathic pain, such as that associated with stroke, diabetic neuropathy, luetic neuropathy, postherpetic neuralgia, trigeminal neuralgia, fibromyalgia, or painful neuropathy induced iatrogenically by drugs; or mixed pain includes pain with both nociceptive and neuropathic components; visceral pain; headache pain includes migraine headache pain; CRPS; CRPS type I; CRPS type II; RSD; reflex neurovascular dystrophy; reflex dystrophy; sympathetically maintained pain syndrome; causalgia; Sudeck atrophy of bone; algoneurodystrophy; shoulder hand syndrome; post-traumatic dystrophy; autonomic dysfunction; autoimmune-related pain; inflammation-related pain; cancer-related pain; phantom limb pain; chronic fatigue syndrome; post-operative pain; spinal cord injury pain; central post-stroke pain; radiculopathy; sensitivity to temperature, light touch or color change to the skin includes allodynia; pain from hyperthermic or hypothermic conditions; and other painful conditions includes diabetic neuropathy, luetic neuropathy, postherpetic neuralgia, trigeminal neuralgia; chronic pain; acute pain; pain from neuromas, pain or itch associated with channelopathies includes small fiber neuralgia, IEM or Raynodes; or itch from various origins includes allergic itch.

13. The use of claim 10, wherein the compound is a voltage-gated sodium channel inhibitor of NaV1.7.

14. Use of a therapeutically effective amount of a compound of any one of claims 1-7, or pharmaceutically acceptable salt, solvate or tautomeric form thereof in the manufacture of a medicament for treating prediabetes or diabetes in a subject, wherein the medicament is to be administered to the subject.

15. The use of claim 10, wherein the pain is neuropathic, nociceptive or inflammatory pain.

16. The compound of claim 1, wherein R_9 and R_{10} together form a unsubstituted 4- to 8-membered heterocycloalkyl ring, wherein said heterocycloalkyl ring is fused with a 5-membered heteroaryl.

17. The compound of claim 1, wherein R_{10} is $(C_3\text{-}C_6)$alkylnyl or $(C_3\text{-}C_6)$ alkenyl.

18. The compound of claim 1, wherein R_9 is $(C_1\text{-}C_3)$ alkyl, wherein R_9 is optionally further substituted with 1 or 2 substituents selected from the group consisting of -COOH, -COOMe, $-CONH_2$, and $-NH_2$.

19. The compound of claim 1, wherein R_9 is $(C_1\text{-}C_3)$ alkyl, wherein R_9 is further substituted with $–CONR_{11}R_{12}$, wherein R_{11} and R_{12} are independently H or $(C_1\text{-}C_6)$ alkyl.