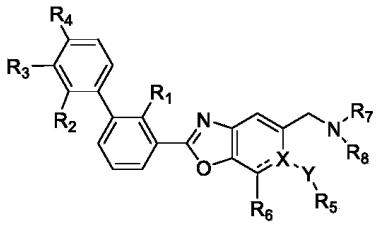
THE CLAIMS:

1. A compound of Formula I, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof,



Formula I

wherein,

X is selected from C, or N;

=== is a single bond or a double bond.

R_1 is selected from H, halogen, CN, -C_{1-8}alkyl, -C_{1-4}haloalkyl, or -OC_{1-8} alkyl;

R_2, R_3 and R_4 are each independently selected from H, -OH, halogen, -CN, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{1-8}alkoxyl, -O-C_{1-4}alkyl-C_{5-10}heterocycle, -C_{3-10}heteroaryl, -NHCO-C_{8-10}heteroaryl, -NHCO-C_{1-4}alkyl-C_{5-10}heterocycle; wherein -C_{1-8}alkyl, -C_{1-8}alkoxyl, -O-C_{1-4}alkyl-C_{5-10}heterocycle, -C_{3-10}heteroaryl, -NHCO-C_{8-10}heteroaryl, -NHCO-C_{1-4}alkyl-C_{5-10}heterocycle substituted with -C_{1-8}alkyl, -C_{1-8}alkoxyl, -C_{3-10}cycloalkyl, -C_{3-10}cycloalkyl-O-C_{1-8}alkyl; or

R_3 and R_4 together with the atoms to which they are attached form a 5- to 6-member heterocyclic ring; wherein the heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O;

Y is selected from absent, O, S, -NR_9-;

R_9 is selected from H, -C_{1-8}alkyl, or -C_{1-8}haloalkyl;

R_5 is selected from H, halogen, CN, -C_{1-8}alkyl, -C_{1-4}haloalkyl, -C_{2-8}alkenyl, sulfonyl, sulfinyl, provided that if Y is O, then R_5 is not -C_{1-8}alkyl;

R_6 is H, or R_5 and R_6 together with the atoms to which they are attached form a 5-to 6-member heterocyclic ring; wherein the heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the heterocyclic ring optionally substituted with oxo, -C_{1-8}alkyl, -C_{0-4}alkyl-COOH, -C_{0-4}alkyl-OH;

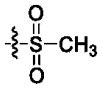
R_7 and R_8 are each independently selected from H, -C_{1-8}alkyl, -C_{1-6}alkyl-COOH, -C_{5-6}aryl, wherein -C_{1-6}alkyl-COOH and -C_{5-6}aryl optionally substituted with -C_{1-8}alkyl, -C_{0-4}alkyl-COOH, -C_{0-4}alkyl-OH; or

R_7 and R_8 together with the atoms to which they are attached form a 3-to 7-member heterocyclic ring; wherein the heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the heterocyclic ring optionally substituted with oxo, -C_{1-8}alkyl, -C_{0-4}alkyl-COOH, -C_{0-4}alkyl-OH;

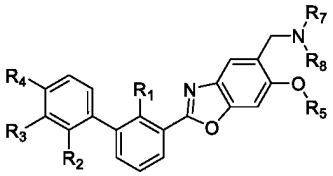
R_5 and R_8 together with the atoms to which they are attached form a 6- to 10- member heterocyclic ring; wherein the heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the heterocyclic ring optionally substituted with oxo, -C_{1-8}alkyl, -C_{0-4}alkyl-COOH, -C_{0-4}alkyl-OH.

2 The compound of claim 1, wherein Y is selected from absent, -O-, -S-, -NH-.

3 The compound of claim 1 or 2, wherein R_1 is selected from CH_3 and CN.

4. The compound of any one of claims 1-3, wherein R_5 is selected from H, -CH_3, , CHF_2, -CF_3, -CH_2CF_3, F, Cl, CN, and provided that if Y is O, then R_5 is not –CH_3.

5. The compound of Formula II, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof,



Formula II

wherein,

R_1 is selected from H, halogen, CN, -C_{1-8}alkyl, -C_{1-4}haloalkyl, or -OC_{1-8}alkyl;

R_2, R_3 and R_4 are each independently selected from H, halogen, CN, -C_{1-8}alkyl, or -C_{1-4}haloalkyl;

R_5 is selected from H, -C_{1-4}haloalkyl, -SO_2-C_{1-4}alkyl;

R_7 and R_8 are each independently selected from H, -C_{1-8}alkyl, -C_{1-6}alkyl-COOH, -C_{5-6}aryl, wherein -C_{1-6}alkyl-COOH and -C_{5-6}aryl optionally substituted with -C_{1-8}alkyl, -C_{0-4}alkyl-COOH, -C_{0-4}alkyl-OH; or

$R_7$and R_8 together with the atoms to which they are attached form a 3-to 7-member heterocyclic ring; wherein the heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the heterocyclic ring
optionally substituted with oxo, -C_{1-8}alkyl, -C_{0-4}alkyl-COOH, -C_{0-4} alkyl-OH.

6. The compound of claim 5, wherein R_1 is selected from CH_3 and CN.

7. The compound of claim 5 or 6, wherein R_2, R_3 and R_4 are each independently selected from H, CN, or F.

8. The compound of any one of claims 5-7, wherein R_5 is -C_{1-4}haloalkyl.

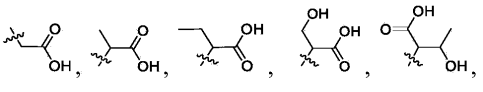
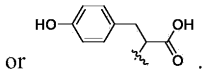
9. The compound of claim 8, wherein R_5 is -C_{1-4}alkyl substituted by 1-3 fluorine atoms.

10. The compound of claim 9, wherein R_5 is methyl or ethyl substituted by 2-3 fluorine atoms.

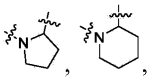
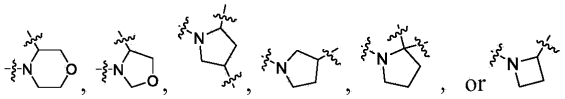
11. The compound of claim 10, wherein R_5 is $-CF_3$, $-CHF_2$, $-CH_2CHF_2$, or $-CH_2CF_3$.

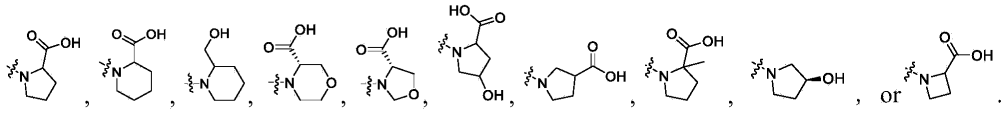
12. The compound of any one of claims 5-7, wherein R_5 is $-SO_2-C_{1-4}$alkyl.

13. The compound of claim 12, wherein R_5 is $-SO_2-CH_3$.

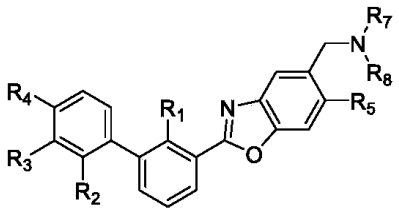
14. The compound of any one of claims 5-13, wherein R_7 and R_{8n} are each independently selected from H, CH_3, ,  or .

15. The compound of any one of claims 5-13, wherein R_7 and R_8 together with the atoms to which they are attached form a 4-to 6-member heterocyclic ring; wherein the heterocyclic ring substituted with-C_{1-4}alkyl, $-C_{0-4}$alkyl-COOH, or $-C_{0-4}$alkyl-OH.

16. The compound of claim 15, wherein heterocyclic ring is ,  or .

17. The compound of claim 15, wherein the substituted heterocyclic ring is selected from  or .

18. A compound of Formula III, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof,



Formula III

wherein,

R_1 is selected from H, halogen, CN, -C_{1-8}alkyl, -C_{1-4}haloalkyl, or -OC_{1-8}alkyl;

R_2, R_3 and R_4 are each independently selected from H, alogen, CN, -C_{1-8}alkyl, or -C_{1-4}haloalkyl;

R_5 is selected from H, halogen, CN, -C_{1-8}alkyl, -C_{1-4}haloalkyl, -NH-C_{1-4}alkyl, -S-C_{1-4}alkyl, sulfonyl, or sulfinyl;

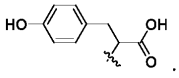
R_7 and R_8 are each independently selected from H, -C_{1-8}alkyl, -C_{1-6}alkyl-COOH, -C_{5-6}aryl, wherein -C_{1-6}alkyl-COOH and -C_{5-6}aryl optionally substituted with -C_{1-8}alkyl, -C_{0-4}alkyl-COOH, -C_{0-4}alkyl-OH; or

R_7 and R_8 together with the atoms to which they are attached form a 3-to 7-member heterocyclic ring; wherein the heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the heterocyclic ring optionally substituted with oxo, -C_{1-8}alkyl, -C_{0-4}alkyl-COOH, -C_{0-4}alkyl-OH.

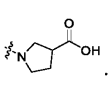
19. The compound of claim 18, R_1 is selected from CH_3, or CN.

20. The compound of claim 18 or 19, wherein R_2, R_3 and R_4 are each independently selected from H, CN, or F.

21. The compound of any one of claims 18-20, wherein R_5 is selected from F, Cl, -CH_3, -C_3, -S-CH_3, -SO-CH_3, -SO_2-CH_3, -CN, or -$NHCH_3$.

22. The compound of any one of claims 18-21, wherein R_7 and R_8 are each independently selected from H, CH_3, , , , , , , or .

23. The compound of any one of claims 18-21, wherein R_7 and R_8 together with the atoms to which they are attached form a 5-to 6-member heterocyclic ring; wherein the heterocyclic ring substituted with -C_{0-4}alkyl-COOH.

24. The compound of claim 23, wherein the substituted heterocyclic ring is selected from , , or .

25. The compound of Formula I, wherein the compound is

1) (S) -1- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

2) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -L-proline;

3) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -D-allothreonine;

4) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -L-allothreonine;

5) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -L-alanine;

6) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -D-alanine;

7) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -D-proline;

8) (1- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) piperidin-2-yl) methanol;

9) (S) -4- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) morpholine-3-carboxylic acid;

10) (S) -2- (((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) amino) butanoic acid;

11) (R) -2- (((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) amino) butanoic acid;

12) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -D-serine;

13) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -L-serine;

14) ((2- (2-cyano- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -L-proline;

15) ((2- (2, 2'-dicyano- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) -L-proline;

16) 2-methyl-1- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylthio) benzo [d] oxazol-5-yl) methyl) pyrrolidine-2-carboxylic acid;

17) ((2- (2-cyano- [1, 1'-biphenyl] -3-yl) -6-methylbenzo [d] oxazol-5-yl) methyl) -D-proline;

18) ((2- (2-cyano- [1, 1'-biphenyl] -3-yl) -6-methylbenzo [d] oxazol-5-yl) methyl) -L-proline;

19) (S) -4- ((2- (2-cyano- [1, 1'-biphenyl] -3-yl) -6-methylbenzo [d] oxazol-5-yl) methyl) morpholine-3-carboxylic acid;

20) ((6-chloro-2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-proline;

21) ((6-hydroxy-2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-proline;

22) (S) -1- ((6-methyl-2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

23) (S) -1- ((6-fluoro-2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) pyrrolidin-3-ol;

24) ((6-fluoro-2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-proline;

25) (S) -1- ((6-fluoro-2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

26) 1- ((6-cyano-2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

27) 1- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylamino) benzo [d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

28) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (trifluoromethyl) benzo [d] oxazol-5-yl) methyl) -L-proline;

29) (S) -1- ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

30) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -D-allothreonine;

31) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-allothreonine;

32) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-tyrosine hydrochloride;

33) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-alanine;

34) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -D-alanine;

35) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) glycine;

36) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-proline;

37) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -D-proline;

38) (1- ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) piperidin-2-yl) methanol;

39) (S) -4- ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) morpholine-3-carboxylic acid;

40) (S) -2- (((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) amino) butanoic acid;

41) (R) -2- (((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) amino) butanoic acid;

42) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -D-serine;

43) ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-serine;

44) ((2- (2-cyano- [1, 1'-biphenyl] -3-yl) -6-(difluoromethoxy) benzo [d] oxazol-5-yl) methyl) -L-proline;

45) ((2- (2, 2'-dicyano- [1, 1'-biphenyl] -3-yl) -6-(difluoromethoxy) benzo [d] oxazol-5-yl) methyl) -L-proline;

46) 1- ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -2-methylpyrrolidine-2-carboxylic acid;

47) ((6- (difluoromethoxy) -2- (3- (2, 3-dihydrobenzo [b] [1, 4] dioxin-6-yl) -2-methylphenyl) benzo [d] oxazol-5-yl) methyl) -L-proline;

48) 1- ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) azetidine-2-carboxylic acid;

49) ((6- (difluoromethoxy) -2- (3- (2, 3-dihydrobenzo [b] [1, 4] dioxin-6-yl) -2-methylphenyl) benzo [d] oxazol-5-yl) methyl) -L-proline;

50) 1- ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -2-methylpyrrolidine-2-carboxylic acid;

51) ((2- (2'-cyano-2-methyl- [1, 1'-biphenyl] -3-yl) -6-(difluoromethoxy) benzo [d] oxazol-5-yl) methyl) proline;

52) ((6- (difluoromethoxy) -2- (2'-fluoro-2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) -L-proline;

53) (S) -3- ((6- (difluoromethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) oxazolidine-4-carboxylic acid;

54) (S) -1- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (2, 2, 2-trifluoroethoxy) benzo [d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

55) 1- ((6- (2, 2-difluoroethoxy) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) benzo [d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

56) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (2, 2, 2-trifluoroethoxy) benzo [d] oxazol-5-yl) methyl) -D-alanine;

57) (S) -4- ((2- (2-cyano- [1, 1'-biphenyl] -3-yl) -6- (2, 2, 2-trifluoroethoxy) benzo [d] oxazol-5-yl) methyl) morpholine-3-carboxylic acid;

58) (S) -4- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (2, 2, 2-trifluoroethoxy) benzo [d] oxazol-5-yl) methyl) morpholine-3-carboxylic acid;

59) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (2, 2, 2-trifluoroethoxy) benzo [d] oxazol-5-yl) methyl) -L-alanine;

60) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (2, 2, 2-trifluoroethoxy) benzo [d] oxazol-5-yl) methyl) -L-proline;

61) 2-methyl-1- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (2, 2, 2-trifluoroethoxy) benzo [d] oxazol-5-yl) methyl) pyrrolidine-2-carboxylic acid;

62) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (2, 2, 2-trifluoroethoxy) benzo [d] oxazol-5-yl) methyl) -D-alanine;

63) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6-(trifluoromethoxy) benzo [d] oxazol-5-yl) methyl) -L-proline;

64) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6-((methylsulfonyl) oxy) benzo [d] oxazol-5-yl) methyl) -L-proline;

65) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylsulfinyl) benzo [d] oxazol-5-yl) methyl) -L-proline;

66) ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6- (methylsulfonyl) benzo [d] oxazol-5-yl) methyl) -L-proline;

67) 8-methyl-2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6, 7, 8, 9-tetrahydrooxazolo [5', 4': 4, 5] benzo [1, 2-f] [1, 4] oxazepine;

68) 1- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -8-oxo-7, 8-dihydrobenzofuro [5, 4-d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid;

69) 1- ((8- (2-methyl- [1, 1'-biphenyl] -3-yl) oxazolo [5, 4-c] [1, 2, 4] triazolo [1, 5-a] pyridin-5-yl) methyl) piperidine-2-carboxylic acid;

70) (S) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6, 7, 8, 9-tetrahydrooxazolo [5', 4': 4, 5] benzo [1, 2-f] [1, 4] oxazepine-7-carboxylic acid;

71) 2- (2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6, 7-dihydrooxazolo [5', 4': 4, 5] benzo [1, 2-f] [1, 4] oxazepin-8 (9H) -yl) acetic acid;

72) (R) -2- (2-methyl- [1, 1'-biphenyl] -3-yl) -6, 7, 8, 9-tetrahydrooxazolo [5', 4': 4, 5] benzo [1, 2-f] [1, 4] oxazepine-7-carboxylic acid;

73) 1- ((2- (2-methyl- [1, 1'-biphenyl] -3-yl) -8-oxo-7, 8-dihydrobenzofuro [5, 4-d] oxazol-5-yl) methyl) piperidine-2-carboxylic acid.

26. A pharmaceutical composition comprising a compound of any one of claims 1-25, or a pharmaceutically acceptable salt or a stereoisomer thereof, and at least one pharmaceutically acceptable carrier or excipient.

~~27. A method of inhibiting PD-1/PD-L1 interaction, said method comprising administering to a patient a compound of any one of claims 1-25, or a pharmaceutically acceptable salt or a stereoisomer thereof.~~

~~28. A method of treating a disease associated with inhibition of PD-1/PD-L1 interaction, said method comprising administering to a patient in need thereof a therapeutically effective amount of a compound of any one of claims 1-25, or a pharmaceutically acceptable salt or a stereoisomer thereof.~~

~~29. The method of claim 28, wherein the disease is colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, pancreatic cancer, melanoma, multiple melanoma, brain cancer, renal cancer, prostate cancer, ovarian cancer or breast cancer.~~

~~30. A method of enhancing, stimulating and/or increasing the immune response in a patient, said method comprising administering to the patient in need thereof a therapeutically effective amount of a compound of any one of claims 1-25, or a pharmaceutically acceptable salt or a stereoisomer thereof.~~

~~31~~27. Use of the pharmaceutical composition of claim ~~30~~26, or the compound of any one of claims 1-25 for the preparation of a medicament.

~~32~~28. The use of claim ~~31~~27, wherein the medicament is used for the treatment or prevention of cancer.

~~33~~29. The use of claim ~~32~~28, wherein the cancer is colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, pancreatic cancer, melanoma, multiple melanoma, brain cancer, renal cancer, prostate cancer, ovarian cancer or breast cancer.

~~34~~30. The use of claim ~~31~~27, wherein the medicament is used as an inhibitor of PD-1/PD-L1 interaction.