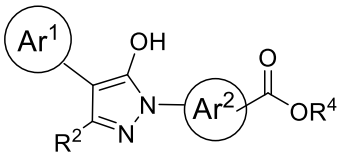
CLAIMS

1. A compound of Formula A:



(A)

or a pharmaceutically acceptable salt thereof, wherein:

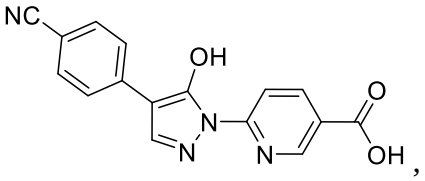
Ar^1 is phenyl or a six-membered nitrogen-containing heteroaryl, wherein said phenyl or heteroaryl is optionally substituted with halogen, CN, OH, C_{1-3} alkyl optionally substituted with one or more halogens, or C_{1-3} alkoxy;

R^2 is H or C_{1-3} alkyl;

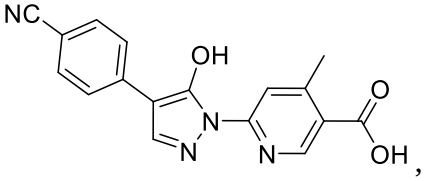
Ar^2 is a six-membered nitrogen-containing heteroaryl, optionally substituted with halogen, OH, amine, or C_{1-3} alkyl;

R^4 is hydrogen or C_{1-4} alkyl; and

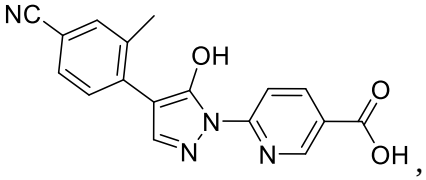
wherein Formula (A) excludes the following compounds:



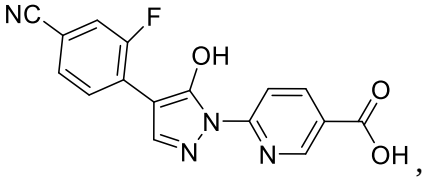
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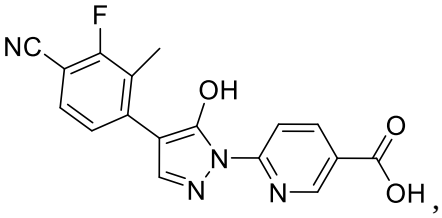
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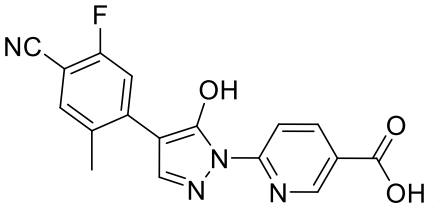
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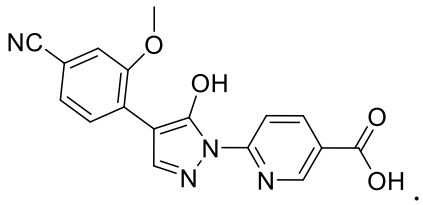
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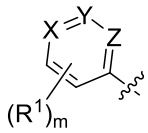
,



, and



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


, wherein

X, Y, and Z are independently CH or N, wherein N is optionally oxidized;

each R^1 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

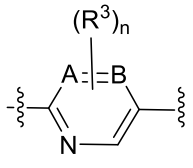
m is 1, 2, 3, or 4.

3. The compound of claim 1 or 2, wherein Ar^1 is a phenyl substituted by at least one R^1 that is CN or halogen.

4. The compound of claim 3, wherein Ar^1 is substituted by one or two R^1 groups independently selected from C_{1-3} alkyl optionally substituted with one or more halogens, halogen, CN or OH.

5. The compound of claim 1 or 2, wherein Ar^1 is a pyridyl N-oxide or is a pyridyl optionally substituted by at least one R^1 that is C_{1-3} alkoxy or halogen.

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


, wherein

A and B are independently CH or N, wherein N is optionally oxidized;

each R^3 is independently selected from the group consisting of hydrogen, halogen, OH, amine, and C_{1-3} alkyl; and

n is 0, 1, or 2.

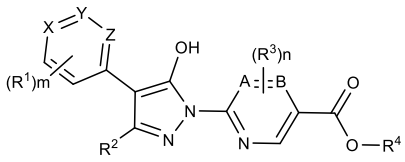
7. The compound of any one of claims 1-6, wherein Ar^2 is a group that is pyridyl or pyrazinyl, and wherein said group is unsubstituted or comprises a substituent that is halogen, C_{1-3} alkyl, or OH.

8. The compound of any one of claims 1-7, wherein R^2 is H or CH_3.

9. The compound of any one of claims 1-8, wherein R^4 is H.

10. The compound of any one of claims 1-8, wherein R^4 is C_{1-4} alkyl.

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



(I)

or a pharmaceutically acceptable salt thereof, wherein:

X, Y, Z, A and B are independently CH or N, wherein N is optionally oxidized;

m is 1, 2, 3, or 4;

n is 0, 1, or 2;

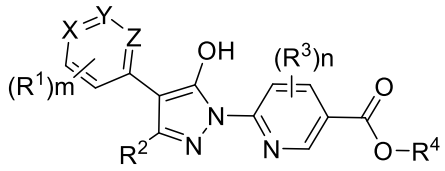
each R^1 is independently selected from the group consisting of hydrogen, halogen, CN, OH, C_{1-3} alkyl optionally substituted with one or more halogens, and C_{1-3} alkoxy;

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

each R^3 is independently selected from the group consisting of hydrogen, halogen, OH, amine, and C_{1-3} alkyl; and

R^4 is hydrogen or C_{1-4} alkyl.

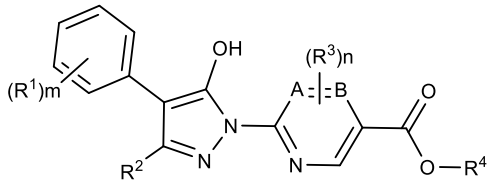
12. The compound of claim 11, having the structure of Formula (Ia):



(Ia)

or a pharmaceutically acceptable salt thereof.

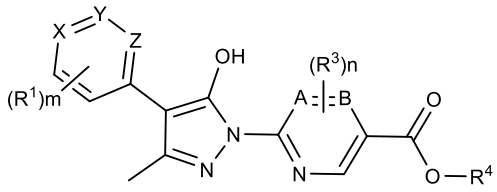
13. The compound of claim 11, having the structure of Formula (Ib):



(Ib)

or a pharmaceutically acceptable salt thereof.

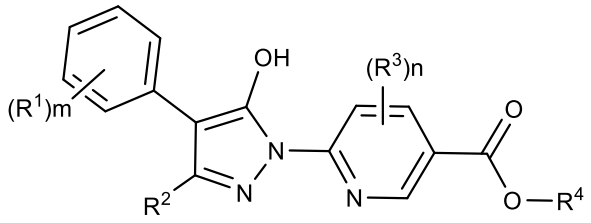
14. The compound of claim 11, having the structure of Formula (Ic):



(Ic)

or a pharmaceutically acceptable salt thereof.

15. The compound of claim 1, having a structure according to Formula (II):



(II)

or a pharmaceutically acceptable salt thereof, wherein:

m is 1, 2, 3, or 4;

n is 0, 1, or 2;

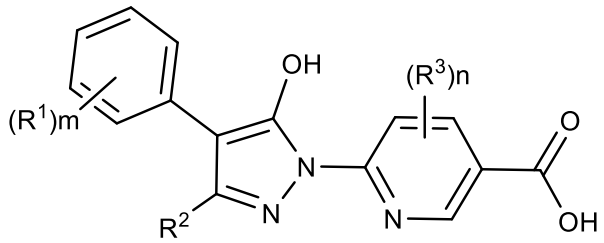
R^1, each time taken, is independently selected from the group consisting of hydrogen, halogen, CN, OH, C_{1-3} alkyl optionally substituted with one or more halogens, and C_{1-3} alkoxy;

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

R^3, each time taken, is independently selected from the group consisting of hydrogen, halogen, OH, amine, or C_{1-3} alkyl; and

R^4 is hydrogen or C_{1-4} alkyl.

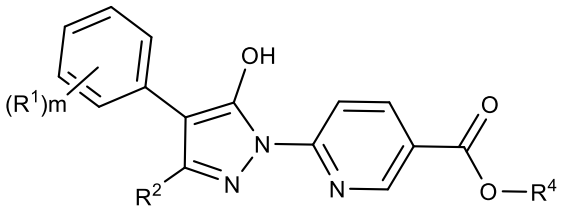
16. The compound of claim 15, having the structure of Formula (IIa):



(IIa)

or a pharmaceutically acceptable salt thereof

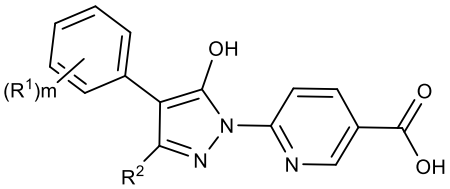
17. The compound of claim 15, having the structure of Formula (IIb):



(IIb)

or a pharmaceutically acceptable salt thereof.

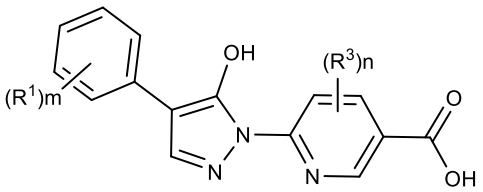
18. The compound of claim 15, having the structure of Formula (IIc):



(IIc)

or a pharmaceutically acceptable salt thereof.

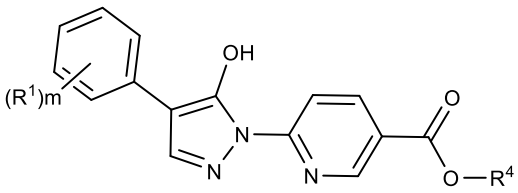
19. The compound of claim 15, having the structure of Formula (IId):



(IId)

or a pharmaceutically acceptable salt thereof.

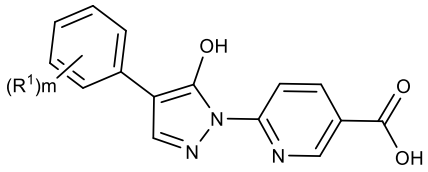
20. The compound of claim 15, having the structure of Formula (IIe):



(IIe)

or a pharmaceutically acceptable salt thereof.

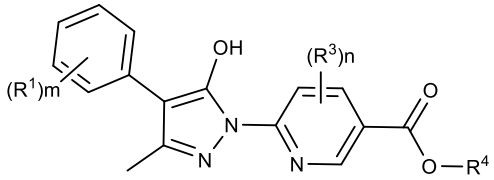
21. The compound of claim 15, having the structure of Formula (IIf):



(IIf)

or a pharmaceutically acceptable salt thereof.

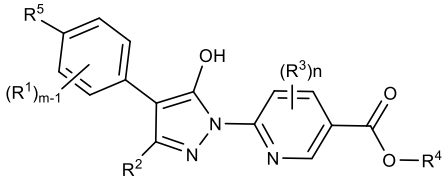
22. The compound of claim 15, having the structure of Formula (IIg):



(IIg)

or a pharmaceutically acceptable salt thereof.

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



(III)

or a pharmaceutically acceptable salt thereof, wherein:

m is 1, 2, 3, or 4;

n is 0, 1, or 2;

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

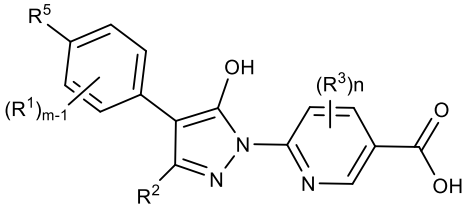
R^2 is hydrogen or C_{1-3} alkyl;

R^3, each time taken, is independently selected from the group consisting of hydrogen, halogen, OH, amine, and C_{1-3} alkyl;

R^4 is hydrogen or C_{1-4} alkyl;

R^5 is CN or halogen.

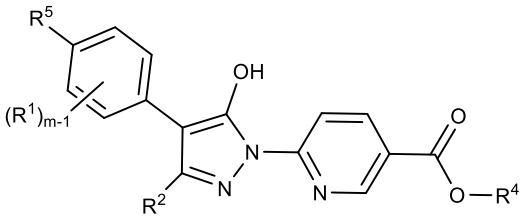
24. The compound of claim 23, having the structure of Formula (IIIa):



(IIIa)

or a pharmaceutically acceptable salt thereof.

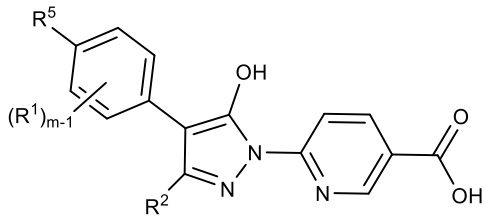
25. The compound of claim 23, having the structure of Formula (IIIb):



(IIIb)

or a pharmaceutically acceptable salt thereof.

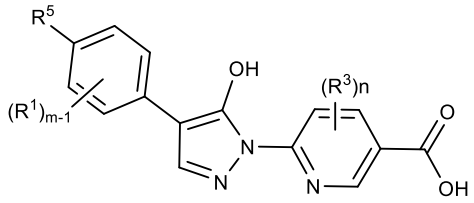
26. The compound of claim 23, having the structure of Formula (IIIc):



(IIIc)

or a pharmaceutically acceptable salt thereof.

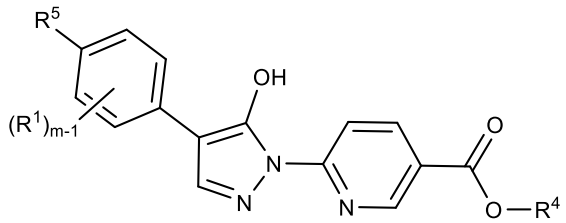
27. The compound of claim 23, having the structure of Formula (IIId)



(IIId)

or a pharmaceutically acceptable salt thereof.

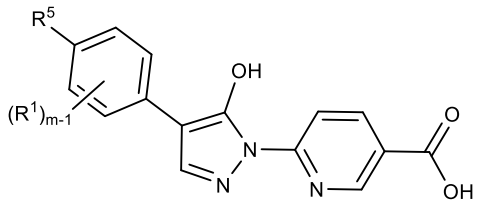
28. The compound of claim 23, having the structure of Formula (IIIe):



(IIIe)

or a pharmaceutically acceptable salt thereof.

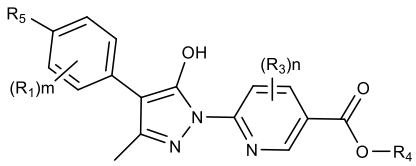
29. The compound of claim 23, having the structure of Formula (IIIf):



(IIIf)

or a pharmaceutically acceptable salt thereof.

30. The compound of claim 23, having the structure of Formula III(g):



III(g)

or a pharmaceutically acceptable salt thereof.

31. The compound of claim 11, 12, or 14, wherein X is CH.

32. The compound of claim 11, 12, or 14, wherein X is N.

33. The compound of claim 32, wherein N is optionally oxidized.

34. The compound of claim 11, 12, or 14, wherein Y is CH.

35. The compound of claim 11, 12, or 14, wherein Y is N.

36. The compound of claim 11, 12, or 14, wherein Z is CH.

37. The compound of claim 11, 12, or 14, wherein Z is N.

38. The compound of claim 11, 12, or 14, wherein A is CH.

39. The compound of claim 11, 12, or 14, wherein A is N.

40. The compound of claim 11, 12, or 14, wherein B is CH.

41. The compound of claim 11, 12, or 14, wherein B is N.

42. The compound of any one of claims 11-30, wherein m is 1.

43. The compound of any one of claims 11-30, wherein m is 2.

44. The compound of any one of claims 11-30, wherein m is 3.

45. The compound of any one of claims 11-22, wherein m is 4.

46. The compound of any one of claims 11-16, 19, 22-24, 27 and 30, wherein n is 0.

47. The compound of any one of claims 11-16, 19, 22-24, 27 and 30, wherein n is 1.

48. The compound of any one of claims 11-16, 19, 22-24, 27 and 30, wherein n is 2.

49. The compound of any one of claims 11-30, wherein R^1 is hydrogen.

50. The compound of any one of claims 11-30, wherein R^1 is halogen.

51. The compound of claim 50, wherein R^1 is F.

52. The compound of claim 50, wherein R^1 is Cl.

53. The compound of claim 50, wherein R^1 is Br.

54. The compound of any one of claims 11-30, wherein R^1 is CN.

55. The compound of any one of claims 11-30, wherein R^1 is OH.

56. The compound of any one of claims 11-30, wherein R^1 is C_{1-3} alkyl optionally substituted with one or more halogens.

57. The compound of claim 56, wherein R^1 is C_{1-3} alkyl.

58. The compound of claim 56, wherein R^1 is methyl.

59. The compound of claim 56 wherein R^1 is ethyl.

60. The compound of claim 56, wherein R^1 is CF_3.

61. The compound of any one of claims 11-30, wherein R^1 is C_{1-3} alkoxy.

62. The compound of claim 61, wherein R^1 is methoxy.

63. The compound of any one of claims 11-18 and 23-26, wherein R^2 is hydrogen.

64. The compound of any one of claims 11-18 and 23-26, wherein R^2 is C_{1-3} alkyl.

65. The compound of claim 64, wherein R^2 is methyl.

66. The compound of any one of claims 11-16, 19, 22-24, 27 and 30, wherein R^3 is hydrogen.

67. The compound of any one of claims 11-16, 19, 22-24, 27 and 30, wherein R^3 is halogen.

68. The compound of claim 56, wherein R^3 is F.

69. The compound of any one of claims 11-16, 19, 22-24, 27 and 30, wherein R^3 is OH.

70. The compound of any one of claims 11-16, 19, 22-24, 27 and 30, wherein R^3 is amine.

71. The compound of claim 70, wherein R^3 is NH_2.

72. The compound of any one of claims 11-16, 19, 22-24, 27 and 30, wherein R^3 is C_{1-3} alkyl.

73. The compound of claim 72, wherein R^3 is methyl.

74. The compound of any one of claims 11-15, 17, 20, 22, 25, 28, and 30, wherein R^4 is hydrogen.

75. The compound of any one of claims 11-15, 17, 20, 22, 25, and 30, wherein R^4 is C_{1-4} alkyl.

76. The compound of claim 75, wherein R^4 is methyl.

77. The compound of claim 75, wherein R^4 is ethyl.

78. The compound of claim 75, wherein R^4 is isopropyl.

79. The compound of claim 75, wherein R^4 is *tert*-butyl.

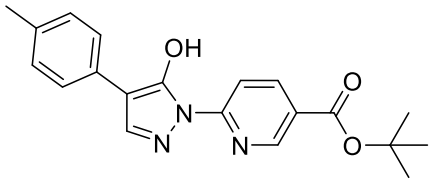
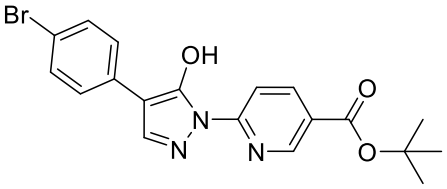
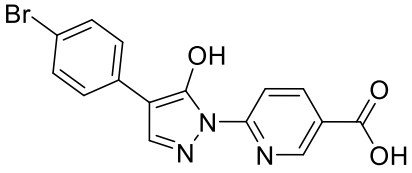
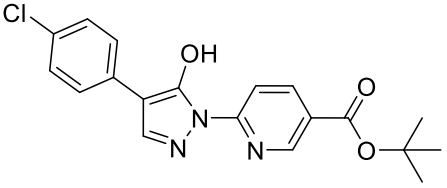
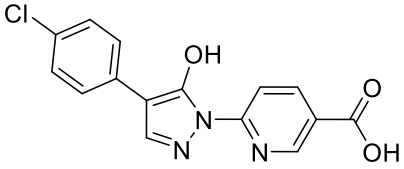
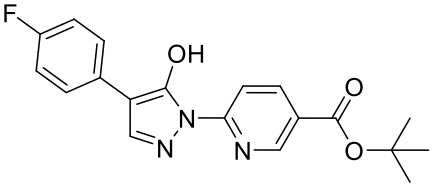
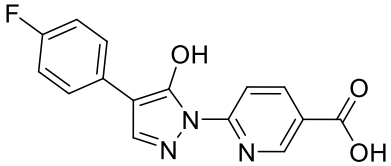
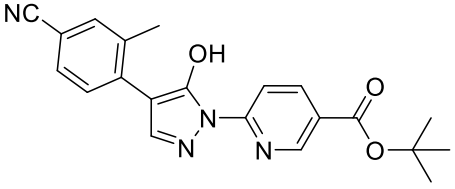
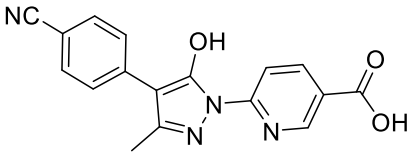
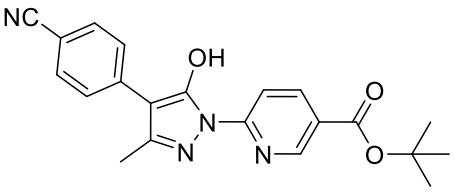
80. The compound of any one of claims 23-30, wherein R^5 is F.

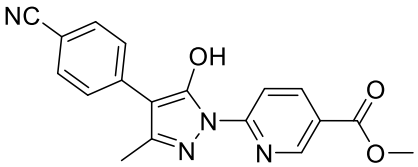
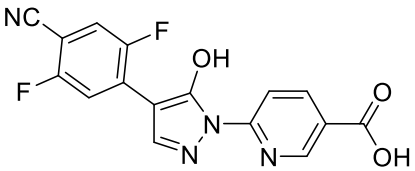
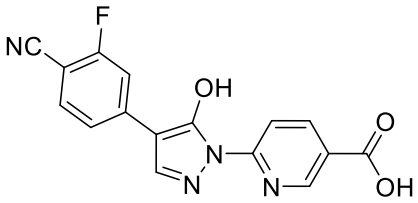
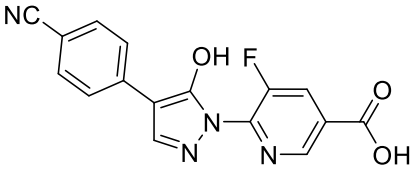
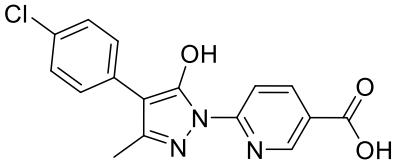
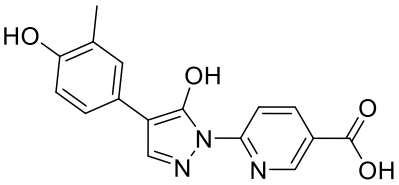
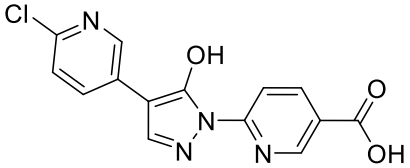
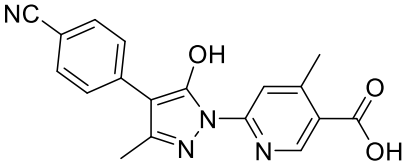
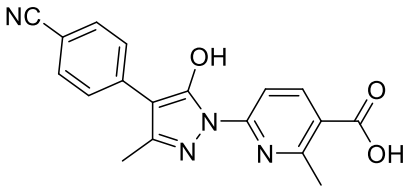
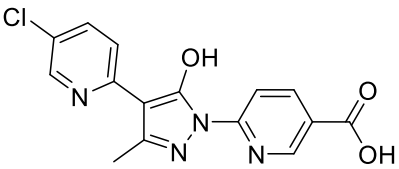
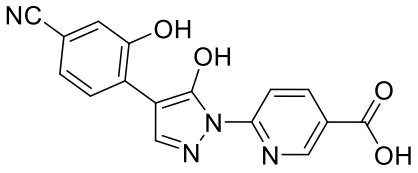
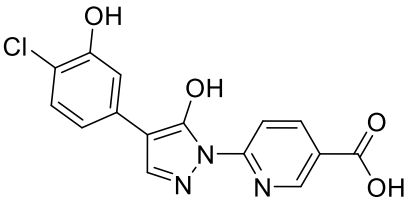
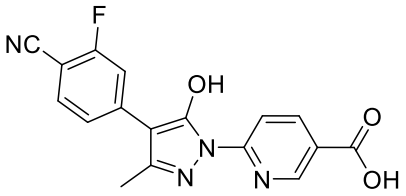
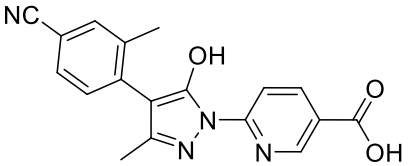
81. The compound of any one of claims 23-30, wherein R^5 is Cl.

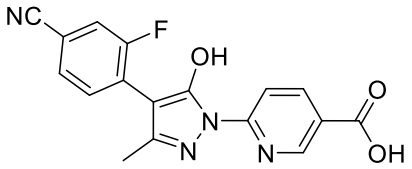
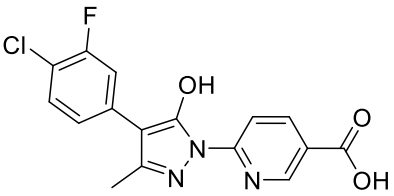
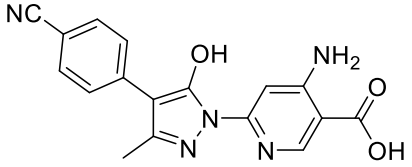
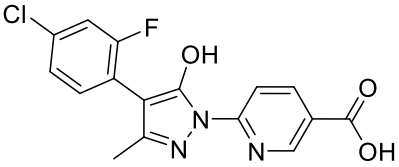
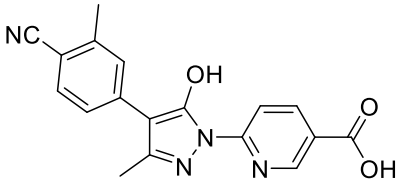
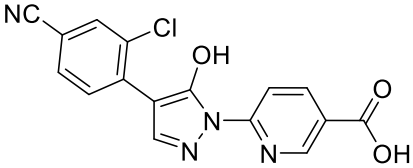
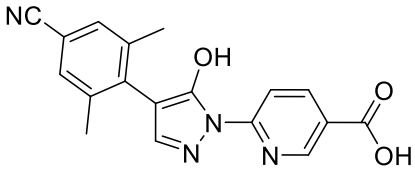
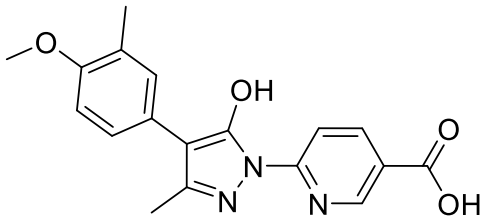
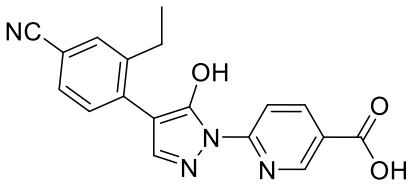
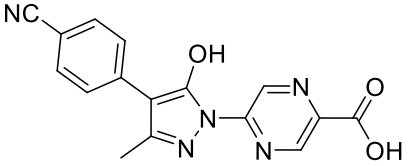
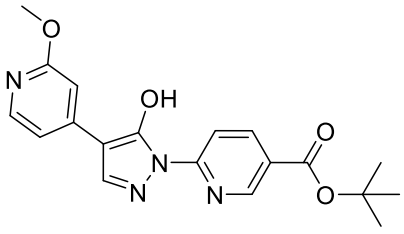
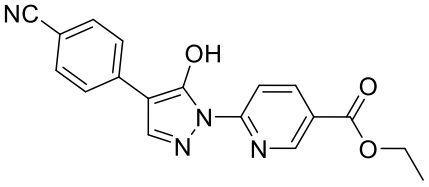
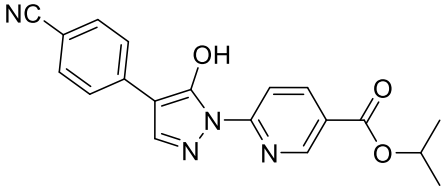
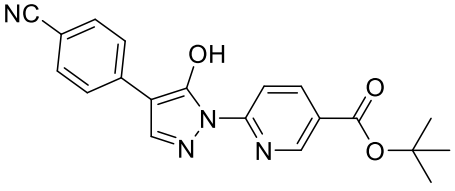
82. The compound of any one of claims 23-30, wherein R^5 is Br.

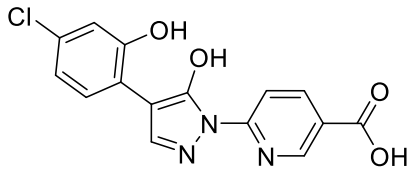
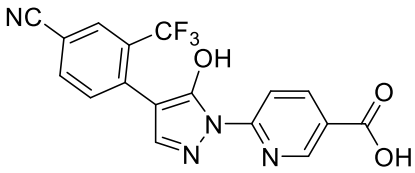
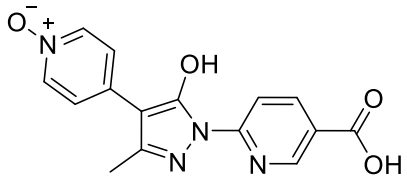
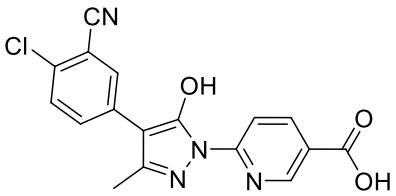
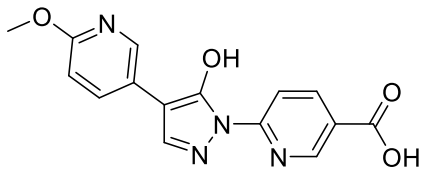
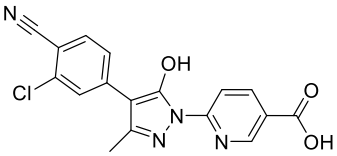
83. The compound of any one of claims 23-30, wherein R^5 is CN.

84. The compound of claim 1, which is selected from the group consisting of:

Compd. No.	Structure	Cmpd. No.	Structure
1		2	
3		4	
5		6	
7		8	
9		10	

11		12	
13		14	
15		16	
17		18	
19		20	
21		22	
23		24	

25		26	
27		28	
29		30	
31		32	
33		34	
35		36	
37		38	

39		40	
41		42	
43		44	

or a pharmaceutically acceptable salt thereof

85. The compound of any one of claims 1-84, or a pharmaceutically acceptable salt thereof wherein at least one hydrogen atom is replaced with a deuterium atom.

86. A pharmaceutical composition comprising the compound of any one of claims 1-85, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

87. Use of a compound of any one of claims 1-85 in the manufacture of a medicament for treating a disease mediated by PHD activity in a subject.

88. The use of claim 87, wherein the disease mediated by PHD activity is an ischemic reperfusion injury.

89. The use of claim 88, wherein the ischemic reperfusion injury is selected from stroke, myocardial infarction, and acute kidney injury.

90. The use of claim 87, wherein the disease mediated by PHD activity is inflammatory bowel disease.

91. The use of claim 90, wherein the inflammatory bowel disease is ulcerative colitis.

92. The use of claim 90, wherein the inflammatory bowel disease is Crohn’s disease.

93. The use of claim 87, wherein the disease mediated by PHD activity is cancer.

94. The use of claim 93, wherein the cancer is colorectal cancer.

95. The use of claim 87, wherein the disease mediated by PHD activity is liver disease.

96. The use of claim 87, wherein the disease mediated by PHD activity is atherosclerosis.

97. The use of claim 87, wherein the disease mediated by PHD activity is cardiovascular disease.

98. The use of claim 87, wherein the disease mediated by PHD activity is a disease or condition of the eye.

99. The use of claim 98, 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.

100. The use of claim 87, wherein the disease is anemia.

101. The use of claim 100, wherein the anemia is anemia associated with chronic kidney disease.

102. The use of claim 87, wherein the disease is chronic kidney disease.

103. The use of claim 87, wherein the disease is associated with hyperoxia.

104. The use of claim 103, wherein the disease is retinopathy of prematurity.

105. The use of claim 103, wherein the disease is bronchopulmonary dysplasia (BPD).

106. The use of claim 87, 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.