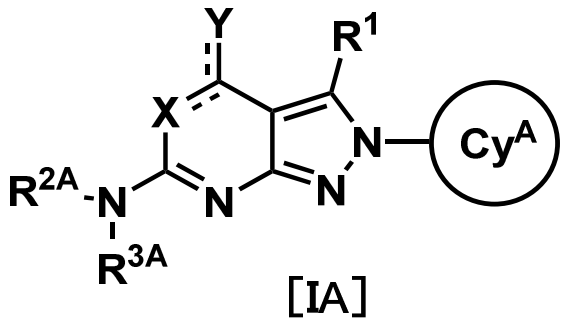
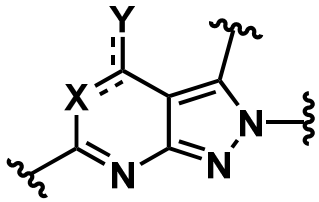
CLAIMS

1. A compound of Formula [IA]:

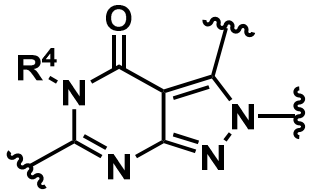


[IA] ,

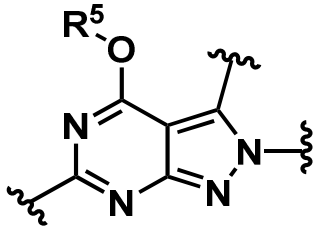
or a pharmaceutically acceptable salt thereof,
wherein a partial structure of the following formula:



is
(1) a structure of the following formula:



wherein R^4 is hydrogen or C_{1-4} alkyl, in which the alkyl group may be optionally substituted with hydroxy or cyano, or
(2) a structure of the following formula:



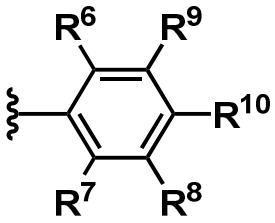
wherein R^5 is C_{1-6} alkyl, in which the alkyl group may be optionally substituted with:

(a) hydroxy,
(b) cyano,
(c) C_{1-4} alkoxy, or

(d) C_{3-6} cycloalkyl, or C_{1-4} haloalkyl;

Ring group Cy^A is

(1) a group of the following formula:



wherein R^6 and R^7 are, each independently,

(a) hydrogen,

(b) hydroxy,

(c) cyano,

(d) C_{1-6} alkyl, in which the alkyl group may be optionally substituted with one or two substituents independently selected from the group consisting of:

(1) hydroxy,

(2) C_{1-4} alkoxy, and

(3) C_{3-6} cycloalkyl,

(e) C_{1-6} alkoxy, in which the alkoxy group may be optionally substituted with C_{3-6} cycloalkyl,

(f) halogen,

(g) C_{1-4} haloalkyl,

(h) –CHO,

(i) $-O-C_{1-4}$ haloalkyl,

(j) $-O-C_{3-6}$ cycloalkyl,

(k) $-CO-C_{1-4}$ alkyl,

(m) $-CO-C_{3-6}$ cycloalkyl,

(n) $-NR^{11}R^{12}$, in which R^{11} and R^{12} are, each independently, hydrogen or 2,4-dimethoxybenzyl, or alternatively, R^{11} and R^{12} may combine together with the nitrogen atom to which they attach and the $-NR^{11}R^{12}$ group may form 5- to 6-membered heterocycloalkyl comprising one or two heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, or

(o) C_{3-6} cycloalkyl;

R^8 and R^9 are, each independently,

(a) hydrogen,

(b) C_{1-4} alkyl, or

(c) C_{1-4} haloalkyl;

R^{10} is

(a) hydrogen,

(b) cyano,

(c) C_{1-6} alkyl,

(d) C_{2-6} alkenyl,

(e) C_{2-5} alkynyl,

(f) C_{1-4} alkoxy,

(g) halogen,

(h) C_{1-6} haloalkyl,

(i) C_{2-6} haloalkenyl,

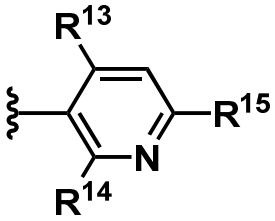
(j) $-O-C_{1-4}$ haloalkyl,

(k) C_{3-6} cycloalkyl, in which the cycloalkyl group may be optionally substituted with C_{1-4} haloalkyl,

(m) C_{5-6} cycloalkenyl, or

(n) 4- to 6-membered heterocycloalkyl comprising one or two heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms;

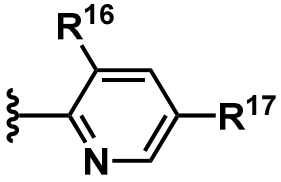
(2) a group of the following formula:



wherein R^{13} and R^{14} are, each independently, hydrogen or C_{1-4} alkyl, and

R^{15} is C_{1-4} haloalkyl or C_{3-6} cycloalkyl;

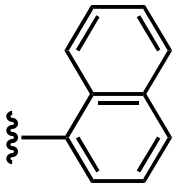
(3) a group of the following formula:



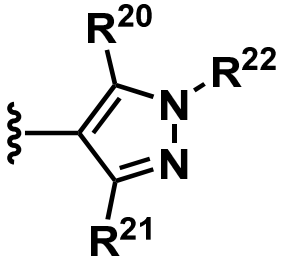
wherein R^{16} is C_{1-6} alkyl or halogen, and

R^{17} is halogen or C_{1-4} haloalkyl;

(4) a group of the following formula:


; or

(5) a group of the following formula:



wherein R^{20} and R^{21} are, each independently, C_{1-4} alkyl or C_{1-4} haloalkyl, and

R^{22} is C_{1-6} alkyl or C_{3-6} cycloalkyl;

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

R^{2A} and R^{3A} are, each independently,

(1) hydrogen,

(2) C_{1-6} alkyl, in which the alkyl group may be optionally substituted with

(a) hydroxy,

(b) C_{1-4} alkoxy, in which the alkoxy group may be optionally substituted with hydroxy,

(c) C_{3-6} cycloalkyl, or

(d) phenyl, in which the phenyl group may be optionally substituted with C_{1-4} alkoxy,

(3) C_{1-4} alkoxy,

(4) C_{1-4} haloalkyl,

(5) $-CD_3$,

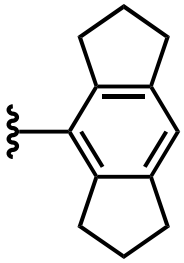
(6) $-CO-C_{1-4}$ alkyl,

(7) C_{3-6} cycloalkyl,

(8) 4- to 6-membered heterocycloalkyl comprising one or two heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, in which the heterocycloalkyl group may be optionally substituted with C_{1-4} alkyl,

(9) phenyl, or

(10) a group of the following formula:

, or

alternatively, R^{2A} and R^{3A} may combine together with the nitrogen atom to which they attach and the $-NR^{2A}R^{3A}$ group may form:

(a) 4- to 7-membered heterocycloalkyl comprising one to three heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur atoms, in which the heterocycloalkyl group may be optionally substituted with one to four substituents independently selected from the group consisting of:

(1) hydroxy,

(2) cyano,

(3) C_{1-6} alkyl, in which the alkyl group may be optionally substituted with

(a) hydroxy,

(b) C_{1-4} alkoxy, or

(c) phenyl,

(4) C_{1-4} alkoxy,

(5) halogen,

(6) C_{1-4} haloalkyl,

(7) $-O-C_{1-4}$ haloalkyl,

(8) $-CO-C_{1-4}$ alkyl, in which the alkyl group may be optionally substituted with C_{1-4} alkoxy,

(9) $-CO-C_{1-6}$ alkoxy,

(10) $-CO-C_{3-6}$ cycloalkyl,

(11) $-CONH-C_{1-4}$ alkyl,

(12) $-NHCO-C_{1-4}$ alkyl,

(13) $-NR^{18}R^{19}$, in which R^{18} and R^{19} are, each independently, C_{1-4} alkyl,

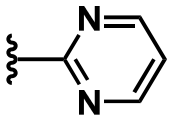
(14) $-SO_2-C_{1-4}$ alkyl,

(15) $-SO_2-C_{3-6}$ cycloalkyl,

(16) C_{3-6} cycloalkyl,

(17) phenyl,

(18) a group of the following formula:



, and

(19) oxo,

(b) 7- to 9-membered spiro heterocycloalkyl comprising one to three heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, in which the spiro heterocycloalkyl group may be optionally substituted with hydroxy,

(c) 6- to 9-membered saturated or partially unsaturated fused ring group comprising one or two heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, in which the fused ring group may be optionally substituted with one or two substituents independently selected from the group consisting of:

(1) halogen,

(2) $-CO-C_{1-4}$ alkyl, and

(3) $-CO-C_{1-6}$ alkoxy,

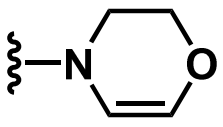
(d) 6- to 8-membered bridged heterocycloalkyl comprising one or two heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, in which the bridged heterocycloalkyl group may be optionally substituted with one or two substituents independently selected from the group consisting of:

(1) halogen,

(2) $-CO-C_{1-4}$ alkyl, in which the alkyl group may be optionally substituted with C_{1-4} alkoxy, and

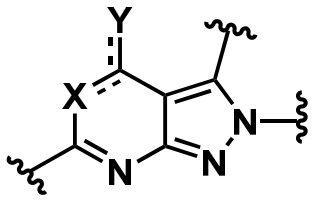
(3) $-SO_2-C_{1-4}$ alkyl, or

(e) a group of the following formula:

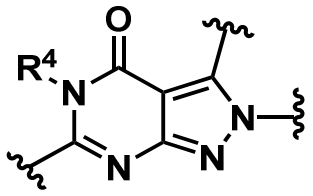


.

2. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein the partial structure of the following formula:



is (1) a structure of the following formula:

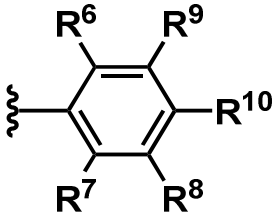


wherein R^4 has the same meaning as defined in claim 1.

3. The compound according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^1 is hydrogen.

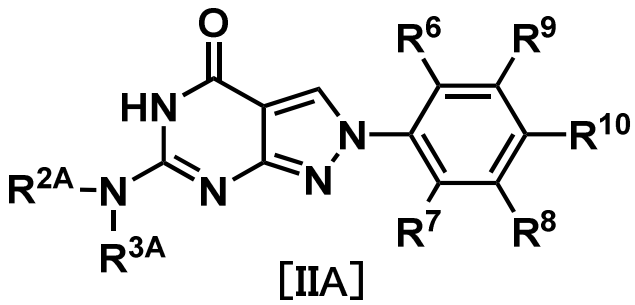
4. The compound according to any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen.

5. The compound according to any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Ring group Cy^A is (1) a group of the following formula:



wherein each symbol has the same meaning as defined in claim 1.

6. The compound according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, having a structure of the following formula [IIA]:

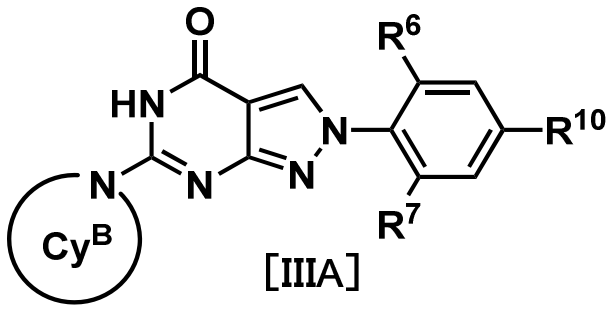


[IIA]

wherein each symbol has the same meaning as defined in claim 1.

7. The compound according to any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R^8 and R^9 are hydrogen.

8. The compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, having a structure of the following formula [IIIA]:



[IIIA]

wherein R^6, R^7, and R^{10} have the same meanings as defined in claim 1, and

Ring group Cy^B is

(1) 4- to 7-membered heterocycloalkyl comprising one to three heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur atoms, in which the heterocycloalkyl group may be optionally substituted with one to four substituents independently selected from the group consisting of:

(a) hydroxy,

(b) cyano,

(c) C_{1-6} alkyl, in which the alkyl group may be optionally substituted with

(1) hydroxy,

(2) C_{1-4} alkoxy, or

(3) phenyl,

(d) C_{1-4} alkoxy,

(e) halogen,

(f) C_{1-4} haloalkyl,

(g) $-O-C_{1-4}$ haloalkyl,

(h) $-CO-C_{1-4}$ alkyl, in which the alkyl group may be optionally substituted with C_{1-4} alkoxy,

(i) $-CO-C_{1-6}$ alkoxy,

(j) $-CO-C_{3-6}$ cycloalkyl,

(k) $-CONH-C_{1-4}$ alkyl,

(m) $-NHCO-C_{1-4}$ alkyl,

(n) $-NR^{18}R^{19}$, in which R^{18} and R^{19} are, each independently, C_{1-4} alkyl,

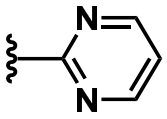
(o) $-SO_2-C_{1-4}$ alkyl,

(p) $-SO_2-C_{3-6}$ cycloalkyl,

(q) C_{3-6} cycloalkyl,

(r) phenyl,

(s) a group of the following formula:



, and

(t) oxo,

(2) 7- to 9-membered spiro heterocycloalkyl comprising one to three heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, in which the spiro heterocycloalkyl group may be optionally substituted with hydroxy,

(3) 6- to 9-membered saturated or partially unsaturated fused ring group comprising one or two heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, in which the fused ring group may be optionally substituted with one or two substituents independently selected from the group consisting of:

(a) halogen,

(b) $-CO-C_{1-4}$ alkyl, and

(c) $-CO-C_{1-6}$ alkoxy,

(4) 6- to 8-membered bridged heterocycloalkyl comprising one

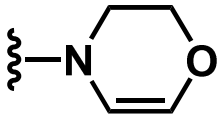
or two heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, in which the bridged heterocycloalkyl group may be optionally substituted with one or two substituents independently selected from the group consisting of:

(a) halogen,

(b) $-CO-C_{1-4}$ alkyl, in which the alkyl group may be optionally substituted with C_{1-4} alkoxy, and

(c) $-SO_2-C_{1-4}$ alkyl, or

(5) a group of the following formula:



.

9. The compound according to claim 8, or a pharmaceutically acceptable salt thereof, wherein Ring group Cy^B is

(1) 4- to 7-membered heterocycloalkyl comprising one to three heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur atoms, in which the heterocycloalkyl group may be optionally substituted with one to four substituents independently selected from the group consisting of:

(a) hydroxy,

(b) cyano,

(c) C_{1-6} alkyl, in which the alkyl group may be optionally substituted with

(1) hydroxy,

(2) C_{1-4} alkoxy, or

(3) phenyl,

(d) C_{1-4} alkoxy,

(e) halogen,

(f) C_{1-4} haloalkyl,

(g) $-O-C_{1-4}$ haloalkyl,

(h) $-CO-C_{1-4}$ alkyl, in which the alkyl group may be optionally substituted with C_{1-4} alkoxy,

(i) $-CO-C_{1-6}$ alkoxy,

(j) $-CO-C_{3-6}$ cycloalkyl,

(k) $-CONH-C_{1-4}$ alkyl,

(m) $-NHCO-C_{1-4}$ alkyl,

(n) $-NR^{18}R^{19}$, in which R^{18} and R^{19} are, each independently, C_{1-4} alkyl,

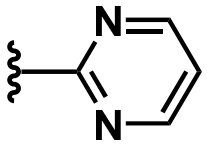
(o) $-SO_2-C_{1-4}$ alkyl,

(p) $-SO_2-C_{3-6}$ cycloalkyl,

(q) C_{3-6} cycloalkyl,

(r) phenyl,

(s) a group of the following formula:



, and

(t) oxo, or

(2) 6- to 8-membered bridged heterocycloalkyl comprising one or two heteroatoms independently selected from the group consisting of nitrogen and oxygen atoms, in which the bridged heterocycloalkyl group may be optionally substituted with one or two substituents independently selected from the group consisting of:

(a) halogen,

(b) $-CO-C_{1-4}$ alkyl, in which the alkyl group may be optionally substituted with C_{1-4} alkoxy, and

(c) $-SO_2-C_{1-4}$ alkyl.

10. The compound according to claim 9, or a pharmaceutically acceptable salt thereof, wherein Ring group Cy^B is 4- to 7-membered heterocycloalkyl comprising one to three heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur atoms, in which the heterocycloalkyl group may be optionally substituted with one to four substituents independently selected from the group consisting of:

(1) hydroxy,

(2) cyano,

(3) C_{1-6} alkyl, in which the alkyl group may be optionally substituted with

(a) hydroxy,

(b) C_{1-4} alkoxy, or

(c) phenyl,

(4) C_{1-4} alkoxy,

(5) halogen,

(6) C_{1-4} haloalkyl,

(7) $-O-C_{1-4}$ haloalkyl,

(8) $-CO-C_{1-4}$ alkyl, in which the alkyl group may be optionally substituted with C_{1-4} alkoxy,

(9) $-CO-C_{1-6}$ alkoxy,

(10) $-CO-C_{3-6}$ cycloalkyl,

(11) $-CONH-C_{1-4}$ alkyl,

(12) $-NHCO-C_{1-4}$ alkyl,

(13) $-NR^{18}R^{19}$, in which R^{18} and R^{19} are, each independently, independently, C_{1-4} alkyl,

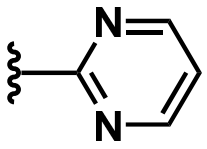
(14) $-SO_2-C_{1-4}$ alkyl,

(15) $-SO_2-C_{3-6}$ cycloalkyl,

(16) C_{3-6} cycloalkyl,

(17) phenyl,

(18) a group of the following formula:



, and

(19) oxo.

11. The compound according to claim 10, or a pharmaceutically acceptable salt thereof, wherein Ring group Cy^B is 4- to 7-membered heterocycloalkyl comprising one to three heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur atoms, in which the heterocycloalkyl group may be optionally substituted with one to four substituents independently selected from the group consisting of:

(1) cyano,

(2) C_{1-6} alkyl, in which the alkyl group may be optionally substituted with hydroxy or C_{1-4} alkoxy,

(3) C_{1-4} alkoxy,

(4) halogen,

(5) $-CO-C_{1-4}$ alkyl, in which the alkyl group may be optionally substituted with C_{1-4} alkoxy,

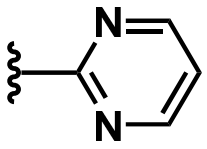
(6) $-CO-C_{1-6}$ alkoxy,

(7) $-CO-C_{3-6}$ cycloalkyl,

(8) $-SO_2-C_{1-4}$ alkyl,

(9) $-SO_2-C_{3-6}$ cycloalkyl,

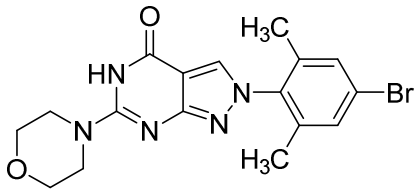
(10) a group of the following formula:



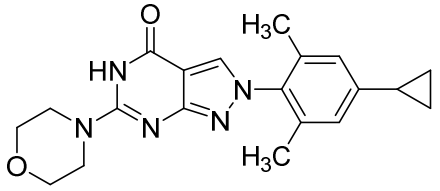
, and

(11) oxo.

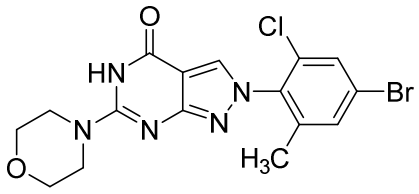
12. The compound according to claim 1 selected from the group consisting of:



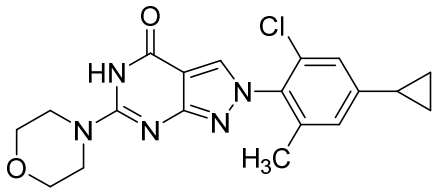
,



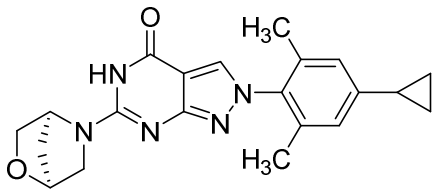
,



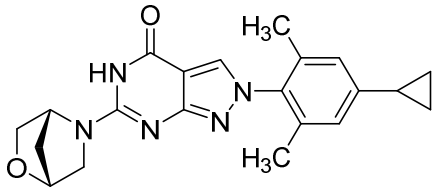
,



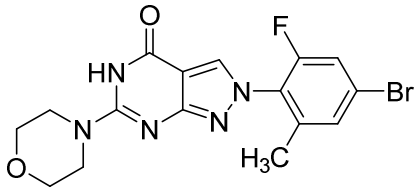
,



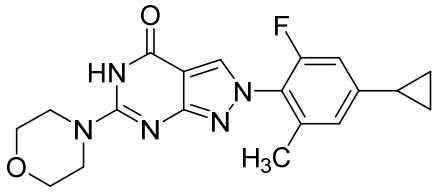
,



,

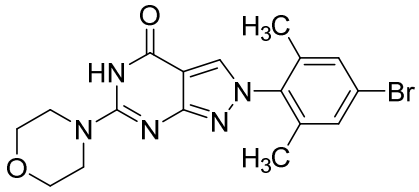


, and



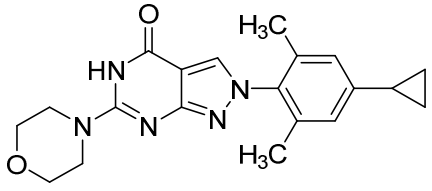
, or a pharmaceutically acceptable salt thereof.

13. A compound having the following structure:



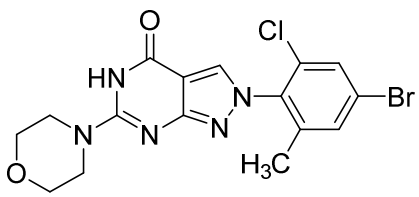
, or a pharmaceutically acceptable salt thereof.

14. A compound having the following structure:



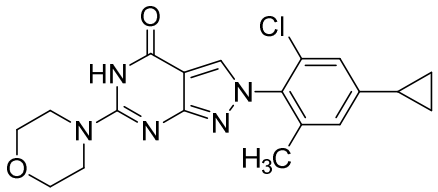
, or a pharmaceutically acceptable salt thereof.

15. A compound having the following structure:



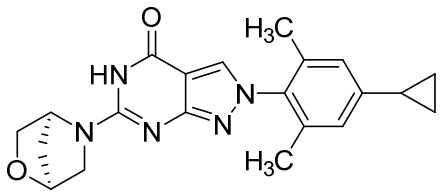
, or a pharmaceutically acceptable salt thereof.

16. A compound having the following structure:



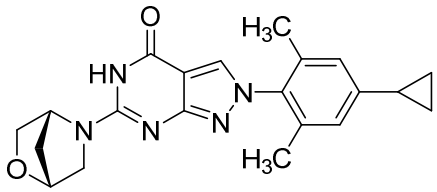
, or a pharmaceutically acceptable salt thereof.

17. A compound having the following structure:



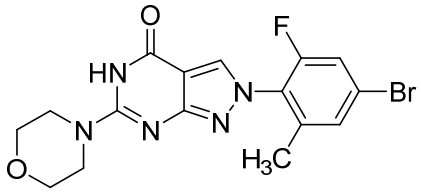
, or a pharmaceutically acceptable salt thereof.

18. A compound having the following structure:



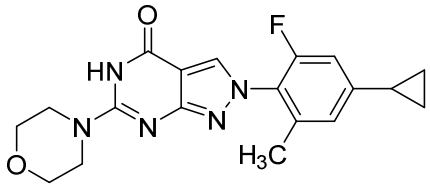
, or a pharmaceutically acceptable salt thereof.

19. A compound having the following structure:



, or a pharmaceutically acceptable salt thereof.

20. A compound having the following structure:



, or a pharmaceutically acceptable salt thereof.

21. A pharmaceutical composition comprising a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

22. An NLRP3 inflammasome inhibitor, comprising a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof.

23. A medicament for use in treating or preventing a disease selected from the group consisting of multiple sclerosis, inflammatory bowel disease, arteriosclerosis, Cryopyrin-associated periodic syndrome, nonalcoholic steatohepatitis, gout, ischemic heart disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and traumatic brain injury, comprising a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof.

24. The medicament for use according to claim 23, wherein inflammatory bowel disease is ulcerative colitis or Crohn's disease.

25. The medicament for use according to claim 23, wherein Cryopyrin-associated periodic syndrome is familial cold autoinflammatory syndrome, Muckle-Wells syndrome, chronic infantile neurologic cutaneous and articular syndrome, or Neonatal onset multisystem inflammatory disease.

26. A method of inhibiting NLRP3 inflammasome, comprising administering a therapeutically effective amount of a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, to a mammal.

27. A method of treating or preventing a disease selected from the group consisting of multiple sclerosis, inflammatory bowel disease, arteriosclerosis, Cryopyrin-associated periodic syndrome, nonalcoholic steatohepatitis, gout, ischemic heart disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and traumatic brain injury, comprising administering a therapeutically effective amount of a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, to a mammal.

28. The method according to claim 27, wherein inflammatory bowel disease is ulcerative colitis or Crohn's disease.

29. The method according to claim 27, wherein Cryopyrin-associated periodic syndrome is familial cold autoinflammatory syndrome, Muckle-Wells syndrome, chronic infantile neurologic cutaneous and articular syndrome, or Neonatal onset multisystem inflammatory disease.

30. Use of a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, in the manufacture of an NLRP3 inflammasome inhibitor.

31. Use of a compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or preventing a disease selected from the group consisting of multiple sclerosis, inflammatory bowel disease, arteriosclerosis, Cryopyrin-associated periodic syndrome, nonalcoholic steatohepatitis, gout, ischemic heart disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and traumatic brain injury.

32. The use according to claim 31, wherein inflammatory bowel disease is ulcerative colitis or Crohn's disease.

33. The use according to claim 31, wherein Cryopyrin-associated periodic syndrome is familial cold autoinflammatory

syndrome, Muckle-Wells syndrome, chronic infantile neurologic cutaneous and articular syndrome, or Neonatal onset multisystem inflammatory disease.

34. A compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, for use in inhibiting NLRP3 inflammasome.

35. A compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, for use in treating or preventing a disease selected from the group consisting of multiple sclerosis, inflammatory bowel disease, arteriosclerosis, Cryopyrin-associated periodic syndrome, nonalcoholic steatohepatitis, gout, ischemic heart disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and traumatic brain injury.

36. The compound according to claim 35, or a pharmaceutically acceptable salt thereof, wherein inflammatory bowel disease is ulcerative colitis or Crohn's disease.

37. The compound according to claim 35, or a pharmaceutically acceptable salt thereof, wherein Cryopyrin-associated periodic syndrome is familial cold autoinflammatory syndrome, Muckle-Wells syndrome, chronic infantile neurologic cutaneous and articular syndrome, or Neonatal onset multisystem inflammatory disease.