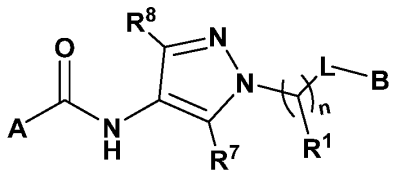
CLAIMS

What is claimed is:

1. A compound of Formula (I-2):



(I-2)

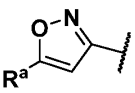
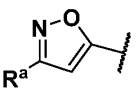
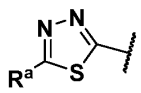
or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H, C_1-C_6alkyl, C_3-C_8cycloalkyl, or C_1-C_6 haloalkyl;

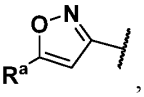
n is 0 or 1;

L is -CH_2- or is absent;

B is C_3-C_6cycloalkyl, 3-6 membered heterocyclyl, or 5-6 membered heteroaryl, wherein the C_3-C_6cycloalkyl and 5-6 membered heteroaryl are each independently optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_1-$_6$alkyl, C_1-$_6$alkoxy and C_1-C_6 haloalkyl;

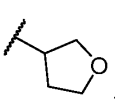
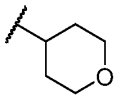
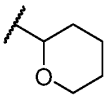
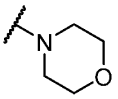
A is , , or ;

R^a is 5- or 6-membered heteroaryl optionally substituted with one to four halo;

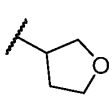
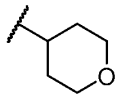
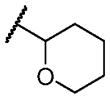
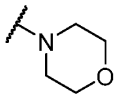
provided that, when A is , one of (*i.*)-(*vii.*) applies:

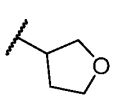
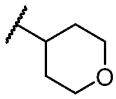
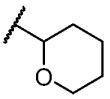
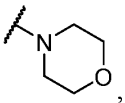
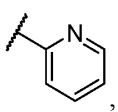
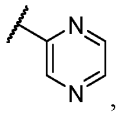
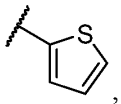
(*i*) B is C_3-C_6cycloalkyl, optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_1-$_6$alkyl, C_1-$_6$alkoxy and C_1-C_6 haloalkyl;

(*ii*) B is 3-6 membered heterocyclyl having one or more annular heteroatoms, wherein the 3-6 membered heterocyclyl is optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_1-$_6$alkoxy and C_1-C_6 haloalkyl, and wherein the one or more annular heteroatoms are nitrogen;

(*iii*) B is , ,  or , each of which is optionally substituted with one or more groups selected from the group consisting of halo, CN, -

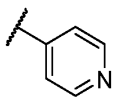
OH, -NH_2, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl, n is 1, R^1 is CH_3, and L is absent;

(*iv*) B is , ,  or , each of which is substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl;

(*v*) B is , ,  or , each of which is optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl, and R^a is , , or , each of which optionally substituted with one to four halo;

(*vi*) B is 4-6 membered bridged heterocyclyl, optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl;

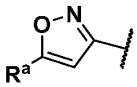
or

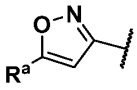
(*vii*) B is 5-membered heteroaryl or , each of which is optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl;

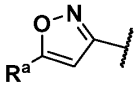
R^7 is H, C_1-C_6alkyl or or C_1-C_6haloalkyl; and

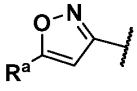
R^8 is H or C_1-C_6alkyl.

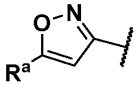
2. The compound of claim 1, wherein the 5- or 6-membered heteroaryl of R^a is selected from the group consisting of 2-furyl, 2-pyridinyl, 2-pyrimidinyl, 4-pyrimidinyl, and 2-pyrazinyl.

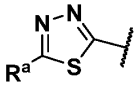
3. The compound of claim 1 or 2, wherein A is  and R^a is 2-furyl.

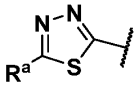
4. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyridinyl.

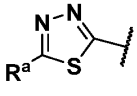
5. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyrimidinyl.

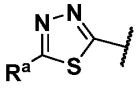
6. The compound of claim 1 or 2, wherein A is  and R^a is 4-pyrimidinyl.

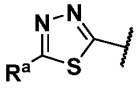
7. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyrazinyl.

8. The compound of claim 1 or 2, wherein A is  and R^a is 2-furyl.

9. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyridinyl.

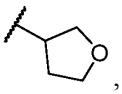
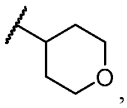
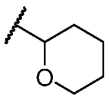
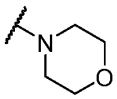
10. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyrimidinyl.

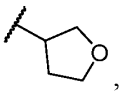
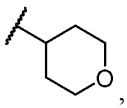
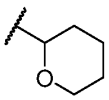
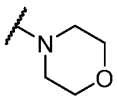
11. The compound of claim 1 or 2, wherein A is  and R^a is 4-pyrimidinyl.

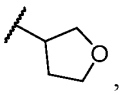
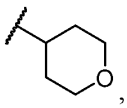
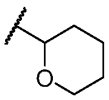
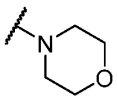
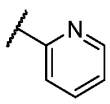
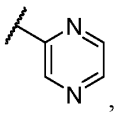
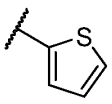
12. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyrazinyl.

13. The compound of any one of claims 1-12, wherein B is C_3-C_6cycloalkyl, optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl.

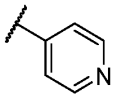
14. The compound of any one of claims 1-12, wherein B is 3-6 membered heterocyclyl having one or more annular heteroatoms, wherein the 3-6 membered heterocyclyl is optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, $-NH_2$, C_{1-6}alkoxy and C_1-C_6 haloalkyl, and wherein the one or more annular heteroatoms are nitrogen.

15. The compound of any one of claims 1-12, wherein B is , ,  or , each of which is optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, $-NH_2$, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl, n is 1, R^1 is CH_3, and L is absent.

16. The compound of any one of claims 1-12, wherein B is , ,  or , each of which is substituted with one or more groups selected from the group consisting of halo, CN, -OH, $-NH_2$, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl.

17. The compound of any one of claims 1-12, wherein B is , ,  or , each of which is optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, $-NH_2$, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl, and R^a is , , or , each of which optionally substituted with one to four halo.

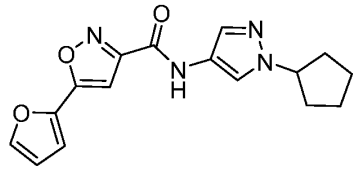
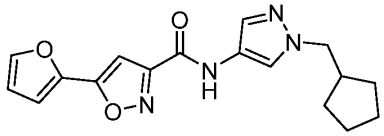
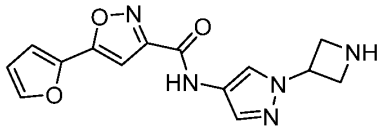
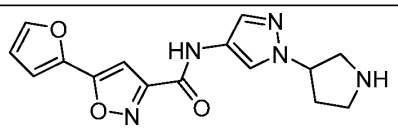
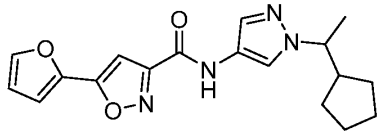
18. The compound of any one of claims 1-12, wherein B is 4-6 membered bridged heterocyclyl, optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl.

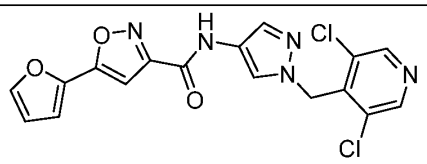
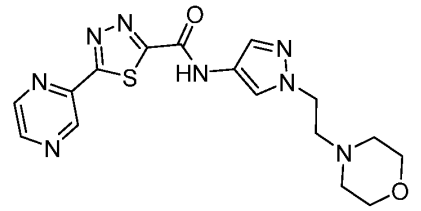
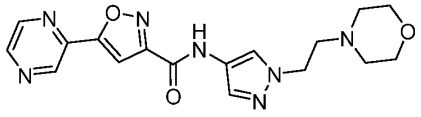
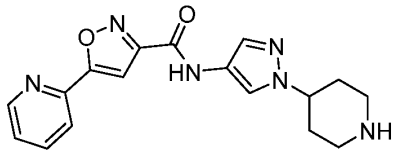
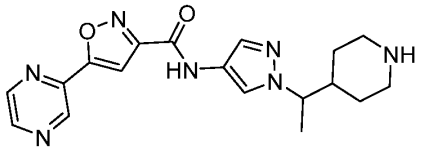
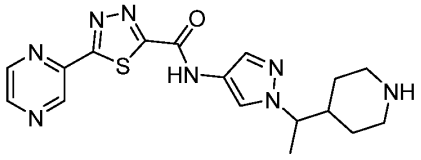
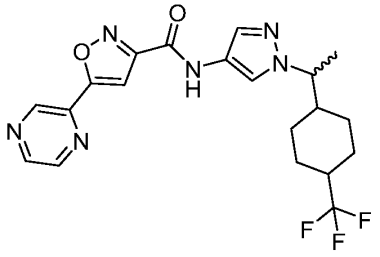
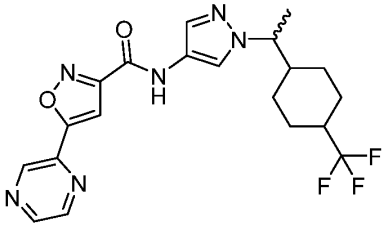
19. The compound of any one of claims 1-12, wherein B is 5-membered heteroaryl or , each of which is optionally substituted with one or more groups selected from the group consisting of halo, CN, -OH, -NH_2, C_{1-6}alkyl, C_{1-6}alkoxy and C_1-C_6 haloalkyl.

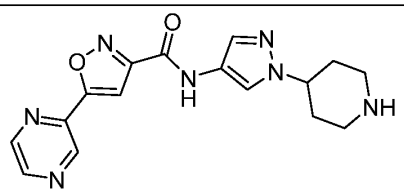
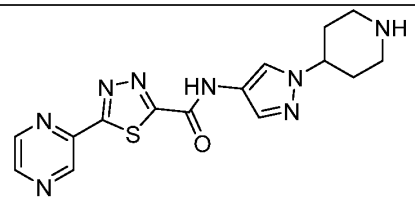
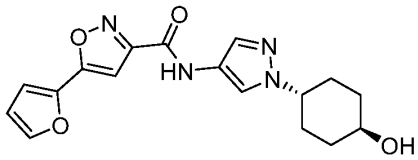
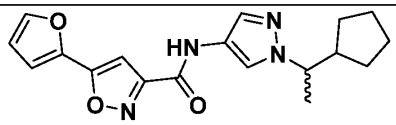
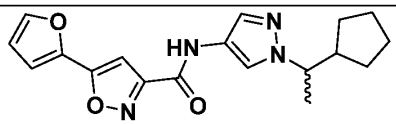
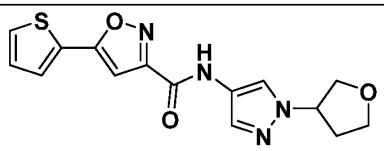
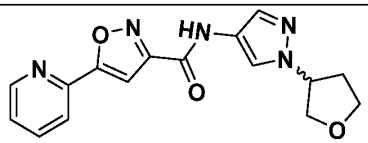
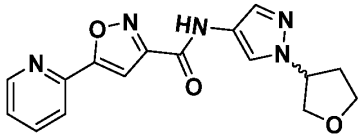
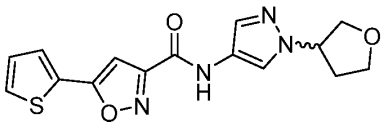
20. The compound of any one of claims 1-19, wherein n is 0 and L is absent.

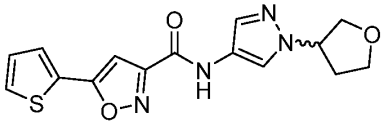
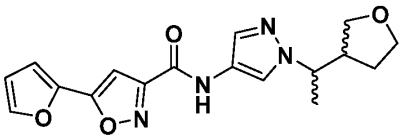
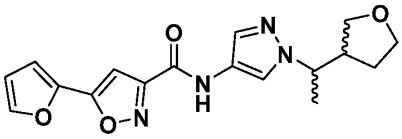
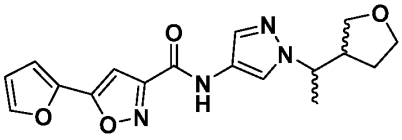
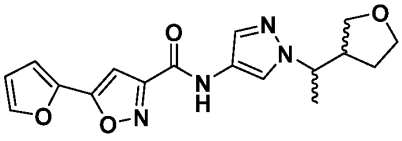
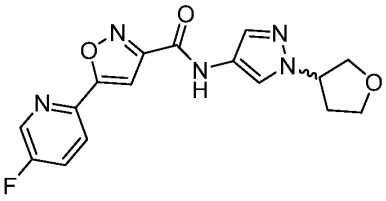
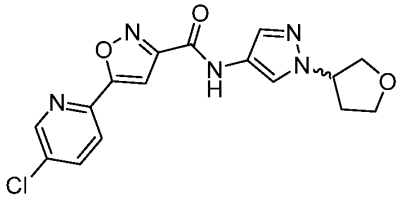
21. The compound of any one of claims 1-19, wherein n is 1, R^1 is CH_3, and L is absent.

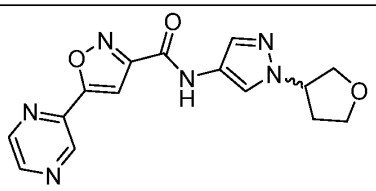
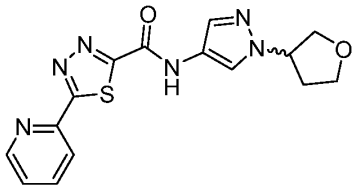
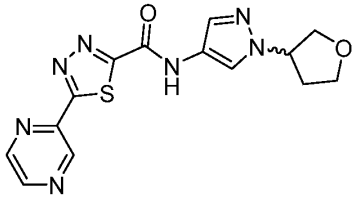
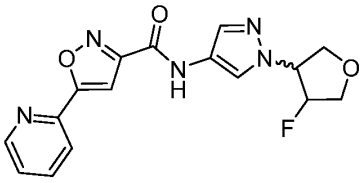
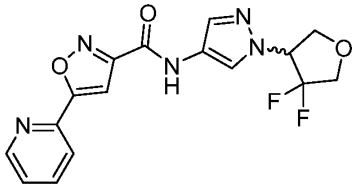
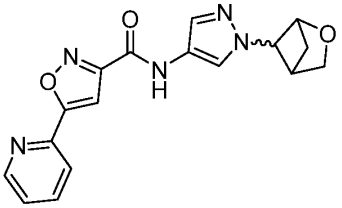
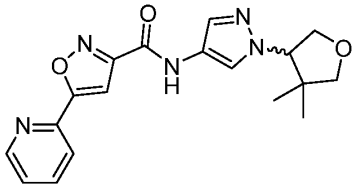
22. A compound selected from the group consisting of:

3-1	
3-2	
3-3	
3-4	
3-5	

3-6	
3-7	
3-8	
3-9	
3-10	
3-11	
3-12	
3-13	 Isomer of compound 3-12

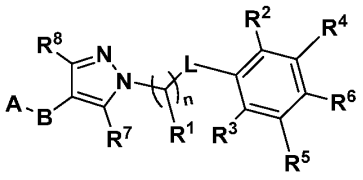
3-14	
3-15	
3-16	
3-17	 Isomer A of compound 3-5
3-18	 Isomer B of compound 3-5
3-19	
3-20	
3-21	 Isomer of compound 3-20
3-22	

	Isomer A of compound 3-19
3-23	 Isomer B of compound 3-19
3-24	
3-25	 Isomer A of compound 3-24
3-26	 Isomer B of compound 3-24
3-27	 Isomer C of compound 3-24
3-28	
3-29	

3-30	
3-31	
3-32	
3-33	
3-34	
3-35	
3-36	

or a pharmaceutically acceptable salt thereof.

23. A compound of formula (I-1):



(I-1)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H, C_1-C_6alkyl, C_3-C_8cycloalkyl, or C_1-C_6 haloalkyl;

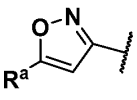
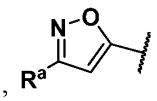
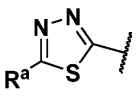
n is 0 or 1;

L is -CH_2- or is absent;

B is -CH_2CH_2-, -CH=CH-, or -C≡C-;

R^2, R^3, R^4, R^5, and R^6 are each independently H, halo, CN, -OH, -NH_2, C_1-$_6$alkoxy, C_1-C_6alkyl, or C_1-C_6haloalkyl;

or R^2, R^4, R^5, and R^6 are each independently H, halo, CN, -OH, -NH_2, C_1-$_6$alkoxy, C_1-C_6alkyl, or C_1-C_6haloalkyl and R^3 is taken together with R^1 and the atoms to which they are attached to form a 5- or 6-membered carbocyclic ring, wherein the 5- or 6-membered carbocyclic ring is unsubstituted or substituted with one to three groups selected from the group consisting of halo, CN, -OH, C_1-C_6alkyl, and C_1-C_6haloalkyl;

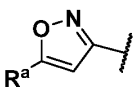
A is , , or ;

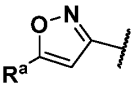
R^a is 5- or 6-membered heteroaryl, wherein the 5- or 6-membered heteroaryl is unsubstituted or substituted with one to four groups selected from the group consisting of OH, halo, C_1-C_6alkyl and C_1-C_6alkoxy,

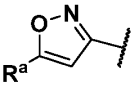
R^7 is H, C_1-C_6alkyl or or C_1-C_6haloalkyl; and

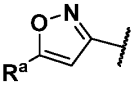
R^8 is H or C_1-C_6alkyl.

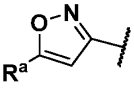
24. The compound of claim 23, wherein the 5- or 6-membered heteroaryl of R^a is selected from the group consisting of 2-furyl, 2-pyridinyl, 2-pyrimidinyl, 4-pyrimidinyl, and 2-pyrazinyl.

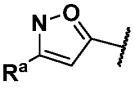
25. The compound of claim 23 or 24, wherein A is  and R^a is 2-furyl.

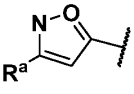
26. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyridinyl.

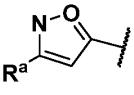
27. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyrimidinyl.

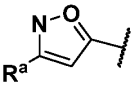
28. The compound of claim 23 or 24, wherein A is  and R^a is 4-pyrimidinyl.

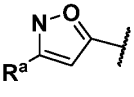
29. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyrazinyl.

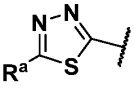
30. The compound of claim 23 or 24, wherein A is  and R^a is 2-furyl.

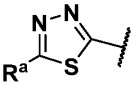
31. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyridinyl.

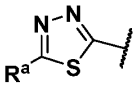
32. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyrimidinyl.

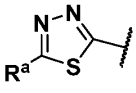
33. The compound of claim 23 or 24, wherein A is  and R^a is 4-pyrimidinyl.

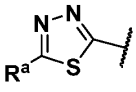
34. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyrazinyl.

35. The compound of claim 23 or 24, wherein A is  and R^a is 2-furyl.

36. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyridinyl.

37. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyrimidinyl.

38. The compound of claim 23 or 24, wherein A is  and R^a is 4-pyrimidinyl.

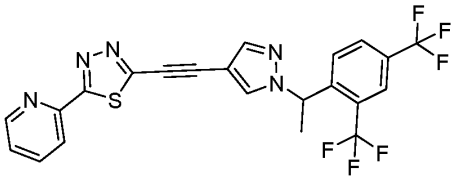
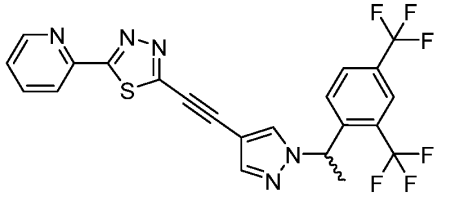
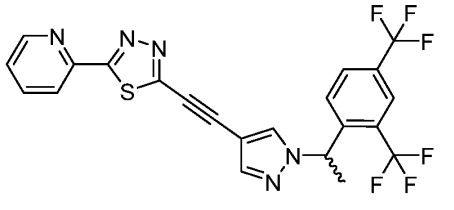
39. The compound of claim 23 or 24, wherein A is  and R^a is 2-pyrazinyl.

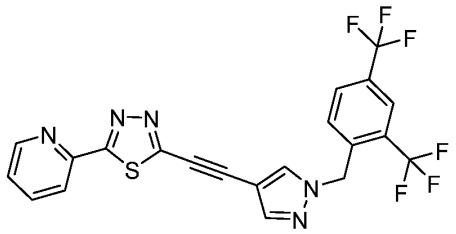
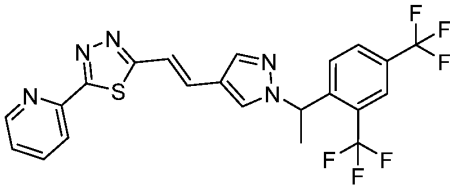
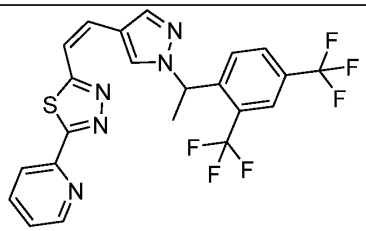
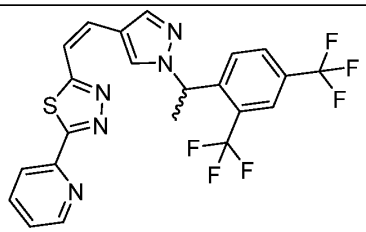
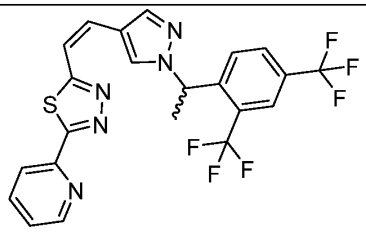
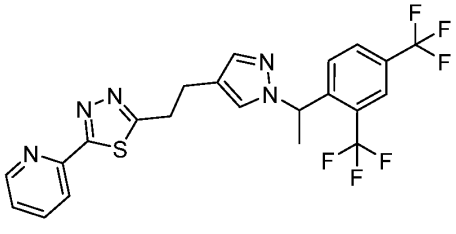
40. The compound of any one of claims 23-39, wherein n is 1, R^1 is H and L is absent.

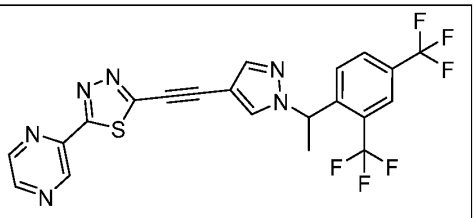
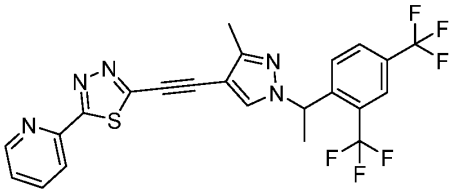
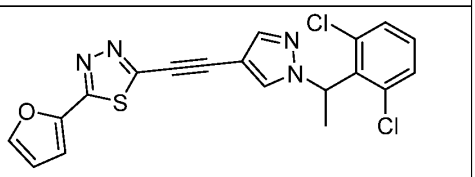
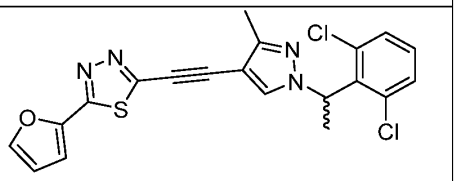
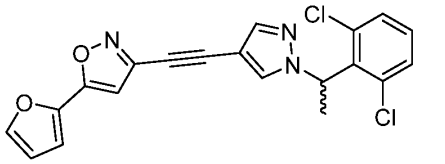
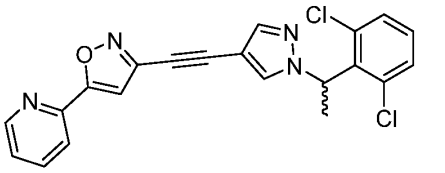
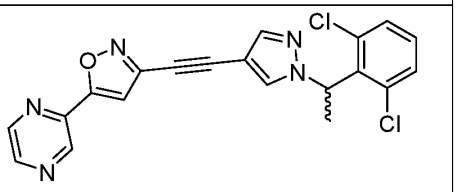
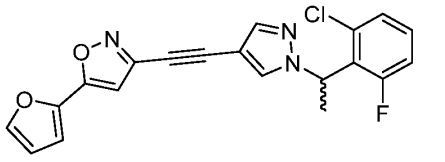
41. The compound of any one of claims 23-40, wherein R^7 and R^8 are H.

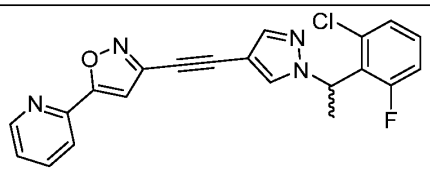
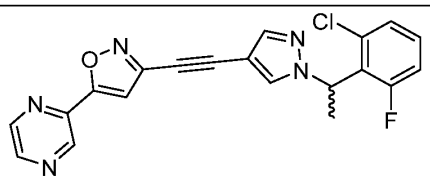
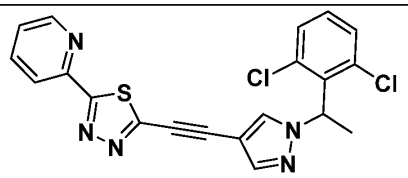
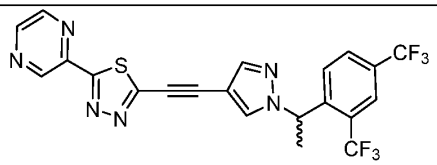
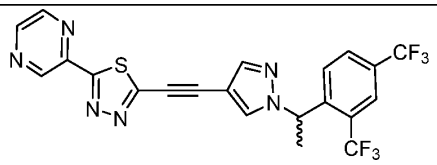
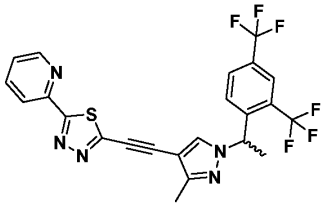
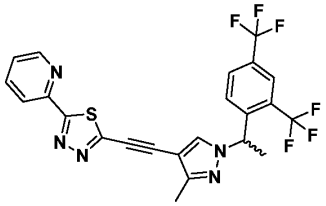
42. The compound of any one of claims 23-41, wherein B is -CH=CH-, or -C≡C-.

43. A compound selected from the group consisting of:

2-1	
2-2	 Isomer A of Compound 1
2-3	

	Isomer B of Compound 1
2-4	
2-5	
2-6	
2-7	 Isomer A of Compound 6
2-8	 Isomer B of Compound 6
2-9	

2-10	
2-11	
2-12	
2-13	
2-14	
2-15	
2-16	
2-17	

2-18	
2-19	
2-20	
2-21	 Isomer A of compound 2-10
2-22	 Isomer B of compound 2-10
2-23	 Isomer A of compound 2-11
2-24	 Isomer B of compound 2-11

or a pharmaceutically acceptable salt thereof.

44. A pharmaceutical composition comprising a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

45. A method of treating a disease or disorder mediated by activating transcription factor 6 (ATF6) in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44.

46. A method of treating a disease or disorder characterized by activation of ATF6 in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44.

47. The method of claims 45 or 46, wherein ATF6 is ATF6α.

48. The method of any one of claims 45-47, wherein the disease or disorder is cancer, a neurodegenerative disease, or a vascular disease.

49. The method of any one of claims 45-47, wherein the disease or disorder is a viral infection, hereditary cerebellar atrophy and ataxia, or Alzheimer's disease, type 2 diabetes mellitus, diabetic nephropathy, myocardial atrophy, heart failure, atherosclerosis, ischemia, ischemic heart disease, or cerebral ischemia.

50. A method of treating cancer in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44.

51. A method of treating a disease or disorder associated with angiogenesis in an individual in need thereof, comprising administering to the individual a therapeutically

effective amount of a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44.

52. A method of treating a metabolic disorder in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44.

53. A method of modulating ATF6 in an individual comprising administering to the individual a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44.

54. A method of modulating ATF6 in a cell comprising administering or delivering to the cell a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44, or a metabolite of the foregoing.

55. A method of activating ATF6 in an individual comprising administering to the individual a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44.

56. A method of activating ATF6 in a cell comprising administering or delivering to the cell a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44, or a metabolite of the foregoing.

57. A method of inhibiting ATF6 in an individual comprising administering to the individual a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44.

58. A method of inhibiting ATF6 in a cell comprising administering or delivering to the cell a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44, or a metabolite of the foregoing.

59. Use of a compound of any one of claims 1-43, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 44, in the manufacture of a medicament for the prevention and/or treatment of a disorder or disease mediated by ATF6.

60. A compound according to any one of claims 1 to 43, or a pharmaceutically acceptable salt thereof, for use in therapy.

61. A compound according to any one of claims 1 to 43, or a pharmaceutically acceptable salt thereof, for use in a method of treating a disease or disorder mediated by activating transcription factor 6 (ATF6) in an individual in need thereof.

62. A compound according to any one of claims 1 to 43, or a pharmaceutically acceptable salt thereof, for use in a method of treating a disease or disorder characterized by activation of ATF6 in an individual in need thereof.

63. A compound, or a pharmaceutically acceptable salt thereof, for use according to claim 61 or 62, wherein ATF6 is ATF6α.

64. A compound, or a pharmaceutically acceptable salt thereof, for use according to any one of claims 61 to 63, wherein the disease or disorder is cancer, a neurodegenerative disease, or a vascular disease.

65. A compound, or a pharmaceutically acceptable salt thereof, for use according to any one of claims 61 to 63, wherein the disease or disorder is a viral infection, hereditary cerebellar atrophy and ataxia, or Alzheimer's disease, type 2 diabetes mellitus, diabetic nephropathy, myocardial atrophy, heart failure, atherosclerosis, ischemia, ischemic heart disease, or cerebral ischemia.

66. A compound according to any one of claims 1 to 43, or a pharmaceutically acceptable salt thereof, for use in a method of treating a disease or disorder associated with angiogenesis in an individual in need thereof.

67. A compound according to any one of claims 1 to 43, or a pharmaceutically acceptable salt thereof, for use in a method of treating a metabolic disorder in an individual in need thereof.