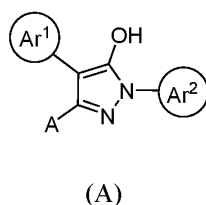


CLAIMS

1. A compound of Formula A,



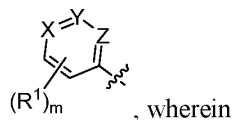
or a pharmaceutically acceptable salt thereof, wherein:

A is C₁₋₃ alkyl or C₃₋₆ cycloalkyl;

Ar¹ is aryl or heteroaryl, optionally substituted with one or more groups selected from halogen, CN, OH, C₁₋₃ alkyl optionally substituted with CN or one or more halogens, and C₁₋₃ alkoxy; and

Ar² is pyrid-2-yl, optionally substituted with one or more groups selected from halogen; amino; amide; OH; a sulfonyl group; a sulfinyl group; a carbonyl group; a phosphoryl group; C₃₋₆ cycloalkyl; C₃₋₆ heterocycloalkyl optionally substituted with a sulfonyl group or =O; C₁₋₃ alkyl optionally substituted with carbonyl or one or more halogens; and heteroaryl optionally substituted with C₁₋₃ alkyl or phenyl.

2. The compound of claim 1, wherein A is C₁₋₃ alkyl.
3. The compound of claim 1 or 2, wherein Ar¹ is



X is N or CR^{1a},

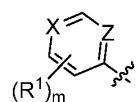
Y and Z are independently CH or N;

R^{1a} is H, CN, halogen, C_{1-3} alkoxy, OH, or C_{1-3} alkyl optionally substituted with CN;

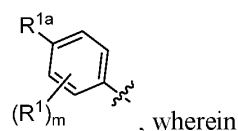
R^1 , each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C_{1-3} alkyl optionally substituted with one or more halogens, and C_{1-3} alkoxy; and

m is 1, 2, 3 or 4.

4. The compound of claim 3, wherein Ar^1 is

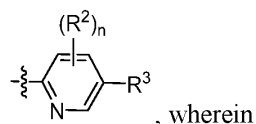


5. The compound of claim 3 or 4, wherein Ar^1 is



R^{1a} is H, CN, halogen, C_{1-3} alkoxy, OH, or C_{1-3} alkyl optionally substituted with CN.

6. The compound of any one of claims 1-5, wherein Ar^2 is



R^2 , each time taken, is independently selected from the group consisting of hydrogen, halogen, NR^4R^5 , OH, C_{1-3} alkyl, and C_{3-6} cycloalkyl;

R^3 is SO_2R^6 , SOR^7R^8 , SOR^9 , COR^{10} , $(CH_2)_pCOOH$, NHR^{11} , $POR^{12}R^{13}$, halogen, cycloalkyl, heterocycloalkyl optionally substituted with SO_2R^{14} or $=O$, heteroaryl optionally substituted with C_{1-3} alkyl or phenyl, or C_{1-3} alkyl optionally substituted with one or more halogens;

R^6 is C_{1-3} alkyl, $NHCOR^{15}$, $NR^{16}R^{17}$, or phenyl;

R^7 is C_{1-3} alkyl, C_{3-5} cycloalkyl, phenyl, or $NR^{18}R^{19}$;

R^8 is NH, NCN, or NCH_3 ;

R^{10} is C_{1-3} alkyl or $NHSO_2R^{20}$;

R^{11} is COR^{21} or SO_2R^{22} ;

R^9 , R^{12} , R^{13} , R^{14} , R^{15} , and R^{20} are each independently C_{1-3} alkyl;

R^{21} is heterocycloalkyl, cycloalkyl, or C_{1-3} alkyl;

R^{22} is $NR^{23}R^{24}$ or C_{1-3} alkyl optionally substituted with carboxyl;

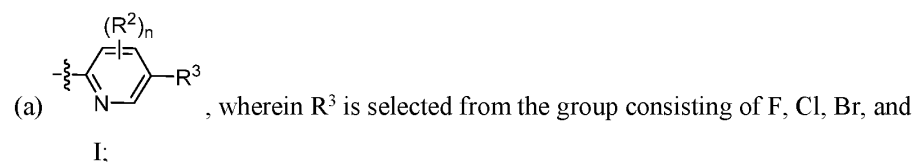
R^4 , R^5 , R^{18} , R^{19} , R^{23} and R^{24} are each independently H or C_{1-3} alkyl;

R^{16} and R^{17} are each independently H, C_{1-3} alkyl, aryl, cycloalkyl, or wherein R^{16} and R^{17} together with the carbon to which they are attached form a heterocycloalkyl;

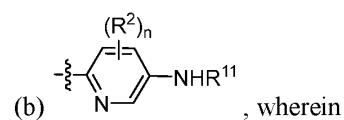
p is 1, 2, or 3; and

n is 0, 1, 2 or 3.

7. The compound of claim 6, wherein Ar^2 is



or



R^{11} is COR^{21} or SO_2R^{22} ;

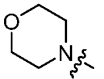
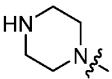
R^{21} is heterocycloalkyl, cycloalkyl, or C_{1-3} alkyl;

R^{22} is $NR^{23}R^{24}$ or C_{1-3} alkyl optionally substituted with carboxyl; and

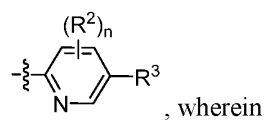
R^{23} and R^{24} are independently H or C_{1-3} alkyl.

8. The compound of claim 7, wherein R^{22} is CH_3 , CH_2CH_3 , CH_2COOH , $NHCH_3$, or $N(CH_3)_2$;

or

wherein R^{21} is , , , or CH_2CH_3 .

9. The compound of claim 6, wherein Ar^2 is



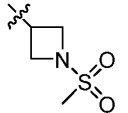
(a) R^3 is cycloalkyl or heterocycloalkyl optionally substituted with SO_2R^{14} or $=O$; and

R^{14} is C_{1-3} alkyl;

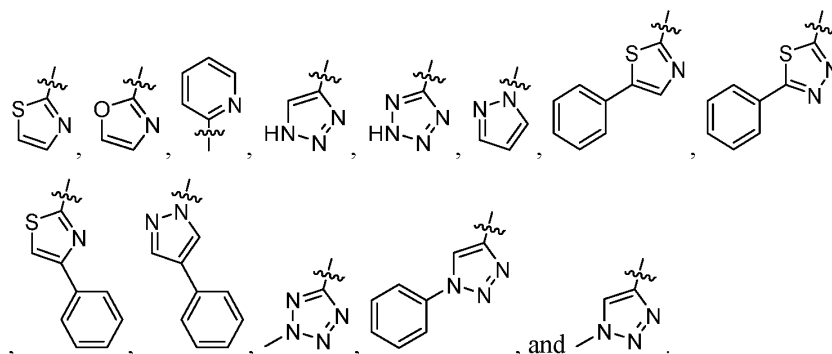
or

(b) R^3 is heteroaryl optionally substituted with C_{1-3} alkyl or phenyl.

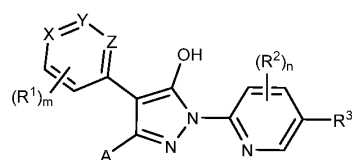
10. The compound of claim 9, wherein the cycloalkyl or optionally substituted

heterocycloalkyl is selected from the group consisting of , , , , and ; or

wherein the optionally substituted heteroaryl is selected from the group consisting of



11. The compound of claim 1, having a structure according to Formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

X is N or CR^{1a};

Y and Z are independently CH or N;

A is C₁₋₃ alkyl or cycloalkyl;

R¹, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C₁₋₃ alkyl optionally substituted one or more halogens, and C₁₋₃ alkoxy;

R^{1a} is H, CN, halogen, C₁₋₃ alkoxy, OH, or C₁₋₃ alkyl optionally substituted with CN;

R², each time taken, is independently selected from the group consisting of hydrogen, halogen, NR⁴R⁵, OH, C₁₋₃ alkyl, and C₃₋₆ cycloalkyl;

R³ is SO₂R⁶, SOR⁷R⁸, SOR⁹, COR¹⁰, (CH₂)_pCOOH, NHR¹¹, POR¹²R¹³, halogen, cycloalkyl, heterocycloalkyl optionally substituted with SO₂R¹⁴ or =O,

heteroaryl optionally substituted with C₁₋₃ alkyl or phenyl, or C₁₋₃ alkyl optionally substituted with one or more halogens;

R⁴ and R⁵ are each independently H or C₁₋₃ alkyl;

R⁶ is C₁₋₃ alkyl, NHCOR¹⁵, NR¹⁶R¹⁷, or phenyl;

R⁷ is C₁₋₃ alkyl, C₃₋₅ cycloalkyl, phenyl, or NR¹⁸R¹⁹;

R⁸ is NH, NCN, or NCH₃;

R⁹ is C₁₋₃ alkyl;

R¹⁰ is C₁₋₃ alkyl or NHSO₂R²⁰;

R¹¹ is COR²¹ or SO₂R²²;

R¹² and R¹³ are each independently C₁₋₃ alkyl;

R¹⁴ is C₁₋₃ alkyl;

R¹⁵ is C₁₋₃ alkyl;

R¹⁶ and R¹⁷ are each independently H, C₁₋₃ alkyl, aryl, cycloalkyl, or wherein R¹⁶ and R¹⁷ together with the carbon to which they are attached form a heterocycloalkyl;

R¹⁸ and R¹⁹ are each independently H or C₁₋₃ alkyl;

R²⁰ is C₁₋₃ alkyl;

R²¹ is heterocycloalkyl, cycloalkyl, or C₁₋₃ alkyl;

R²² is NR²³R²⁴ or C₁₋₃ alkyl optionally substituted with carboxyl;

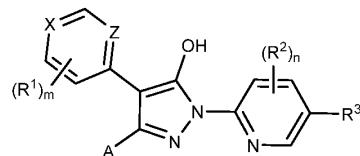
R²³ and R²⁴ are each independently H or C₁₋₃ alkyl;

m is 1, 2, 3, or 4;

n is 0, 1, 2 or 3; and

p is 1, 2, or 3.

12. The compound of claim 1, having a structure according to Formula II:



(II)

or a pharmaceutically acceptable salt thereof, wherein:

X is N or CR^{1a};

Z is CH or N;

A is C₁₋₃ alkyl or cycloalkyl;

R¹, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C₁₋₃ alkyl optionally substituted one or more halogens, and C₁₋₃ alkoxy;

R^{1a} is H, CN, halogen, C₁₋₃ alkoxy, OH, or C₁₋₃ alkyl optionally substituted with CN;

R², each time taken, is independently selected from the group consisting of hydrogen, halogen, NR⁴R⁵, OH, C₁₋₃ alkyl, and C₃₋₆ cycloalkyl;

R³ is SO₂R⁶, SOR⁷R⁸, SOR⁹, COR¹⁰, (CH₂)_pCOOH, NHR¹¹, POR¹²R¹³, halogen, cycloalkyl, heterocycloalkyl optionally substituted with SO₂R¹⁴ or =O, heteroaryl optionally substituted with C₁₋₃ alkyl or phenyl, or C₁₋₃ alkyl optionally substituted with one or more halogens;

R⁴ and R⁵ are each independently H or C₁₋₃ alkyl;

R⁶ is C₁₋₃ alkyl, NHCOR¹⁵, NR¹⁶R¹⁷, or phenyl;

R⁷ is C₁₋₃ alkyl, C₃₋₅ cycloalkyl, phenyl, or NR¹⁸R¹⁹;

R⁸ is NH, NCN, or NCH₃;

R^9 is C_{1-3} alkyl;

R^{10} is C_{1-3} alkyl or $NHSO_2R^{20}$;

R^{11} is COR^{21} or SO_2R^{22} ;

R^{12} and R^{13} are each independently C_{1-3} alkyl;

R^{14} is C_{1-3} alkyl;

R^{15} is C_{1-3} alkyl;

R^{16} and R^{17} are each independently H, C_{1-3} alkyl, aryl, cycloalkyl, or wherein R^{16} and R^{17} together with the carbon to which they are attached form a heterocycloalkyl;

R^{18} and R^{19} are independently H or C_{1-3} alkyl;

R^{20} is C_{1-3} alkyl;

R^{21} is heterocycloalkyl, cycloalkyl, or C_{1-3} alkyl;

R^{22} is $NR^{23}R^{24}$ or C_{1-3} alkyl optionally substituted with carboxyl;

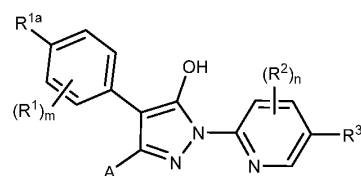
R^{23} and R^{24} are independently H or C_{1-3} alkyl;

m is 1, 2, 3, or 4;

n is 0, 1, 2 or 3; and

p is 1, 2, or 3.

13. The compound of claim 1, having a structure according to Formula III:



(III)

or a pharmaceutically acceptable salt thereof, wherein:

A is C₁₋₃ alkyl or cycloalkyl;

R¹, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C₁₋₃ alkyl optionally substituted one or more halogens, and C₁₋₃ alkoxy;

R^{1a} is H, CN, halogen, C₁₋₃ alkoxy, OH, or C₁₋₃ alkyl optionally substituted with CN;

R², each time taken, is independently selected from the group consisting of hydrogen, halogen, NR⁴R⁵, OH, C₁₋₃ alkyl, and C₃₋₆ cycloalkyl;

R³ is SO₂R⁶, SOR⁷R⁸, SOR⁹, COR¹⁰, (CH₂)_pCOOH, NHR¹¹, POR¹²R¹³, halogen, cycloalkyl, heterocycloalkyl optionally substituted with SO₂R¹⁴ or =O, heteroaryl optionally substituted with C₁₋₃ alkyl or phenyl, or C₁₋₃ alkyl optionally substituted with one or more halogens;

R⁴ and R⁵ are each independently H or C₁₋₃ alkyl;

R⁶ is C₁₋₃ alkyl, NHCOR¹⁵, NR¹⁶R¹⁷, or phenyl;

R⁷ is C₁₋₃ alkyl, C₃₋₅ cycloalkyl, phenyl, or NR¹⁸R¹⁹;

R⁸ is NH, NCN, or NCH₃;

R⁹ is C₁₋₃ alkyl;

R¹⁰ is C₁₋₃ alkyl or NHSO₂R²⁰;

R¹¹ is COR²¹ or SO₂R²²;

R¹² and R¹³ are each independently C₁₋₃ alkyl;

R¹⁴ is C₁₋₃ alkyl;

R¹⁵ is C₁₋₃ alkyl;

R^{16} and R^{17} are each independently H, C_{1-3} alkyl, aryl, cycloalkyl, or wherein R^{16} and R^{17} together with the carbon to which they are attached form a heterocycloalkyl;

R^{18} and R^{19} are independently H or C_{1-3} alkyl;

R^{20} is C_{1-3} alkyl;

R^{21} is heterocycloalkyl, cycloalkyl, or C_{1-3} alkyl;

R^{22} is $NR^{23}R^{24}$ or C_{1-3} alkyl optionally substituted with carboxyl;

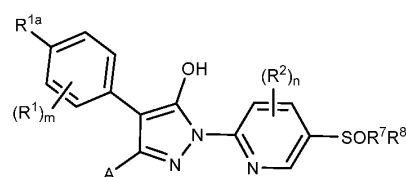
R^{23} and R^{24} are independently H or C_{1-3} alkyl;

m is 1, 2, 3, or 4;

n is 0, 1, 2 or 3; and

p is 1, 2, or 3.

14. The compound of claim 1, having a structure according to Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, wherein:

A is C_{1-3} alkyl or cycloalkyl;

R^1 , each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C_{1-3} alkyl optionally substituted one or more halogens, and C_{1-3} alkoxy;

R^{1a} is H, CN, halogen, C_{1-3} alkoxy, OH, or C_{1-3} alkyl optionally substituted with CN;

R^2 , each time taken, is independently selected from the group consisting of hydrogen, halogen, NR^4R^5 , OH, C_{1-3} alkyl, and C_{3-6} cycloalkyl;

R^4 and R^5 are each independently H or C_{1-3} alkyl;

R^7 is C_{1-3} alkyl, C_{3-5} cycloalkyl, phenyl, or $NR^{18}R^{19}$;

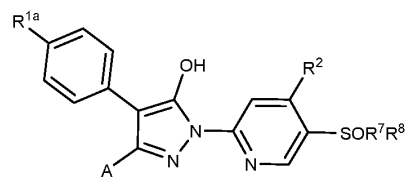
R^8 is NH, NCN, or NCH_3 ;

R^{18} and R^{19} are each independently H or C_{1-3} alkyl;

m is 1, 2, 3, or 4; and

n is 0, 1, 2 or 3.

15. The compound of claim 14, wherein R^1 is C_{1-3} alkyl.
16. The compound of claim 15, wherein R^1 is CH_3 .
17. The compound of claim 14 having a structure of Formula IVa:



(IVa)

or a pharmaceutically acceptable salt thereof, wherein:

A is C_{1-3} alkyl;

R^{1a} is CN or halogen;

R^2 is selected from the group consisting of hydrogen or C_{1-3} alkyl;

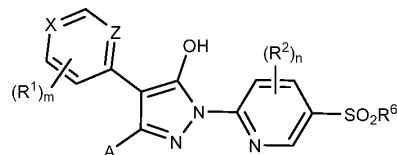
R^7 is C_{1-3} alkyl, C_{3-5} cycloalkyl, phenyl, or $NR^{18}R^{19}$;

R^8 is NH, NCN, or NCH_3 ; and

R^{18} and R^{19} are each independently H or C_{1-3} alkyl.

18. The compound of any one of claims 14-17, wherein R^{1a} is CN.
19. The compound of any one of claims 14-17, wherein R^{1a} is halogen.
20. The compound of claim 19, wherein R^{1a} is Cl.
21. The compound of any one of claims 14-20, wherein A is C₁₋₃ alkyl.
22. The compound of claim 21, wherein A is CH₃.
23. The compound of any one of claims 14-22, wherein R² is C₁₋₃ alkyl.
24. The compound of claim 23, wherein R² is CH₃.
25. The compound of any one of claims 14-24, wherein R⁷ is C₁₋₃ alkyl.
26. The compound of claim 25, wherein R⁷ is CH₃.
27. The compound of claim 25, wherein R⁷ is CH(CH₃)₂.
28. The compound of claim 25, wherein R⁷ is CH₂CH₃.
29. The compound of any one of claims 14-24, wherein R⁷ is C₃₋₅ cycloalkyl.
30. The compound of claim 29, wherein R⁷ is cyclopropyl.
31. The compound of claim 29, wherein R⁷ is cyclopentyl.
32. The compound of any one of claims 14-24, wherein R⁷ is phenyl.
33. The compound of any one of claims 14-24, wherein R⁷ is NR¹⁸R¹⁹, and wherein R¹⁸ and R¹⁹ are each independently H or C₁₋₃ alkyl.
34. The compound of claim 33, wherein R¹⁸ and R¹⁹ are independently H.
35. The compound of claim 33, wherein R¹⁸ is H and R¹⁹ is C₁₋₃ alkyl.
36. The compound of claim 35, wherein R¹⁹ is CH₃.
37. The compound of claim 33, wherein R¹⁸ and R¹⁹ are independently CH₃.
38. The compound of any one of claims 14-37, wherein R⁸ is NH.

39. The compound of any one of claims 14-37, wherein R^8 is NCN.
40. The compound of any one of claims 14-37, wherein R^8 is NCH_3 .
41. The compound of claim 1, having a structure according to Formula V:



(V)

or a pharmaceutically acceptable salt thereof, wherein:

X is N or CR^{1a} ;

Z is N or CH;

A is C_{1-3} alkyl or cycloalkyl;

R^1 , each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C_{1-3} alkyl optionally substituted one or more halogens, and C_{1-3} alkoxy;

R^{1a} is H, CN, halogen, C_{1-3} alkoxy, OH, or C_{1-3} alkyl optionally substituted with CN;

R^2 , each time taken, is independently selected from the group consisting of hydrogen, halogen, NR^4R^5 , OH, C_{1-3} alkyl, and C_{3-6} cycloalkyl;

R^4 and R^5 are each independently H or C_{1-3} alkyl;

R^6 is C_{1-3} alkyl, $NHCOR^{15}$, $NR^{16}R^{17}$, or phenyl; and

R^{15} is C_{1-3} alkyl;

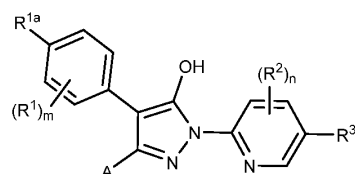
R^{16} and R^{17} are each independently H, C_{1-3} alkyl, aryl, cycloalkyl, or wherein R^{16} and R^{17} together with the carbon to which they are attached form a heterocycloalkyl;

m is 1, 2, 3, or 4; and

n is 0, 1, 2 or 3.

42. The compound of claim 41, wherein X is N.
43. The compound of claim 41, wherein X is CR^{1a}.
44. The compound of any one of claims 41-43, wherein A is C₁₋₃ alkyl.
45. The compound of claim 44, wherein A is CH₃.
46. The compound of claim 44, wherein A is CH₂CH₃.
47. The compound of any one of claims 41-43, wherein A is cycloalkyl.
48. The compound of claim 47, wherein A is cyclopropyl.
49. The compound of any one of claims 41-48, wherein R^{1a} is CN.
50. The compound of any one of claims 41-48, wherein R^{1a} is halogen.
51. The compound of claim 50, wherein R^{1a} is Cl.
52. The compound of claim 50, wherein R^{1a} is F.
53. The compound of claim 50, wherein R^{1a} is Br.
54. The compound of any one of claims 41-48, wherein R^{1a} is C₁₋₃ alkoxy.
55. The compound of claim 54, wherein R^{1a} is methoxy.
56. The compound of any one of claims 41-48, wherein R^{1a} is H.
57. The compound of any one of claims 41-48, wherein R^{1a} is C₁₋₃ alkyl optionally substituted with CN.
58. The compound of claim 57, wherein R^{1a} is CH₂CN.
59. The compound of any one of claims 41-48, wherein R^{1a} is OH.
60. The compound of any one of claims 41-59, wherein Z is CH.
61. The compound of any one of claims 41-59, wherein Z is N.

62. The compound of any one of claims 41-61, wherein R^1 is H.
63. The compound of any one of claims 41-61, wherein R^1 is C_{1-3} alkyl.
64. The compound of claim 63, wherein R^1 is CH_3 .
65. The compound of any one of claims 41-61, wherein R^1 is C_{1-3} alkoxy.
66. The compound of claim 65, wherein R^1 is methoxy.
67. The compound of any one of claims 41-61, wherein R^1 is CN.
68. The compound of any one of claims 41-67, wherein R^2 is H.
69. The compound of any one of claims 41-67, wherein R^2 is C_{1-3} alkyl.
70. The compound of claim 69, wherein R^2 is CH_3 .
71. The compound of any one of claims 41-70, wherein R^6 is C_{1-3} alkyl.
72. The compound of claim 71, wherein R^6 is CH_3 .
73. The compound of any one of claims 41-70, wherein R^6 is $NHCOR^{15}$, and wherein R^{15} is C_{1-3} alkyl.
74. The compound of claim 73, wherein R^{15} is CH_3 .
75. The compound of any one of claims 41-70, wherein R^6 is $NR^{16}R^{17}$, and wherein R^{16} and R^{17} are each independently H, C_{1-3} alkyl, aryl, cycloalkyl, or wherein R^{16} and R^{17} together with the carbon to which they are attached form a heterocycloalkyl.
76. The compound of claim 75, wherein R^6 is NH_2 .
77. The compound of any one of claims 41-70, wherein R^6 is phenyl.
78. The compound of claim 1, having a structure according to Formula VI:



(VI)

or a pharmaceutically acceptable salt thereof, wherein:

A is C₁₋₃ alkyl or cycloalkyl;

R¹, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C₁₋₃ alkyl optionally substituted one or more halogens, and C₁₋₃ alkoxy;

R^{1a} is H, CN, halogen, C₁₋₃ alkoxy, OH, or C₁₋₃ alkyl optionally substituted with CN;

R², each time taken, is independently selected from the group consisting of hydrogen, halogen, NR⁴R⁵, OH, C₁₋₃ alkyl, and C₃₋₆ cycloalkyl;

R³ is cycloalkyl or heterocycloalkyl optionally substituted with SO₂R¹⁴ or =O;

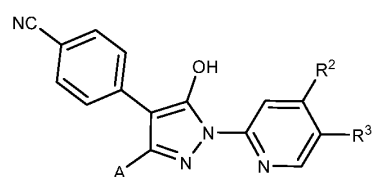
R⁴ and R⁵ are each independently H or C₁₋₃ alkyl;

R¹⁴ is C₁₋₃ alkyl;

m is 1, 2, 3, or 4; and

n is 0, 1, 2 or 3.

79. The compound of claim 78 having a structure of Formula VIa:



(VIa)

or a pharmaceutically acceptable salt thereof, wherein:

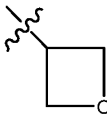
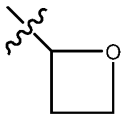
A is C₁₋₃ alkyl;

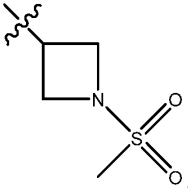
R² is hydrogen or C₁₋₃ alkyl;

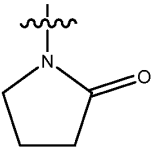
R^3 is cycloalkyl or heterocycloalkyl optionally substituted with SO_2R^{14} or $=O$; and

R^{14} is C_{1-3} alkyl.

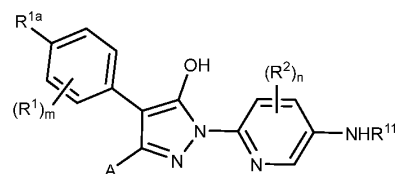
80. The compound of claim 78 or 79, wherein A is C_{1-3} alkyl.
81. The compound of claim 80, wherein A is CH_3 .
82. The compound of any one of claims 78-81, wherein R^2 is H.
83. The compound of any one of claims 78-81, wherein R^2 is C_{1-3} alkyl.
84. The compound of claim 83, wherein R^2 is CH_3 .
85. The compound of any one of claims 78-84, wherein R^3 is cycloalkyl.
86. The compound of claim 85, wherein R^3 is cyclopropyl.
87. The compound of any one of claims 78-84, wherein R^3 is heterocycloalkyl optionally substituted with SO_2R^{14} or $=O$, and wherein R^{14} is C_{1-3} alkyl.

88. The compound of claim 87, wherein R^3 is  or .

89. The compound of claim 87, wherein R^3 is .

90. The compound of claim 87, wherein R^3 is .

91. The compound of claim 1, having a structure according to Formula VII:



(VII)

or a pharmaceutically acceptable salt thereof, wherein:

A is C₁₋₃ alkyl or cycloalkyl;

R¹, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C₁₋₃ alkyl optionally substituted one or more halogens, and C₁₋₃ alkoxy;

R^{1a} is H, CN, halogen, C₁₋₃ alkoxy, OH, or C₁₋₃ alkyl optionally substituted with CN;

R², each time taken, is independently selected from the group consisting of hydrogen, halogen, NR⁴R⁵, OH, C₁₋₃ alkyl, and C₃₋₆ cycloalkyl;

R⁴ and R⁵ are each independently H or C₁₋₃ alkyl;

R¹¹ is COR²¹ or SO₂R²²;

R²¹ is heterocycloalkyl, cycloalkyl, or C₁₋₃ alkyl;

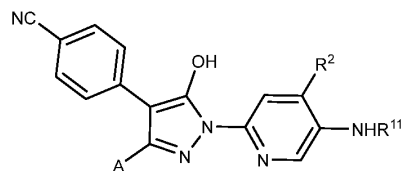
R²² is NR²³R²⁴ or C₁₋₃ alkyl optionally substituted with carboxyl;

R²³ and R²⁴ are independently H or C₁₋₃ alkyl;

m is 1, 2, 3, or 4; and

n is 0, 1, 2 or 3.

92. The compound of claim 91 having a structure of Formula VIIa:



(VIIa)

or a pharmaceutically acceptable salt thereof, wherein:

A is C₁₋₃ alkyl or cycloalkyl;

R² is hydrogen, C₁₋₃ alkyl or C₃₋₆ cycloalkyl;

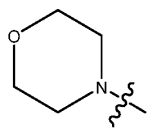
R¹¹ is COR²¹ or SO₂R²²;

R²¹ is heterocycloalkyl, cycloalkyl, or C₁₋₃ alkyl;

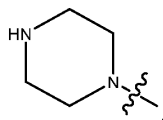
R²² is NR²³R²⁴ or C₁₋₃ alkyl optionally substituted with carboxyl; and

R²³ and R²⁴ are independently H or C₁₋₃ alkyl.

93. The compound of claim 91 or 92, wherein A is C₁₋₃ alkyl.
94. The compound of claim 93, wherein A is CH₃.
95. The compound of any one of claims 91-94, wherein R² is H.
96. The compound of any one of claims 91-94, wherein R² is C₁₋₃ alkyl.
97. The compound of claim 96, wherein R² is CH₃.
98. The compound of any one of claims 91-97, wherein R¹¹ is COR²¹, and wherein R²¹ is heterocycloalkyl, cycloalkyl, or C₁₋₃ alkyl.
99. The compound of claim 98, wherein R²¹ is heterocycloalkyl.



100. The compound of claim 99, wherein R^{21} is



101. The compound of claim 99, wherein R^{21} is

102. The compound of claim 98, wherein R^{21} is cycloalkyl.

103. The compound of claim 102, wherein R^{21} is cyclopropyl.

104. The compound of claim 98, wherein R^{21} is C_{1-3} alkyl.

105. The compound of claim 104, wherein R^{21} is CH_2CH_3 .

106. The compound of any one of claims 91-97, wherein R^{11} is SO_2R^{22} , wherein R^{22} is $NR^{23}R^{24}$ or C_{1-3} alkyl optionally substituted with carboxyl, and wherein R^{23} and R^{24} are independently H or C_{1-3} alkyl.

107. The compound of claim 106, wherein R^{22} is C_{1-3} alkyl optionally substituted with carboxyl.

108. The compound of claim 107, wherein R^{22} is CH_3 .

109. The compound of claim 107, wherein R^{22} is CH_2CH_3 .

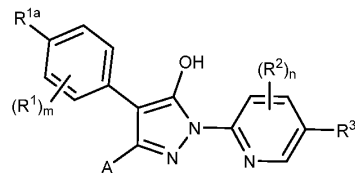
110. The compound of claim 107, wherein R^{22} is CH_2COOH .

111. The compound of claim 106, wherein R^{22} is $NR^{23}R^{24}$, and wherein R^{23} and R^{24} are independently H or C_{1-3} alkyl.

112. The compound of claim 111, wherein R^{22} is $NHCH_3$.

113. The compound of claim 111, wherein R^{22} is $N(CH_3)_2$.

114. The compound of claim 1, having a structure according to Formula VIII:



(VIII)

or a pharmaceutically acceptable salt thereof, wherein:

A is C₁₋₃ alkyl or cycloalkyl;

R¹, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C₁₋₃ alkyl optionally substituted one or more halogens, and C₁₋₃ alkoxy;

R^{1a} is H, CN, halogen, C₁₋₃ alkoxy, OH, or C₁₋₃ alkyl optionally substituted with CN;

R², each time taken, is independently selected from the group consisting of hydrogen, halogen, NR⁴R⁵, OH, C₁₋₃ alkyl, and C₃₋₆ cycloalkyl;

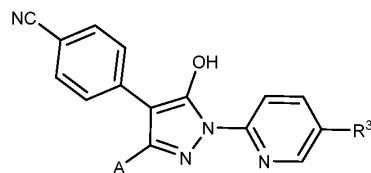
R³ is heteroaryl optionally substituted with C₁₋₃ alkyl or phenyl;

R⁴ and R⁵ are each independently H or C₁₋₃ alkyl;

m is 1, 2, 3, or 4; and

n is 0, 1, 2 or 3.

115. The compound of claim 114 having a structure of Formula VIIIa:



(VIIIa)

or a pharmaceutically acceptable salt thereof, wherein:

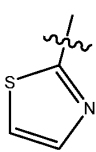
A is C₁₋₃ alkyl or cycloalkyl; and

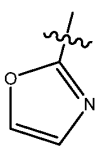
R³ is heteroaryl optionally substituted with C₁₋₃ alkyl or phenyl.

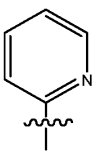
116. The compound of claim 114 or 115, wherein A is C₁₋₃ alkyl.

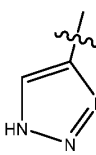
117. The compound of claim 116, wherein A is CH₃.

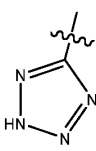
118. The compound of anyone of claims 114-117, wherein R³ is heteroaryl.

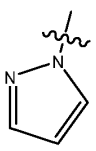
119. The compound of claim 118, wherein R³ is .

120. The compound of claim 118, wherein R³ is .

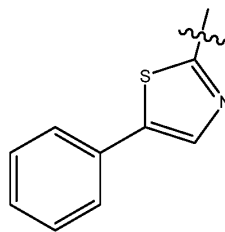
121. The compound of claim 118, wherein R³ is .

122. The compound of claim 118, wherein R³ is .

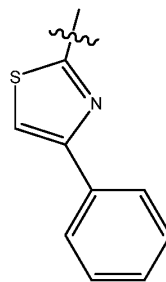
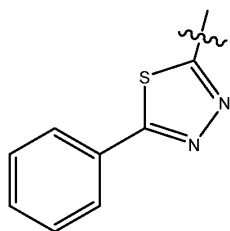
123. The compound of claim 118, wherein R³ is .

124. The compound of claim 118, wherein R³ is .

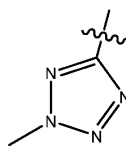
125. The compound of anyone of claims 114-117, wherein R^3 is heteroaryl optionally substituted with C_{1-3} alkyl or phenyl.



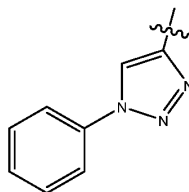
126. The compound of claim 125, wherein R^3 is or



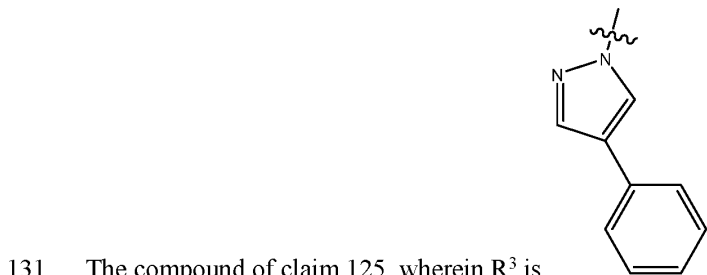
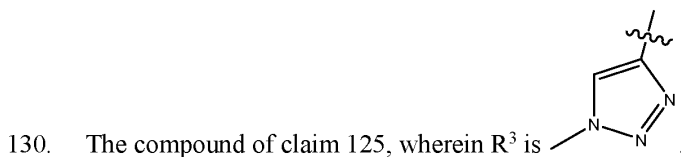
127. The compound of claim 125, wherein R^3 is



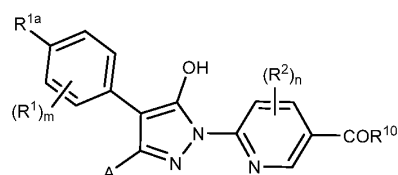
128. The compound of claim 125, wherein R^3 is



129. The compound of claim 125, wherein R^3 is



132. The compound of claim 1, having a structure according to Formula IX:



(IX)

or a pharmaceutically acceptable salt thereof, wherein:

A is C₁₋₃ alkyl or cycloalkyl;

R¹, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C₁₋₃ alkyl optionally substituted one or more halogens, and C₁₋₃ alkoxy;

R^{1a} is H, CN, halogen, C₁₋₃ alkoxy, OH, or C₁₋₃ alkyl optionally substituted with CN;

R², each time taken, is independently selected from the group consisting of hydrogen, halogen, NR⁴R⁵, OH, C₁₋₃ alkyl, and C₃₋₆ cycloalkyl;

R⁴ and R⁵ are each independently H or C₁₋₃ alkyl;

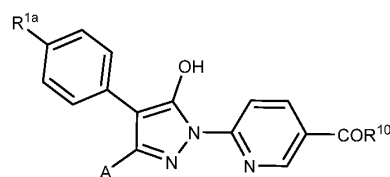
R¹⁰ is C₁₋₃ alkyl or NHSO₂R²⁰;

R^{20} is C_{1-3} alkyl;

m is 1, 2, 3, or 4; and

n is 0, 1, 2 or 3.

133. The compound of claim 132 having a structure of Formula IXa:



(IXa)

or a pharmaceutically acceptable salt thereof, wherein:

A is C_{1-3} alkyl;

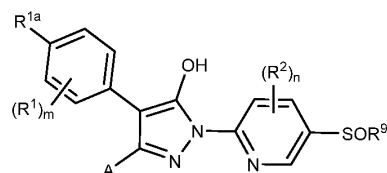
R^{1a} is CN or halogen;

R^{10} is C_{1-3} alkyl or $NHSO_2R^{20}$; and

R^{20} is C_{1-3} alkyl.

134. The compound of claim 132 or 133, wherein R^{1a} is CN.
135. The compound of claim 132 or 133, wherein R^{1a} is halogen.
136. The compound of claim 135, wherein R^{1a} is Cl.
137. The compound of any one of claims 132-136, wherein R^{10} is C_{1-3} alkyl.
138. The compound of claim 137, wherein R^{10} is CH_3 .
139. The compound of claim 137, wherein R^{10} is $CH(CH_3)_2$.
140. The compound of claim 137, wherein R^{10} is CH_2CH_3 .
141. The compound of any one of claims 132-136, wherein R^{10} is $NHSO_2R^{20}$, and wherein R^{20} is C_{1-3} alkyl.

142. The compound of claim 141, wherein R^{20} is CH_3 .
143. The compound of claim 1, having a structure according to Formula X:



(X)

or a pharmaceutically acceptable salt thereof, wherein:

A is C_{1-3} alkyl or cycloalkyl;

R^1 , each time taken, is independently selected from the group consisting of hydrogen, halogen, CN , OH , C_{1-3} alkyl optionally substituted one or more halogens, and C_{1-3} alkoxy;

R^{1a} is H , CN , halogen, C_{1-3} alkoxy, OH , or C_{1-3} alkyl optionally substituted with CN ;

R^2 , each time taken, is independently selected from the group consisting of hydrogen, halogen, NR^4R^5 , OH , C_{1-3} alkyl, and C_{3-6} cycloalkyl;

R^4 and R^5 are each independently H or C_{1-3} alkyl;

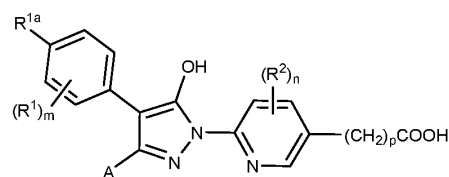
R^9 is C_{1-3} alkyl;

m is 1, 2, 3, or 4; and

n is 0, 1, 2 or 3.

144. The compound of claim 143, wherein R^{1a} is CN .
145. The compound of claim 143 or 144, wherein R^1 is H .
146. The compound of any one of claims 143-145, wherein A is C_{1-3} alkyl.
147. The compound of claim 146, wherein A is CH_3 .

148. The compound of any one of claims 143-147, wherein R^2 is H.
149. The compound of any one of claims 143-148, wherein R^9 is C_{1-3} alkyl.
150. The compound of claim 149, wherein R^9 is CH_3 .
151. The compound of claim 1, having a structure according to Formula XI:



(XI)

or a pharmaceutically acceptable salt thereof, wherein:

A is C_{1-3} alkyl or cycloalkyl;

R^1 , each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C_{1-3} alkyl optionally substituted one or more halogens, and C_{1-3} alkoxy;

R^{1a} is H, CN, halogen, C_{1-3} alkoxy, OH, or C_{1-3} alkyl optionally substituted with CN;

R^2 , each time taken, is independently selected from the group consisting of hydrogen, halogen, NR^4R^5 , OH, C_{1-3} alkyl, and C_{3-6} cycloalkyl;

R^4 and R^5 are each independently H or C_{1-3} alkyl;

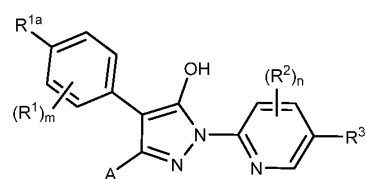
m is 1, 2, 3, or 4;

n is 0, 1, 2 or 3; and

p is 1, 2, or 3.

152. The compound of claim 151, wherein R^{1a} is CN.
153. The compound of claim 151 or 152, wherein R^1 is H.

154. The compound of any one of claims 151-153, wherein A is C₁₋₃ alkyl.
155. The compound of claim 154, wherein A is CH₃.
156. The compound of any one of claims 151-155, wherein R² is H.
157. The compound of anyone of claims 151-156, wherein p is 1.
158. The compound of claim 1, having a structure according to Formula XII:



(XII)

or a pharmaceutically acceptable salt thereof, wherein:

A is C₁₋₃ alkyl or cycloalkyl;

R¹, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C₁₋₃ alkyl optionally substituted one or more halogens, and C₁₋₃ alkoxy;

R^{1a} is H, CN, halogen, C₁₋₃ alkoxy, OH, or C₁₋₃ alkyl optionally substituted with CN;

R², each time taken, is independently selected from the group consisting of hydrogen, halogen, NR⁴R⁵, OH, C₁₋₃ alkyl, and C₃₋₆ cycloalkyl;

R³ is halogen;

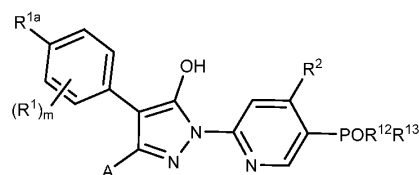
R⁴ and R⁵ are each independently H or C₁₋₃ alkyl;

m is 1, 2, 3, or 4; and

n is 0, 1, 2 or 3.

159. The compound of claim 158, wherein R^{1a} is CN.

160. The compound of claim 158 or 159, wherein R^1 is H.
161. The compound of any one of claims 158-160, wherein R^2 is H.
162. The compound of anyone of claims 158-161, wherein R^3 is Cl.
163. The compound of anyone of claims 158-161, wherein R^3 is Br.
164. The compound of anyone of claims 158-161, wherein R^3 is F.
165. The compound of claim 1, having a structure according to Formula XIII:



(XIII)

or a pharmaceutically acceptable salt thereof, wherein:

A is C_{1-3} alkyl or cycloalkyl;

R^1 , each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C_{1-3} alkyl optionally substituted one or more halogens, and C_{1-3} alkoxy;

R^{1a} is H, CN, halogen, C_{1-3} alkoxy, OH, or C_{1-3} alkyl optionally substituted with CN;

R^2 , each time taken, is independently selected from the group consisting of hydrogen, halogen, NR^4R^5 , OH, C_{1-3} alkyl, and C_{3-6} cycloalkyl;

R^4 and R^5 are each independently H or C_{1-3} alkyl;

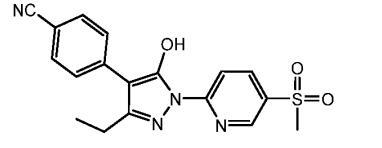
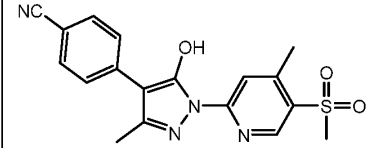
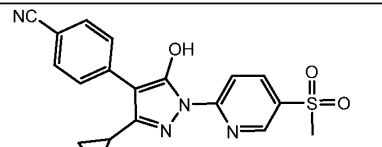
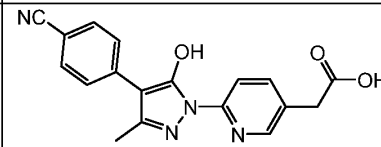
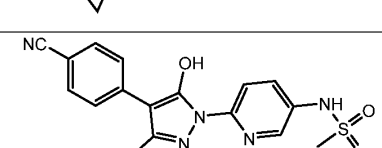
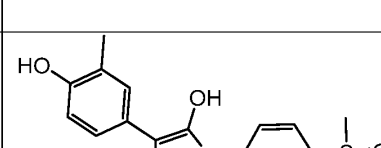
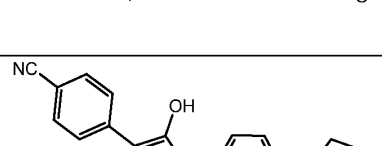
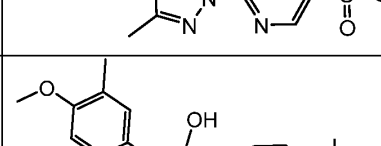
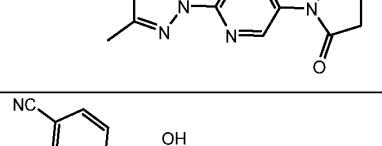
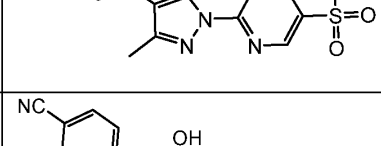
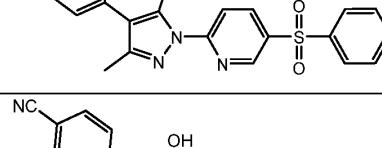
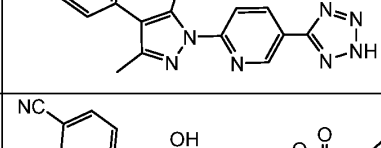
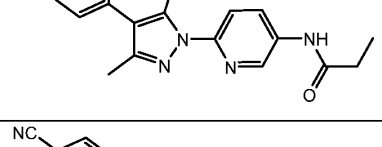
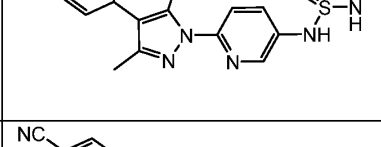
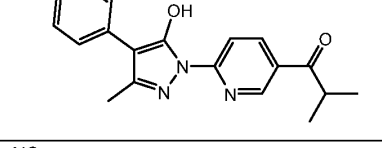
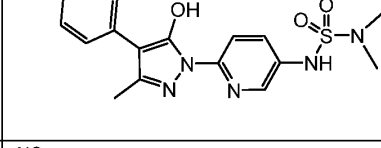
R^{12} is C_{1-3} alkyl;

R^{13} is C_{1-3} alkyl; and

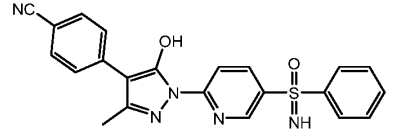
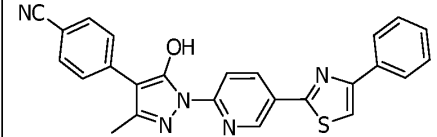
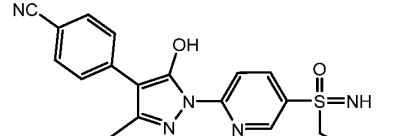
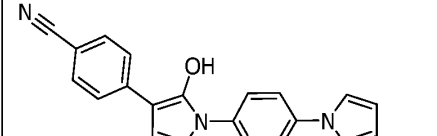
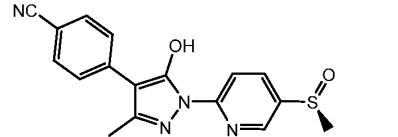
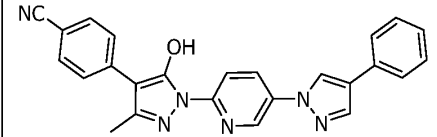
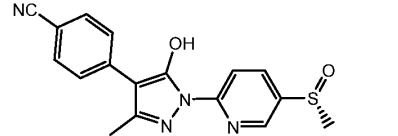
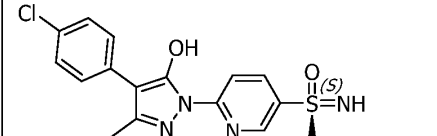
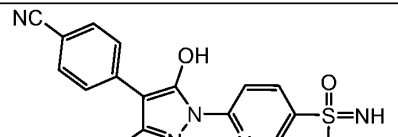
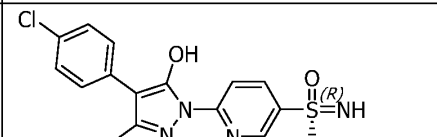
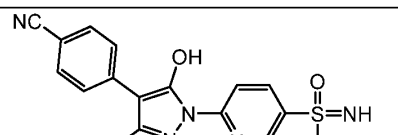
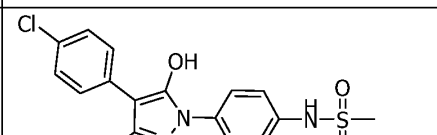
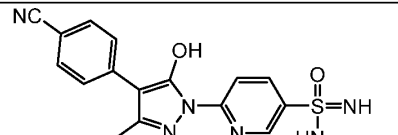
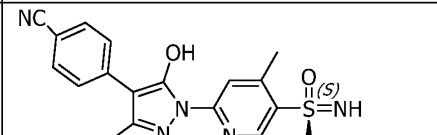
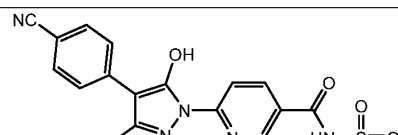
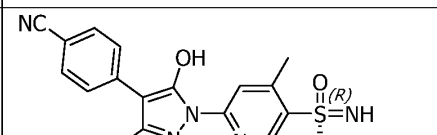
m is 1, 2, 3, or 4.

166. The compound of claim 165, wherein R^{1a} is CN.
167. The compound of claim 165 or 166, wherein R^1 is H.
168. The compound of any one of claims 165-167, wherein A is C_{1-3} alkyl.
169. The compound of claim 168, wherein A is CH_3 .
170. The compound of any one of claims 165-169, wherein R^2 is C_{1-3} alkyl.
171. The compound of claim 170, wherein R^2 is CH_3 .
172. The compound of any one of claims 165-171, wherein R^{12} is C_{1-3} alkyl.
173. The compound of claim 172, wherein R^{12} is CH_3 .
174. The compound of anyone of claims 165-173, wherein R^{13} is C_{1-3} alkyl.
175. The compound of claim 174, wherein R^{13} is CH_3 .
176. The compound of claim 1, wherein the compound is selected from the group consisting of:

Cmpd No.	Structure	Cmpd No.	Structure
1		43	
2		44	
3		45	

4		46	
5		47	
6		48	
7		49	
8		50	
9		51	
10		52	
11		53	

12		54	
13		55	
14		56	
15		57	
16		58	
17		59	
18		60	
19		61	

20		62	
21		63	
22		64	
23		65	
24		66	
25		67	
26		68	
27		69	

28		70	
29		71	
30		72	
31		73	
32		74	
33		75	
34		76	
35		77	

36		78	
37		79	
38		80	
39		81	
40		82	
41		83	
42			

or a pharmaceutically acceptable salt thereof.

177. The compound of any one of claims 1-176, or a pharmaceutically acceptable salt thereof, wherein at least one hydrogen atom is replaced with a deuterium atom.

178. A pharmaceutical composition comprising the compound of any one of claims 1-177, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.
179. A method for treating a disease mediated by PHD activity comprising administering to a subject the compound of any one of claims 1-177, or a pharmaceutically acceptable salt thereof.
180. The method of claim 179, wherein the disease mediated by PHD activity is an ischemic reperfusion injury.
181. The method of claim 180, wherein the ischemic reperfusion injury is selected from stroke, myocardial infarction, and acute kidney injury.
182. The method of claim 179, wherein the disease mediated by PHD activity is inflammatory bowel disease.
183. The method of claim 182, wherein the inflammatory bowel disease is ulcerative colitis.
184. The method of claim 182, wherein the inflammatory bowel disease is Crohn's disease.
185. The method of claim 175, wherein the disease mediated by PHD activity is cancer.
186. The method of claim 181, wherein the cancer is colorectal cancer.
187. The method of claim 179, wherein the disease mediated by PHD activity is liver disease.
188. The method of claim 179, wherein the disease mediated by PHD activity is atherosclerosis.
189. The method of claim 179, wherein the disease mediated by PHD activity is cardiovascular disease.
190. The method of claim 179, wherein the disease mediated by PHD activity is a disease or condition of the eye.

191. The method of claim 190, wherein the disease or condition of the eye is selected from radiation retinopathy, retinopathy of prematurity, diabetic retinopathy, age-related macular degeneration, and ocular ischemia.
192. The method of claim 179, wherein the disease is anemia.
193. The method of claim 192, wherein the anemia is anemia associated with chronic kidney disease.
194. The method of claim 179, wherein the disease is chronic kidney disease.
195. The method of claim 179, wherein the disease is associated with hyperoxia.
196. The method of claim 195, wherein the disease is retinopathy of prematurity.
197. The method of claim 195, wherein the disease is bronchopulmonary dysplasia (BPD).
198. The method of claim 179, wherein the disease is selected from ischemic heart disease, valvular heart disease, congestive heart failure, acute lung injury, pulmonary fibrosis, pulmonary hypertension, chronic obstructive pulmonary disease (COPD), acute liver failure, liver fibrosis, and cirrhosis.