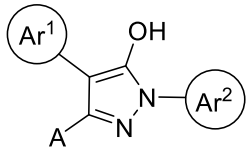
CLAIMS

1. A compound of Formula A,



(A)

or a pharmaceutically acceptable salt thereof, wherein:

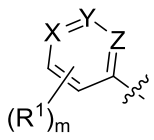
A is C_{1-3} alkyl or C_{3-6} cycloalkyl;

Ar^1 is aryl or heteroaryl, optionally substituted with one or more groups selected from halogen, CN, OH, C_{1-3} alkyl optionally substituted with CN or one or more halogens, and C_{1-3} alkoxy; and

Ar^2 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; C_{3-6} cycloalkyl; C_{3-6} heterocycloalkyl optionally substituted with a sulfonyl group or =O; C_{1-3} alkyl optionally substituted with carbonyl or one or more halogens; and heteroaryl optionally substituted with C_{1-3} alkyl or phenyl.

2. The compound of claim 1, wherein A is C_{1-3} alkyl.

3. The compound of claim 1 or 2, wherein Ar^1 is



, wherein

X is N or CR^{1a};

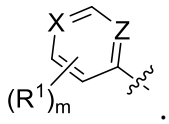
Y and Z are independently CH or N;

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

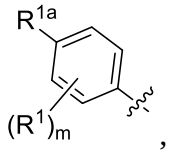
m is 1, 2, 3 or 4.

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



.

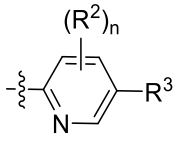
5. The compound of claim 3 or 4, wherein Ar^1 is



, wherein

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



, wherein

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;

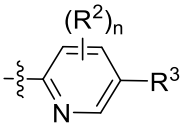
R^4, R^5, R^{18}, R^{19}, R^{23} and R^{24} are each independently H or C_{1-3} alkyl;

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

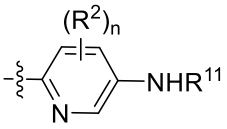
n is 0, 1, 2 or 3.

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

(a) 

, wherein R^3 is selected from the group consisting of F, Cl, Br, and I;

or

(b) 

, wherein

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

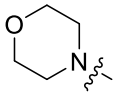
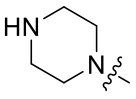
R^{21} is heterocycloalkyl, cycloalkyl, or C_{1-3} alkyl;

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

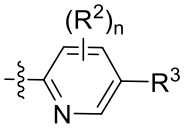
R^{23} and R^{24} are independently H or C_{1-3} alkyl.

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

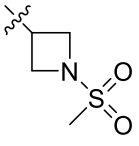
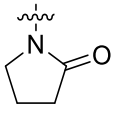
, wherein

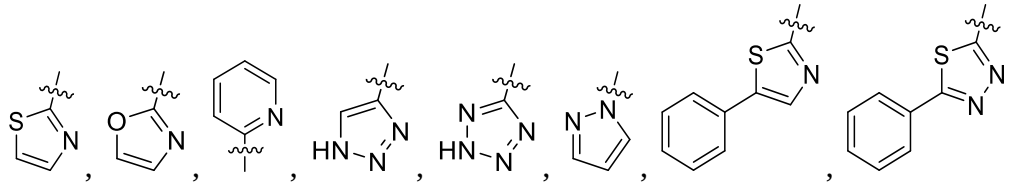
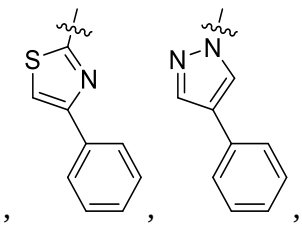
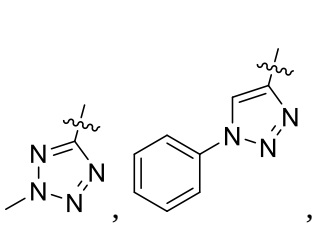
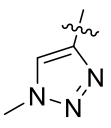
(a) R^3 is cycloalkyl or heterocycloalkyl optionally substituted with SO_2R^{14} or =O; and

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

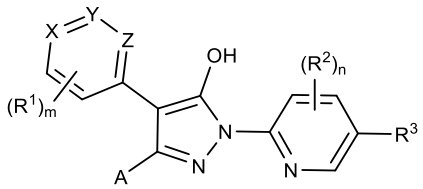
or

(b) R^3 is heteroaryl optionally substituted with $C_{1\text{-}3}$ 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 , , , , and .

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 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^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^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;

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^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 each 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;

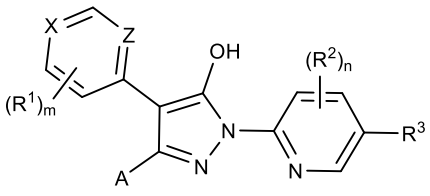
R^{23} and R^{24} are each independently H or C_{1-3} alkyl;

m is 1, 2, 3, or 4;

n is 0, 1, 2 or 3; and

p is 1, 2, or 3.

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 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^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^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;

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^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;

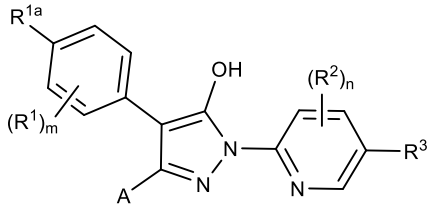
R^{23} and R^{24} are independently H or C_{1-3} alkyl;

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 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^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^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;

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^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;

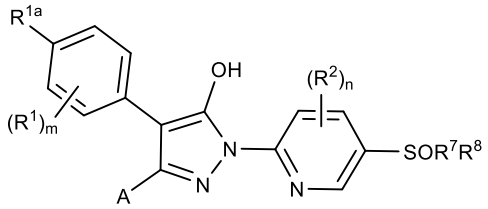
R^{23} and R^{24} are independently H or C_{1-3} alkyl;

m is 1, 2, 3, or 4;

n is 0, 1, 2 or 3; and

p is 1, 2, or 3.

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;

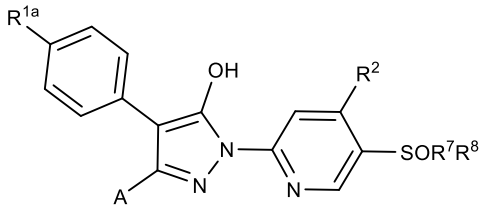
m is 1, 2, 3, or 4; and

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 C_{1-3} alkyl.

22. The compound of claim 21, wherein A is CH_3.

23. The compound of any one of claims 14-22, wherein R^2 is C_{1-3} alkyl.

24. The compound of claim 23, wherein R^2 is CH_3.

25. The compound of any one of claims 14-24, wherein R^7 is C_{1-3} alkyl.

26. The compound of claim 25, wherein R^7 is CH_3.

27. The compound of claim 25, wherein R^7 is $CH(CH_3)_2$.

28. The compound of claim 25, wherein R^7 is CH_2CH_3.

29. The compound of any one of claims 14-24, wherein R^7 is C_{3-5} cycloalkyl.

30. The compound of claim 29, wherein R^7 is cyclopropyl.

31. The compound of claim 29, wherein R^7 is cyclopentyl.

32. The compound of any one of claims 14-24, wherein R^7 is phenyl.

33. The compound of any one of claims 14-24, wherein R^7 is $NR^{18}R^{19}$, and wherein R^{18} and R^{19} are each independently H or C_{1-3} alkyl.

34. The compound of claim 33, wherein R^{18} and R^{19} are independently H.

35. The compound of claim 33, wherein R^{18} is H and R^{19} is C_{1-3} alkyl.

36. The compound of claim 35, wherein R^{19} is CH_3.

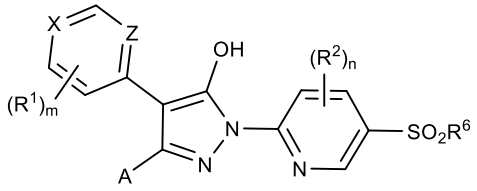
37. The compound of claim 33, wherein R^{18} and R^{19} are independently CH_3.

38. The compound of any one of claims 14-37, wherein R^8 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 C_{1-3} alkyl.

45. The compound of claim 44, wherein A is CH_3.

46. The compound of claim 44, wherein A is CH_2CH_3.

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 C_{1-3} 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 C_{1-3} alkyl optionally substituted with CN.

58. The compound of claim 57, wherein R^{1a} is CH_2CN.

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 anyone 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 anyone of claims 41-70, wherein R^6 is $NHCOR^{15}$, and wherein R^{15} is C_{1-3} alkyl.

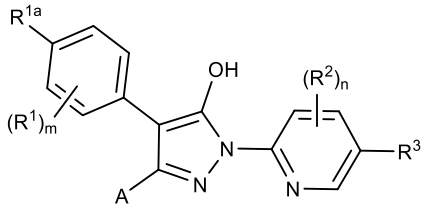
74. The compound of claim 73, wherein R^{15} is CH_3.

75. The compound of anyone 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 anyone 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 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^3 is cycloalkyl or heterocycloalkyl optionally substituted with SO_2R^{14} or =O;

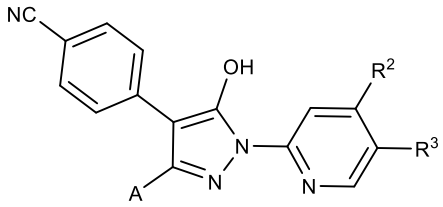
R^4 and R^5 are each independently H or C_{1-3} alkyl;

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

R^2 is hydrogen or C_{1-3} 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.

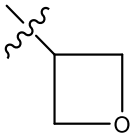
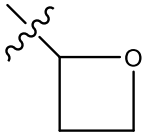
83. The compound of any one of claims 78-81, wherein R^2 is C_{1-3} alkyl.

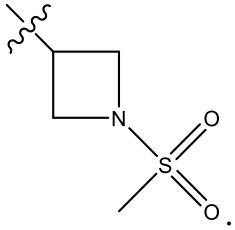
84. The compound of claim 83, wherein R^2 is CH_3.

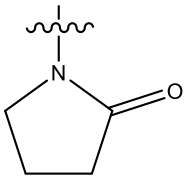
85. The compound of any one of claims 78-84, wherein R^3 is cycloalkyl.

86. The compound of claim 85, wherein R^3 is cyclopropyl.

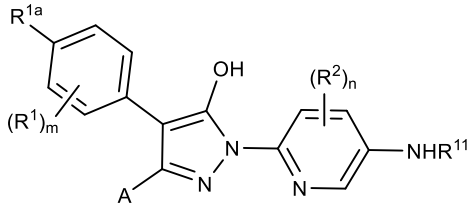
87. The compound of any one of claims 78-84, wherein R^3 is heterocycloalkyl optionally substituted with SO_2R^{14} or =O, and wherein R^{14} is C_{1-3} alkyl.

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

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

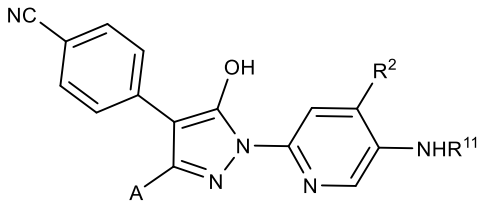
R^{22} is $NR^{23}R^{24}$ or C_{1-3} alkyl optionally substituted with carboxyl;

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

R^2 is hydrogen, C_{1-3} alkyl or C_{3-6} cycloalkyl;

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.

93. The compound of claim 91 or 92, wherein A is C_{1-3} alkyl.

94. The compound of claim 93, wherein A is CH_3.

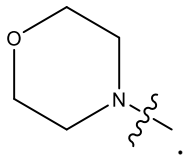
95. The compound of any one of claims 91-94, wherein R^2 is H.

96. The compound of any one of claims 91-94, wherein R^2 is C_{1-3} alkyl.

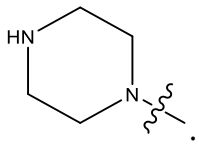
97. The compound of claim 96, wherein R^2 is CH_3.

98. The compound of any one of claims 91-97, wherein R^{11} is COR^{21}, and wherein R^{21} is heterocycloalkyl, cycloalkyl, or C_{1-3} alkyl.

99. The compound of claim 98, wherein R^{21} 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.

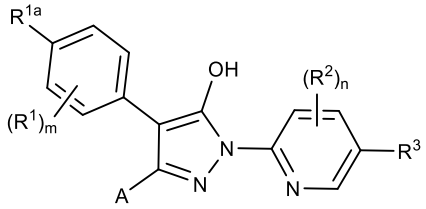
110. The compound of claim 107, wherein R^{22} is CH_2COOH.

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 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;

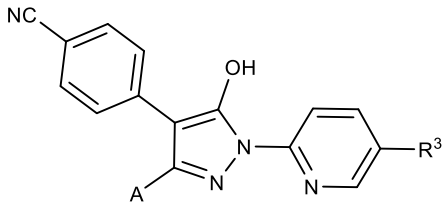
R^3 is heteroaryl optionally substituted with C_{1-3} alkyl or phenyl;

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

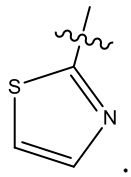
A is C_{1-3} alkyl or cycloalkyl; and

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

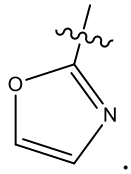
116. The compound of claim 114 or 115, wherein A is C_{1-3} alkyl.

117. The compound of claim 116, wherein A is CH_3.

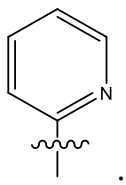
118. The compound of anyone of claims 114-117, wherein R^3 is heteroaryl.

119. The compound of claim 118, wherein R^3 is 

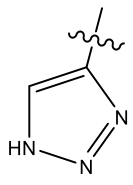
.

120. The compound of claim 118, wherein R^3 is 

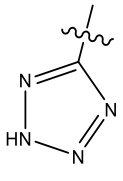
.

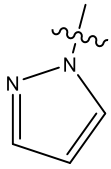
121. The compound of claim 118, wherein R^3 is 

.

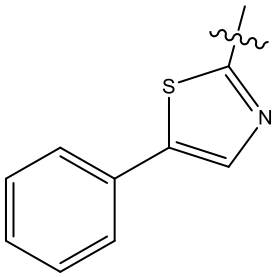
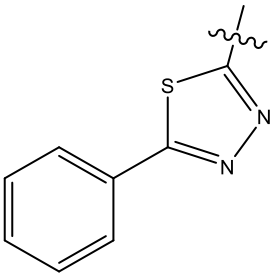
122. The compound of claim 118, wherein R^3 is 

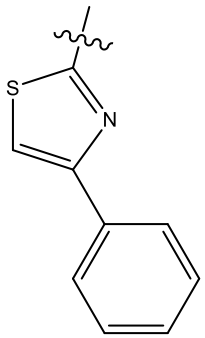
.

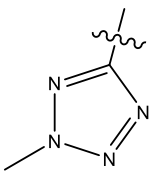
123. The compound of claim 118, wherein R^3 is .

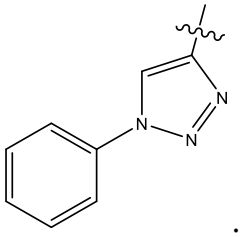
124. The compound of claim 118, wherein R^3 is .

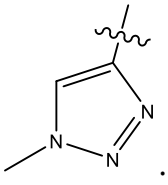
125. The compound of anyone of claims 114-117, wherein R^3 is heteroaryl optionally substituted with C_{1-3} alkyl or phenyl.

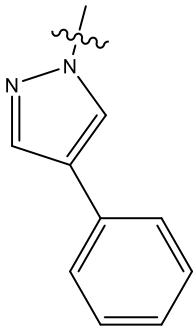
126. The compound of claim 125, wherein R^3 is  or .

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

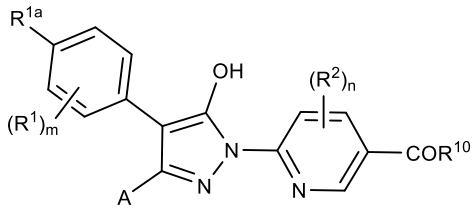
128. The compound of claim 125, wherein R^3 is .

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

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

131. 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 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;

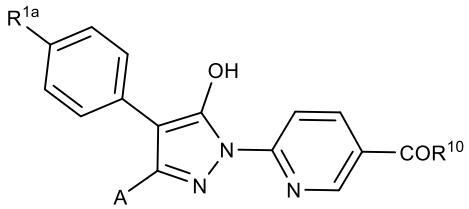
R^{10} is C_{1-3} alkyl or $NHSO_2R^{20}$;

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.

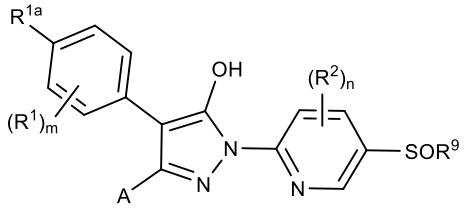
139. The compound of claim 137, wherein R^{10} is $CH(CH_3)_2$.

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 $C_{1\text{-}3}$ 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, $C_{1\text{-}3}$ alkyl optionally substituted one or more halogens, and $C_{1\text{-}3}$ alkoxy;

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

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

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

R^9 is $C_{1\text{-}3}$ 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.

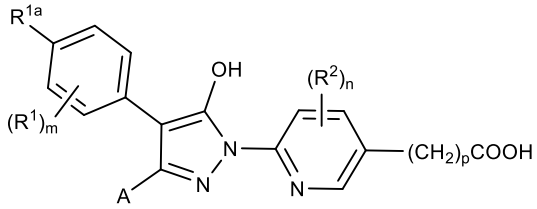
147. The compound of claim 146, wherein A is CH_3.

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.

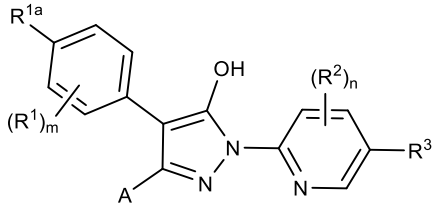
154. The compound of any one of claims 151-153, wherein A is C_{1-3} alkyl.

155. The compound of claim 154, wherein A is CH_3.

156. The compound of any one of claims 151-155, wherein R^2 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 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^3 is halogen;

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

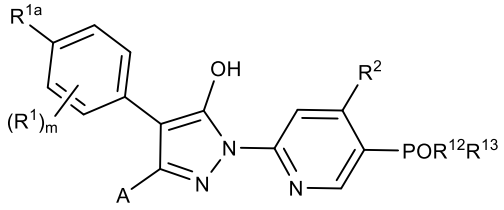
161. The compound of any one of claims 158-160, wherein R^2 is H.

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.

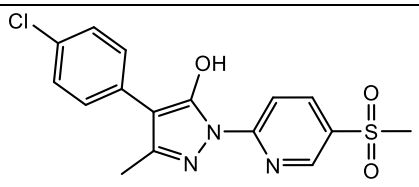
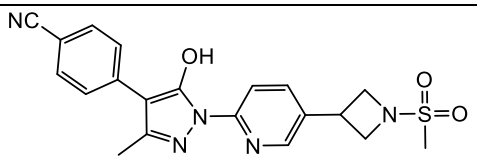
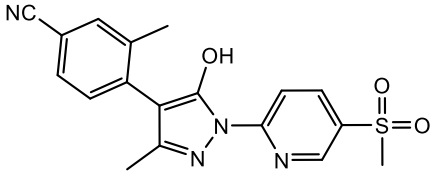
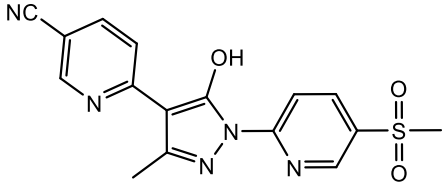
172. The compound of any one of claims 165-171, wherein R^{12} is C_{1-3} alkyl.

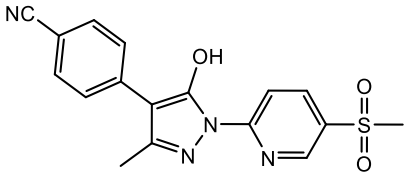
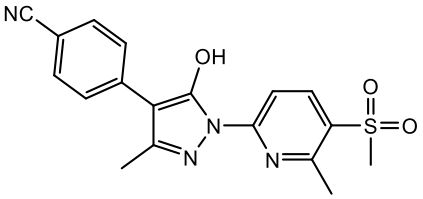
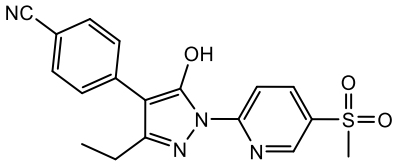
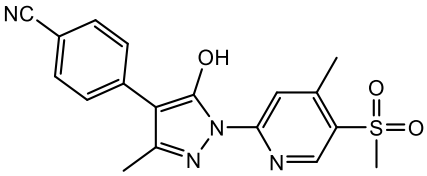
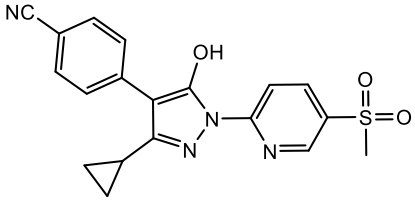
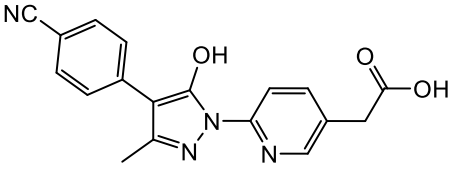
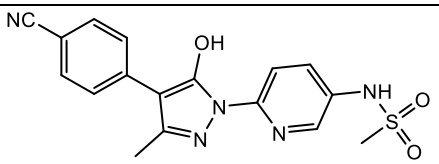
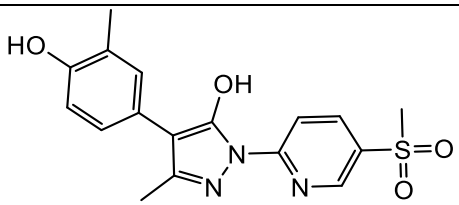
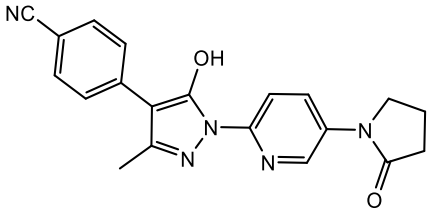
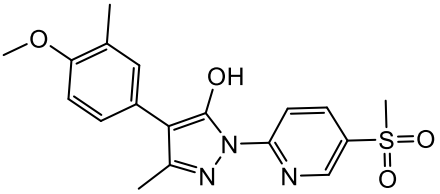
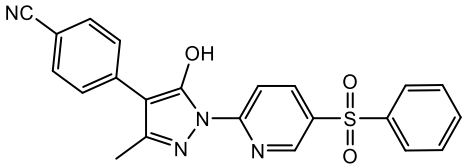
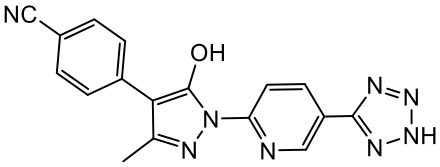
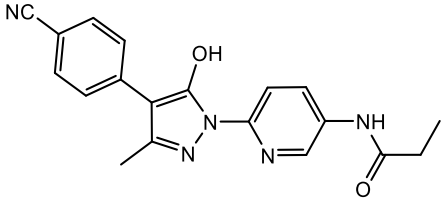
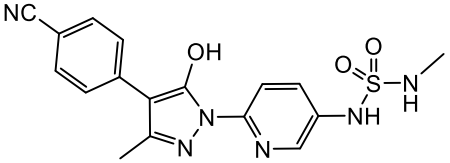
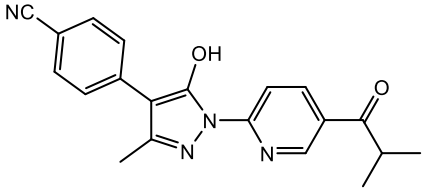
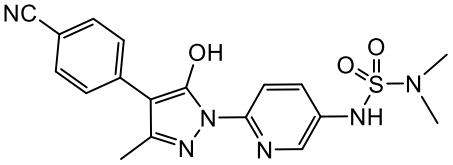
173. The compound of claim 172, wherein R^{12} is CH_3.

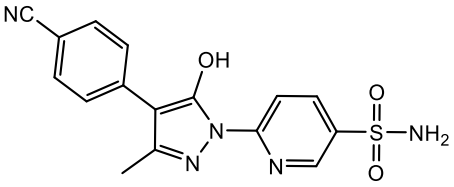
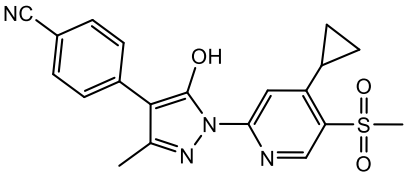
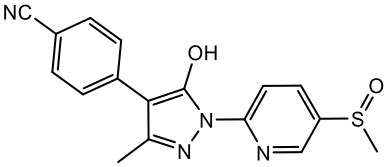
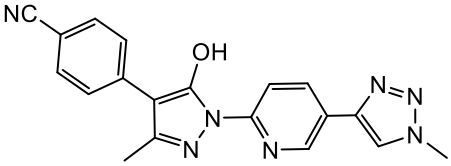
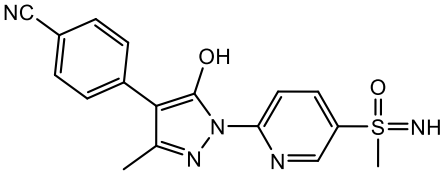
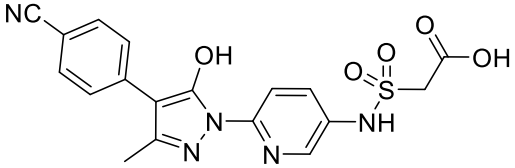
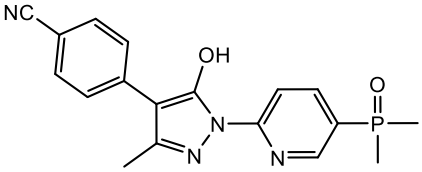
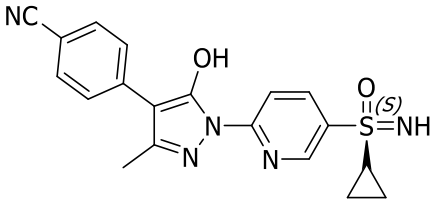
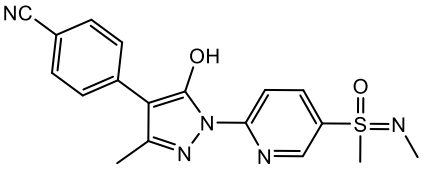
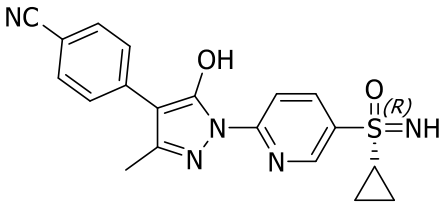
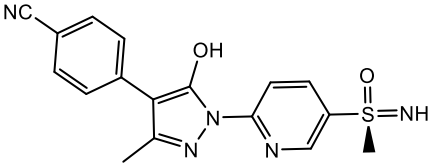
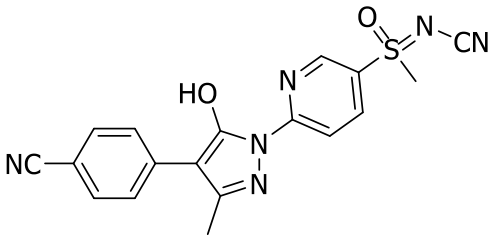
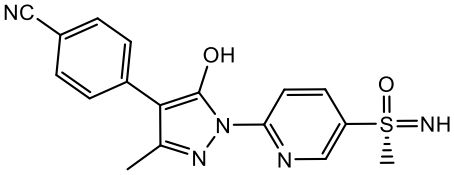
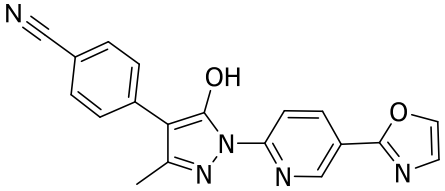
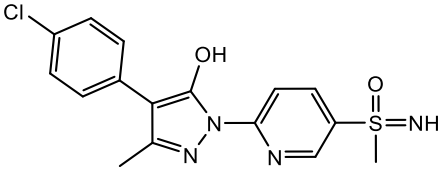
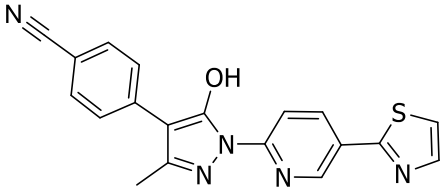
174. The compound of anyone of claims 165-173, wherein R^{13} is C_{1-3} alkyl.

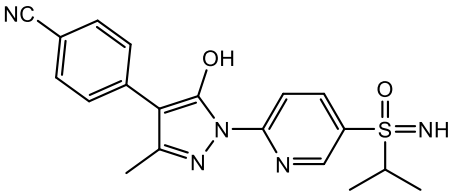
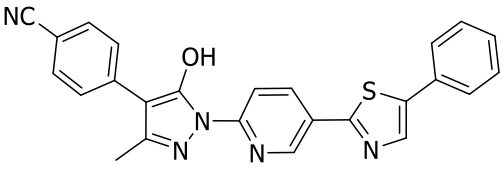
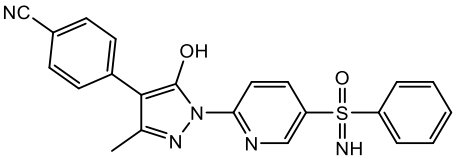
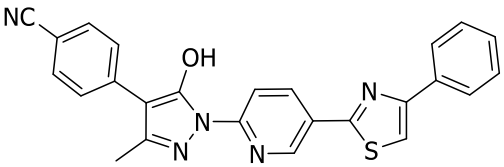
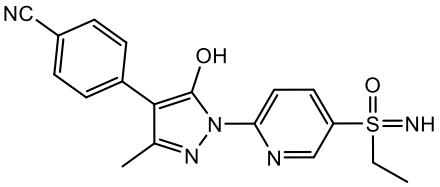
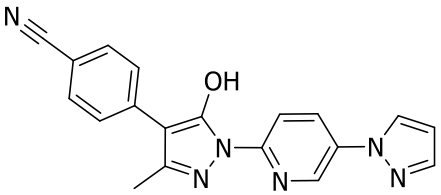
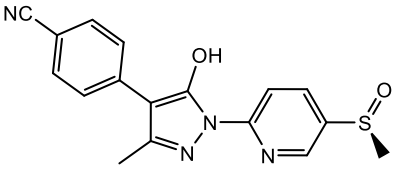
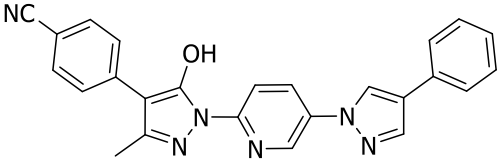
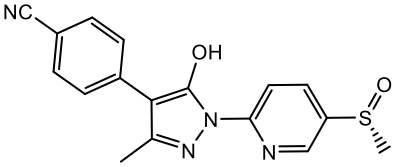
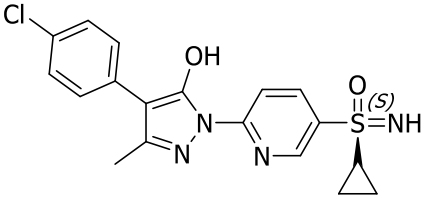
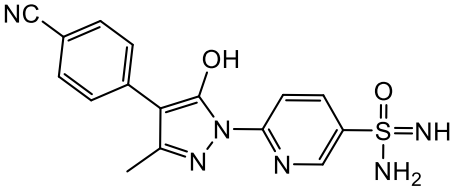
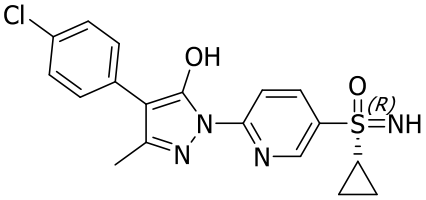
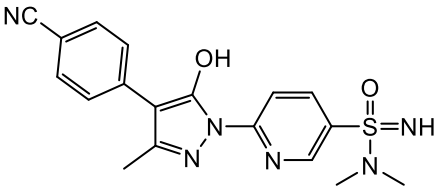
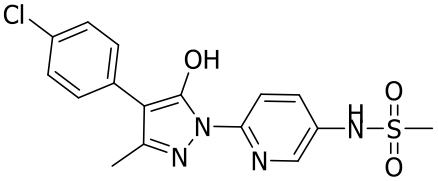
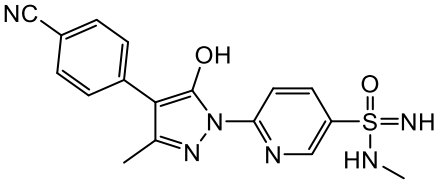
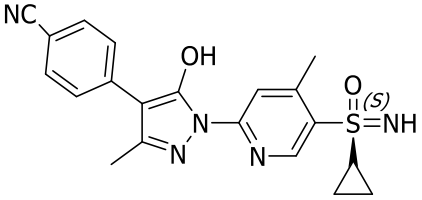
175. The compound of claim 174, wherein R^{13} is CH_3.

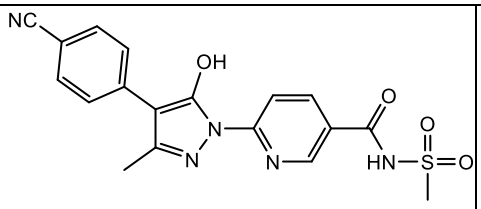
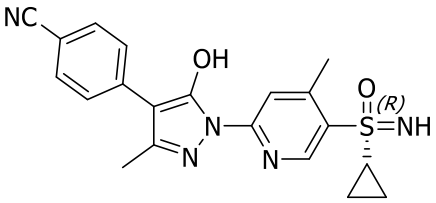
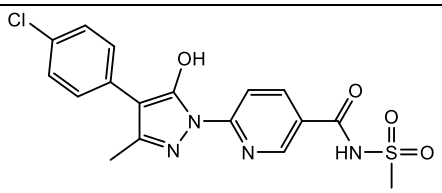
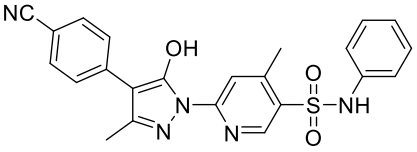
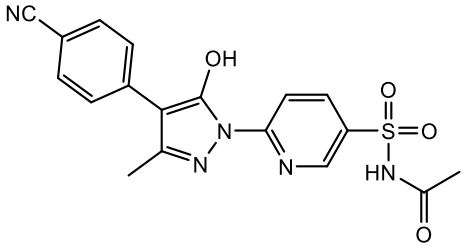
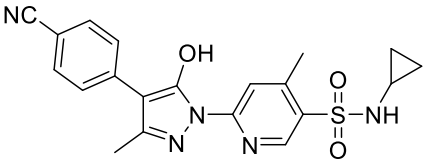
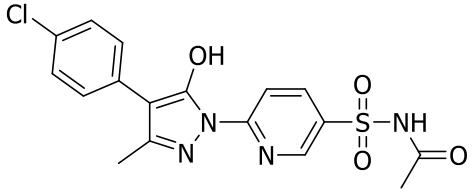
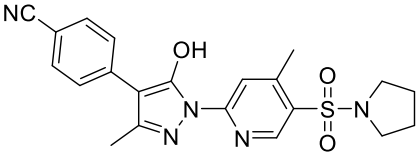
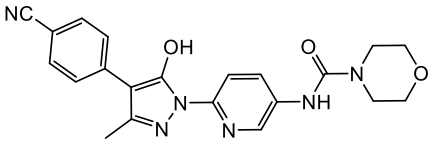
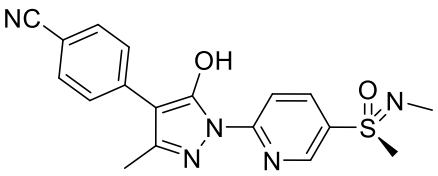
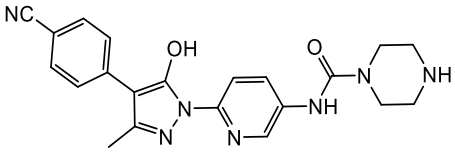
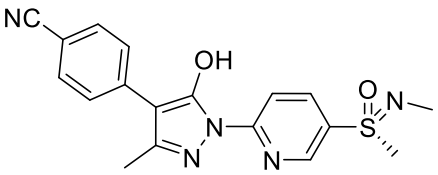
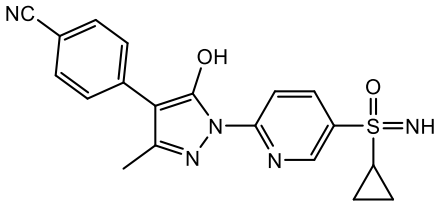
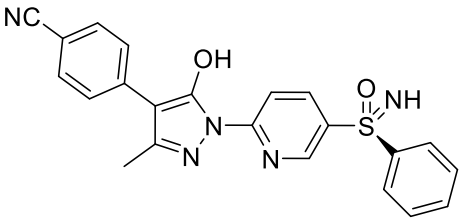
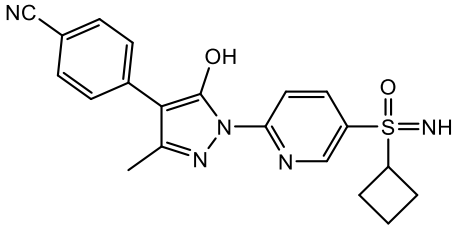
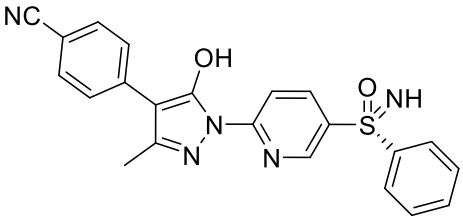
176. The compound of claim 1, wherein the compound is selected from the group consisting of:

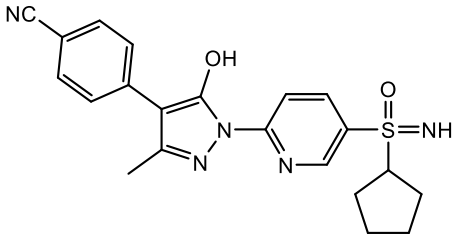
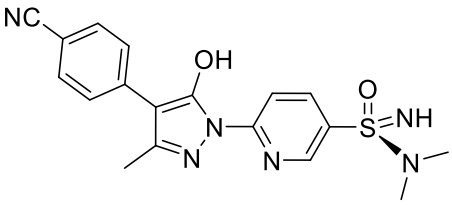
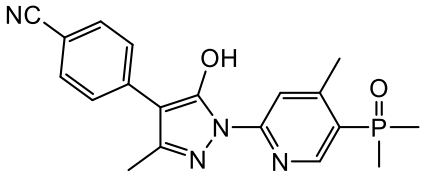
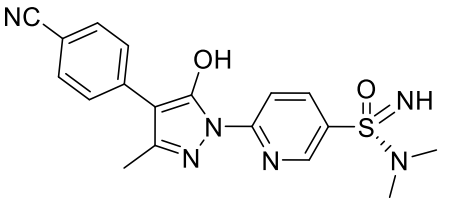
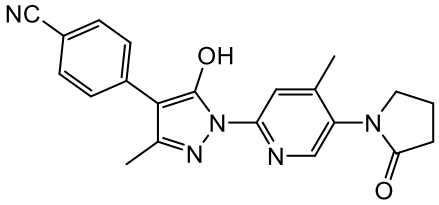
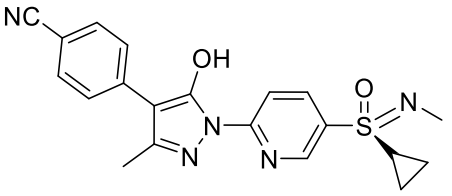
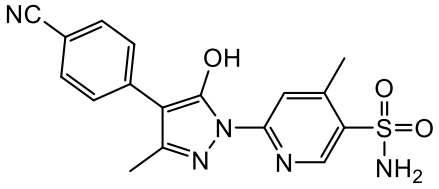
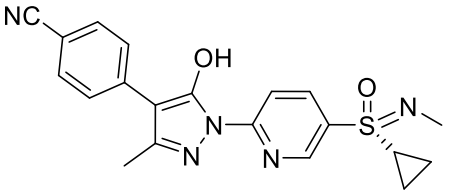
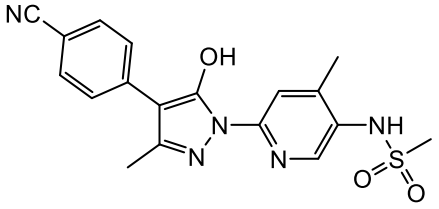
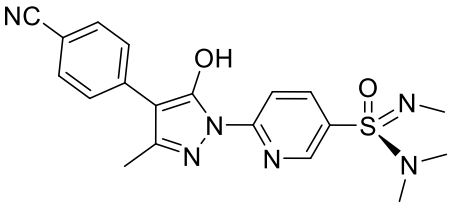
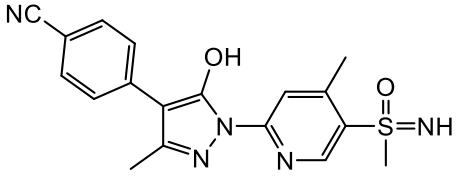
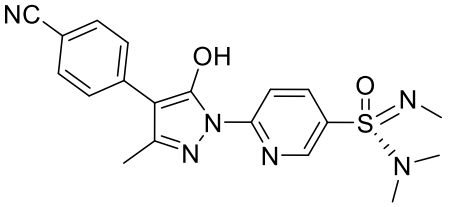
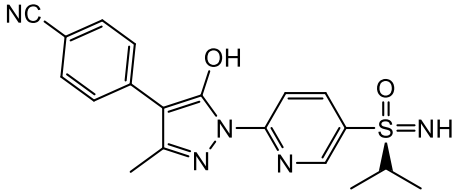
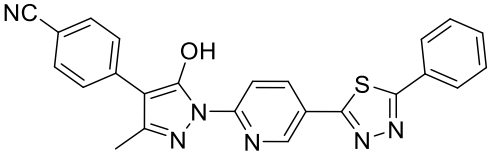
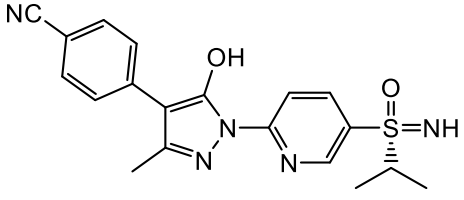
Cmpd No.	Structure	Cmpd No.	Structure
1		43	
2		44	

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~~ Use of a compound of any one of claims 1-177, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a disease mediated by PHD activity in a subject.

180. The use~~method~~ of claim 179, wherein the disease mediated by PHD activity is an ischemic reperfusion injury.

181. The use~~method~~ of claim 180, wherein the ischemic reperfusion injury is selected from stroke, myocardial infarction, and acute kidney injury.

182. The use~~method~~ of claim 179, wherein the disease mediated by PHD activity is inflammatory bowel disease.

183. The use~~method~~ of claim 182, wherein the inflammatory bowel disease is ulcerative colitis.

184. The use~~method~~ of claim 182, wherein the inflammatory bowel disease is Crohn's disease.

185. The use~~method~~ of claim 175, wherein the disease mediated by PHD activity is cancer.

186. The use~~method~~ of claim 181, wherein the cancer is colorectal cancer.

187. The use~~method~~ of claim 179, wherein the disease mediated by PHD activity is liver disease.

188. The use~~method~~ of claim 179, wherein the disease mediated by PHD activity is atherosclerosis.

189. The use~~method~~ of claim 179, wherein the disease mediated by PHD activity is cardiovascular disease.

190. The use~~method~~ of claim 179, wherein the disease mediated by PHD activity is a disease or condition of the eye.

191. The use~~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 use~~method~~ of claim 179, wherein the disease is anemia.

193. The use~~method~~ of claim 192, wherein the anemia is anemia associated with chronic kidney disease.

194. The use~~method~~ of claim 179, wherein the disease is chronic kidney disease.

195. The use~~method~~ of claim 179, wherein the disease is associated with hyperoxia.

196. The use~~method~~ of claim 195, wherein the disease is retinopathy of prematurity.

197. The use~~method~~ of claim 195, wherein the disease is bronchopulmonary dysplasia (BPD).

198. The use~~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.