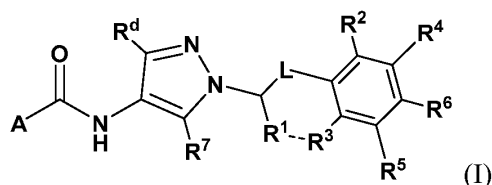


CLAIMS

What is claimed is:

1. A compound of formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

R^d is H or C₁-C₆alkyl;

R^1 is C₁-C₆alkyl, C₃-C₈cycloalkyl, or C₁-C₆ haloalkyl;

L is -CH₂- or is absent;

-- is a bond or is absent;

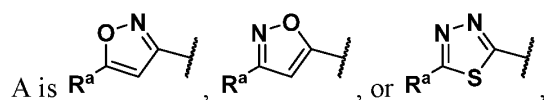
R^2 , R^3 , R^4 , R^5 , and R^6 are each independently H, halo, CN, C₁-C₆alkyl, or C₁-C₆haloalkyl,

wherein at least two of R^2 , R^3 , R^4 , R^5 , and R^6 are halo, CN, C₁-C₆alkyl, or C₁-C₆haloalkyl,

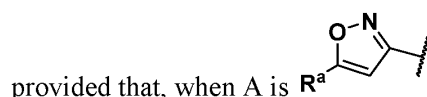
and/or wherein one of R^2 , R^3 , R^4 , R^5 , and R^6 is CN;

or R^2 , R^4 , R^5 , and R^6 are each independently H, halo, CN, C₁-C₆alkyl, or C₁-C₆haloalkyl and

-- is a bond, such that 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, C₁-C₆alkyl, and C₁-C₆haloalkyl;



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, C₁-C₆alkyl and C₁-C₆alkoxy,



and R^a is 2-furyl or 2-thiofuryl, at least one of (i.)-(vi.) applies:

(i.) L is absent, and R^1 is C₁-C₆alkyl;

(ii.) -- is a bond, such that 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, provided that when the 5-

membered carbocyclic ring is formed, at least one of R^2 , R^4 , R^5 , and R^6 is halo, CN, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl;

(iii.) one of R^2 , R^3 , R^4 , R^5 , and R^6 is CN;

(iv.) R^4 and R^5 are each independently Cl, Br, I, CN, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl;

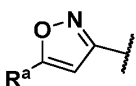
(v.) R^2 and R^3 are each Cl; and

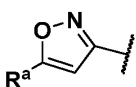
(vi.) at least one of R^2 , R^3 , R^4 , R^5 , and R^6 is F, Br, I, CN, or C_1 - C_6 haloalkyl and R^a is 2-thiofuryl; and

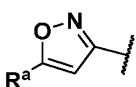
R^7 is H, C_1 - C_6 alkyl or or C_1 - C_6 haloalkyl,

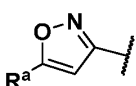
provided that, when R^d is C_1 - C_6 alkyl, R^7 is H, and, when R^7 is C_1 - C_6 alkyl, R^d is H.

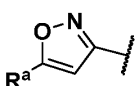
2. The compound of claim 1, wherein the 5- or 6-membered heteroaryl of R^a is selected from the group consisting of 2-furyl, 2-pyridinyl, 2-pyrimidinyl, 4-pyrimidinyl, and 2-pyrazinyl.

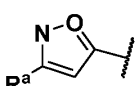
3. The compound of claim 1 or 2, wherein A is  and R^a is 2-furyl.

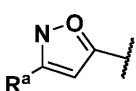
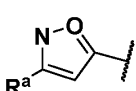
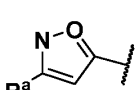
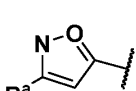
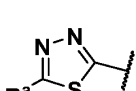
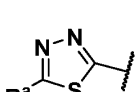
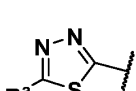
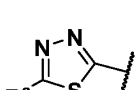
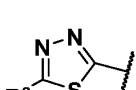
4. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyridinyl.

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

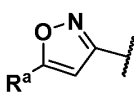
6. The compound of claim 1 or 2, wherein A is  and R^a is 4-pyrimidinyl.

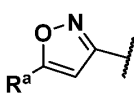
7. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyrazinyl.

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 claim 1 or 2, wherein A is  and R^a is 2-furyl.
14. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyridinyl.
15. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyrimidinyl.
16. The compound of claim 1 or 2, wherein A is  and R^a is 4-pyrimidinyl.
17. The compound of claim 1 or 2, wherein A is  and R^a is 2-pyrazinyl.
18. The compound of any one of claims 1-17, wherein -- is a bond, such that R³ is taken together with R¹ and the atoms to which they are attached to form a 5-membered carbocyclic ring.

19. The compound of any one of claims 1-17, wherein -- is a bond, such that R³ is taken together with R¹ and the atoms to which they are attached to form a 6-membered carbocyclic ring.

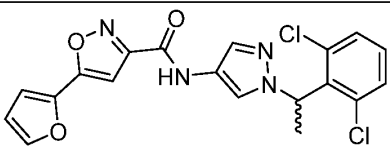
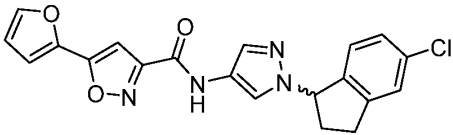
20. The compound of any one of claims 1-3, wherein A is , R^a is 2-furyl, L is absent and R¹ is C₁-C₆alkyl.

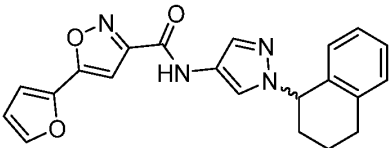
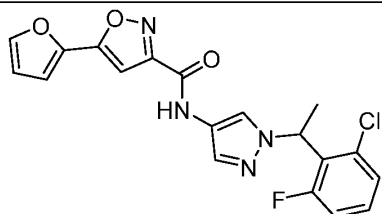
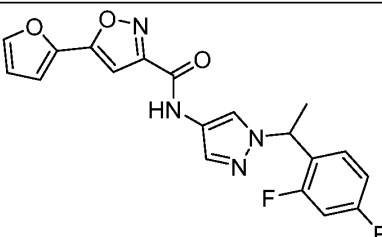
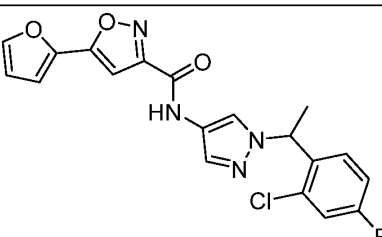
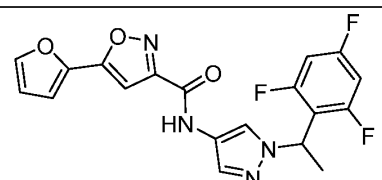
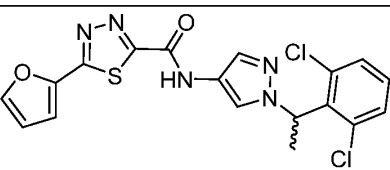
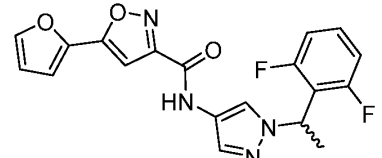
21. The compound of any one of claims 1-3, wherein A is , R^a is 2-furyl, -- is a bond, such that R³ is taken together with R¹ and the atoms to which they are attached to form a 5- or 6-membered carbocyclic ring, provided that, when the 5-membered carbocyclic ring is formed, at least one of R², R⁴, R⁵, and R⁶ is halo, CN, C₁-C₆alkyl, or C₁-C₆haloalkyl.

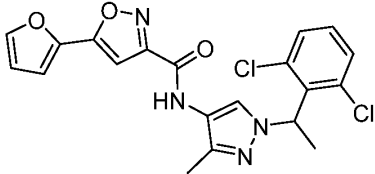
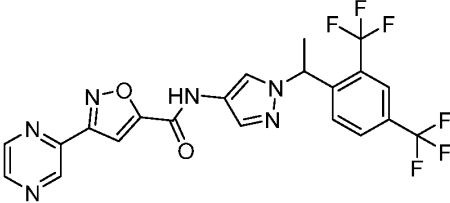
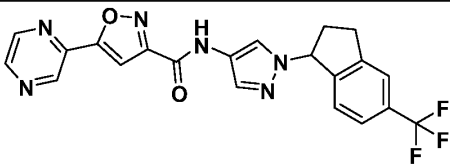
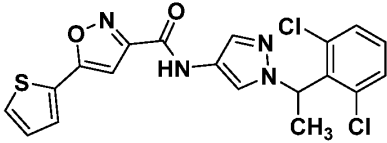
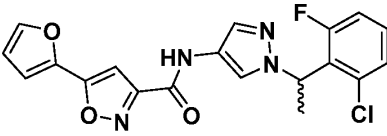
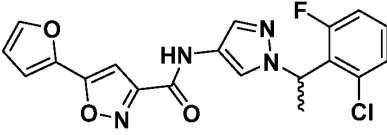
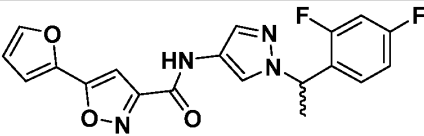
22. The compound of claim 21, wherein L is absent, R³ is taken together with R¹ and the atoms to which they are attached to form the 5-membered carbocyclic ring, and at least one of R², R⁴, R⁵, and R⁶ is halo, CN, C₁-C₆alkyl, or C₁-C₆haloalkyl.

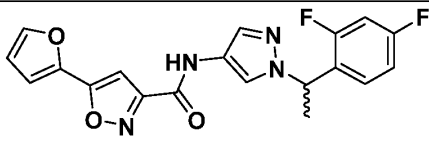
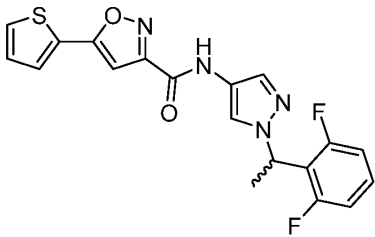
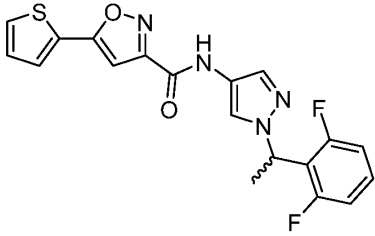
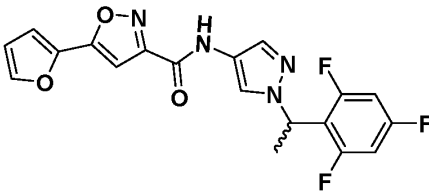
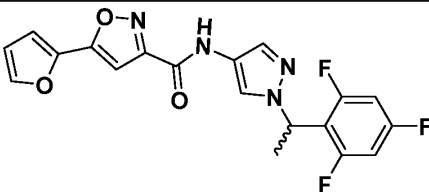
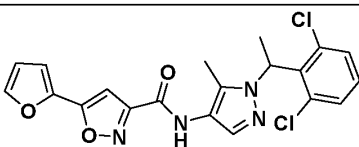
23. The compound of claim 21, wherein L is absent, R³ is taken together with R¹ and the atoms to which they are attached to form the 6-membered carbocyclic ring, and each of R², R⁴, R⁵, and R⁶ is hydrogen.

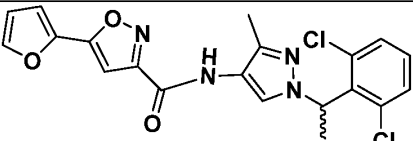
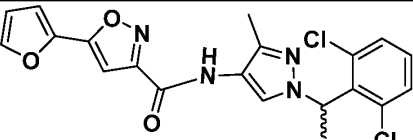
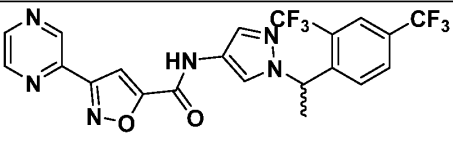
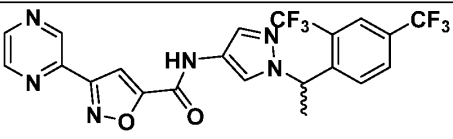
24. A compound selected from the group consisting of:

1-1	
1-2	

1-3	
1-4	
1-5	
1-6	
1-7	
1-8	
1-9	

1-10	
1-11	
1-12	
1-13	
1-14	 Isomer A of compound 1-4
1-15	 Isomer B of compound 1-4
1-16	 Isomer A of compound 1-5

1-17	 Isomer B of compound 1-5
1-18	
1-19	 Isomer of compound 1-18
1-20	 Isomer A of compound 1-7
1-21	 Isomer B of compound 1-7
1-22	

1-23	 Isomer A of compound 1-10
1-24	 Isomer B of compound 1-10
1-25	 Isomer A of compound 1-11
1-26	 Isomer B of compound 1-11

or a pharmaceutically acceptable salt thereof.

25. A pharmaceutical composition comprising a compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

26. 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 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25.

27. 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 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25.

28. The method of claims 26 or 27, wherein ATF6 is ATF6 α .
29. The method of any one of claims 26-28, wherein the disease or disorder is cancer, a neurodegenerative disease, or a vascular disease.
30. The method of any one of claims 26-28, 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.
31. 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 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25.
32. 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 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25.
33. 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 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25.
34. A method of modulating ATF6 in an individual comprising administering to the individual a compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25.
35. A method of modulating ATF6 in a cell comprising administering or delivering to the cell a compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25, or a metabolite of the foregoing.

36. A method of activating ATF6 in an individual comprising administering to the individual a compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25.
37. A method of activating ATF6 in a cell comprising administering or delivering to the cell a compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25, or a metabolite of the foregoing.
38. A method of inhibiting ATF6 in an individual comprising administering to the individual a compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25.
39. A method of inhibiting ATF6 in a cell comprising administering or delivering to the cell a compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25, or a metabolite of the foregoing.
40. Use of a compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 25, in the manufacture of a medicament for the prevention and/or treatment of a disorder or disease mediated by ATF6.
41. A compound according to any one of claims 1 to 24, or a pharmaceutically acceptable salt thereof, for use in therapy.
42. A compound according to any one of claims 1 to 24, 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.
43. A compound according to any one of claims 1 to 24, for use in a method of treating a disease or disorder characterized by activation of ATF6 in an individual in need thereof.
44. A compound, or a pharmaceutically acceptable salt thereof, for use according to claim 42 or 43, wherein ATF6 is ATF6 α .

45. A compound, or a pharmaceutically acceptable salt thereof, for use according to any one of claims 42 to 44, wherein the disease or disorder is cancer, a neurodegenerative disease, or a vascular disease.
46. A compound, or a pharmaceutically acceptable salt thereof, for use according to any one of claims 42 to 44, 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.
47. A compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 24, for use in a method of treating a disease or disorder associated with angiogenesis in an individual in need thereof.
48. A compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 24, for use in a method of treating a metabolic disorder in an individual in need thereof.