[0021a] In one aspect, the present disclosure provides for a compound of formula Ib:

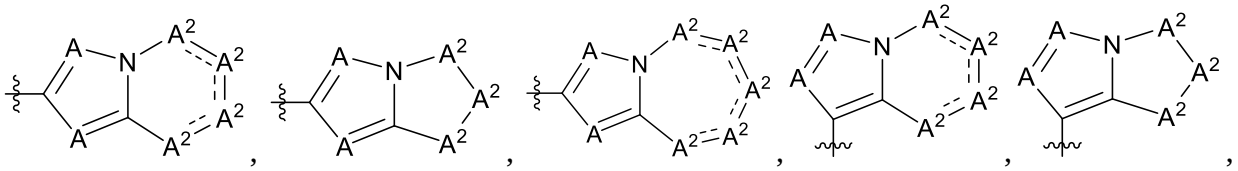
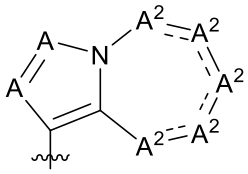

(Ib)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof,

wherein:

X^1 is O;

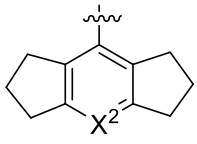
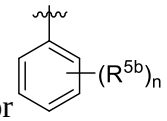
R^1 is selected from the group consisting of:


and ;

wherein ⎓ represents a single bond;

each A is independently CR^{5a} or N;

each A^2 is independently $C(R^{5a})_2$, NR^{5a}, or O; wherein at least one A^2 is NR^{5a} or O;

R^2 is  or ;

X^2 is N or CR^{5b};

R^3 and R^4 are H;

each R^{5a} is independently H, D, halogen, OH, CN, –SR^6, –OR^6, –NHR^6, –NR^6R^7, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, or -CH_2-C_3-C_8cycloalkyl; wherein the C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, and -CH_2-C_3-C_8cycloalkyl are optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or two R^{5a} together with the atoms to which they are attached can form C_3-C_8cycloalkyl, or heterocyclyl; wherein the heterocyclyl contains 1-3 heteroatoms selected from the group consisting of N, S, P and O; wherein the C_3-C_8cycloalkyl or heterocyclyl is optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, NH(C_1-C_6alkyl), or N(C_1-C_6alkyl)$_2$; or

two geminal R^{5a} can form an oxo group;

each R^{5b} is independently H, D, halogen, OH, CN, –SR^6, –OR^6, –NHR^6, –NR^6R^7, or C_1-C_6alkyl; wherein the C_1-C_6alkyl is optionally substituted with D, halogen, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$;

R^6 and R^7 are independently, at each occurrence H, D, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, C_3-C_8cycloalkyl, or heterocyclyl; wherein the heterocyclyl contains 1-5 heteroatoms selected from the group consisting of N, S, P and O; wherein the C_1-C_6alkyl, C_2-C_8alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, or heterocyclyl is optionally substituted with D, halogen, C_1-C_6alkyl,-OH, -O-C_1-C_6alkyl, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or

R^6 and R^7 together with the atom to which they are attached can form heterocyclyl containing 1-3 heteroatoms selected from the group consisting of N, S, P and O; and

n is an integer from 0 to 5.

[0021b] In another aspect, the present disclosure provides for a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, and a pharmaceutically acceptable carrier.

[0022] The present disclosure provides a pharmaceutical composition comprising a compound of the present disclosure, and pharmaceutically acceptable salts, prodrugs, solvates, hydrates, isomers, and tautomers thereof, and a pharmaceutically acceptable carrier, diluent and/or excipient. In one aspect, the present disclosure provides a pharmaceutical composition comprising a compound of the present disclosure, or a pharmaceutically acceptable salt, prodrug, solvate, hydrate, isomer, or tautomer thereof, and a pharmaceutically acceptable carrier.

[0023] The present disclosure provides a method of treatment or prevention of a disease, disorder or condition including the step of administering an effective amount of a compound of the present disclosure, and pharmaceutically acceptable salts, prodrugs, solvates, hydrates, isomers, and tautomers thereof to thereby treat or prevent the disease, disorder or condition in a subject in need thereof.

[0023a] In another aspect, the present disclosure provides for a compound as described herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, for use in therapy.

[0023b] In another aspect, the present disclosure provides for a use of a compound as described herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, in the manufacture of a medicament for the treatment of a disease, disorder, or condition that is of the immune system, the cardiovascular system, the endocrine system, the gastrointestinal tract, the renal system, the respiratory system, the central nervous system, or that is a cancer or other malignancy.

[0023c] In another aspect, the present disclosure provides for a use of a compound as described herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, in the manufacture of a medicament for the treatment of an inflammatory or autoimmune disease, disorder, or condition.

[0023d] In another aspect, the present disclosure provides for a use of a compound as described herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, in the manufacture of a medicament for the treatment of a disease, disorder, or condition selected from the group consisting of constitutive inflammation, the cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), neonatal-onset multisystem inflammatory disease (NOMID), familial Mediterranean fever (FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D, periodic fever syndrome (HIDS), Majeed syndrome, pyogenic arthritis, pyoderma gangrenosum and acne (PAPA), haploinsufficiency of A20 (HA20), pediatric granulomatous arthritis (PGA), PLCG2-associated antibody deficiency and immune dysregulation (PLAID), PLCG2-associated autoinflammation, antibody deficiency and immune dysregulation (APLAID), sideroblastic anemia with B-cell immunodeficiency, periodic fevers, developmental delay (SIFD), Sweet's syndrome, chronic nonbacterial osteomyelitis (CNO), chronic recurrent multifocal osteomyelitis (CRMO) and synovitis, acne, pustulosis, hyperostosis, osteitis syndrome (SAPHO), multiple sclerosis (MS), type-1 diabetes, psoriasis, rheumatoid arthritis, Behcet's disease, Sjogren's syndrome, Schnitzler syndrome, idiopathic pulmonary fibrosis (IPF), chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis, cystic fibrosis, Parkinson's disease, Alzheimer's disease, motor neuron disease, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis, Type 2 diabetes, atherosclerosis, obesity, gout, pseudo-gout, disease of the ocular epithelium, age-related macular degeneration (AMD), corneal infection, uveitis, dry eye, kidney disease, chronic kidney disease, oxalate nephropathy, diabetic nephropathy, non-alcoholic steatohepatitis, alcoholic liver disease, inflammatory reactions in skin, contact hypersensitivity, sunburn, osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis, cyst-causing skin diseases, cancers, lung cancer metastasis, pancreatic cancers,

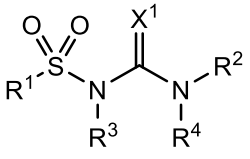
gastric cancers, myelodisplastic syndrome, leukemia, polymyositis, stroke, myocardial infarction, Graft versus Host Disease, hypertension, colitis, bacterial infection, abdominal aortic aneurism, wound healing, pericarditis, Dressler's syndrome, and ischaemia reperfusion injury.

[0023e] In another aspect, the present disclosure provides for a use of a compound as described herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, in the manufacture of a medicament for the treatment of a disease, disorder, or condition selected from the group consisting of cryopyrin-associated periodic syndromes (CAPS), atherosclerosis, gout, pseudo-gout, rheumatoid arthritis, systemic juvenile idiopathic arthritis, non-alcoholic steatohepatitis, myocardial infarction, Parkinson's disease, Alzheimer's disease, multiple sclerosis, and type-1 diabetes.

[0024] The present disclosure provides a compound of the present disclosure, and pharmaceutically acceptable salts, prodrugs, solvates, hydrates, isomers, and tautomers thereof, or the pharmaceutical composition of the present disclosure for use in the treatment or prevention of a disease, disorder or condition in a subject in need thereof.

CLAIMS:

1. A compound of formula Ib:

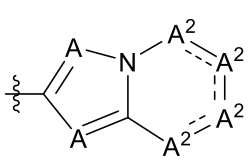
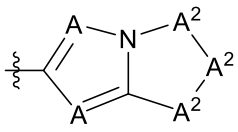
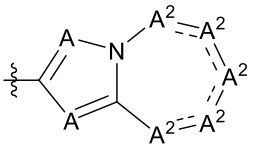
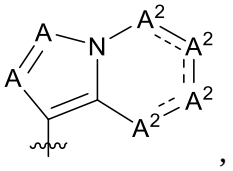
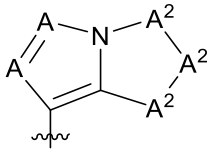
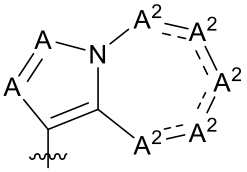

(Ib)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof,

wherein:

X^1 is O;

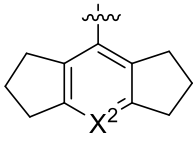
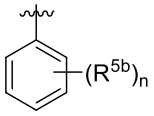
R^1 is selected from the group consisting of:


,

,

,

,

, and

;

wherein ⎓ represents a single bond;

each A is independently CR^{5a} or N;

each A^2 is independently $C(R^{5a})_2$, NR^{5a}, or O; wherein at least one A^2 is NR^{5a} or O;

R^2 is

or

;

X^2 is N or CR^{5b};

R^3 and R^4 are H;

each R^{5a} is independently H, D, halogen, OH, CN, $–SR^6$, $–OR^6$, $–NHR^6$, $–NR^6R^7$, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, or -CH_2-C_3-C_8cycloalkyl; wherein the C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, and -CH_2-C_3-C_8cycloalkyl are optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or

two R^{5a} together with the atoms to which they are attached can form C_3-C_8cycloalkyl, or heterocyclyl; wherein the heterocyclyl contains 1-3 heteroatoms selected from the group

consisting of N, S, P and O; wherein the C_3-C_8cycloalkyl or heterocyclyl is optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, NH(C_1-C_6alkyl), or N(C_1-C_6alkyl)$_2$; or

two geminal R^{5a} can form an oxo group;

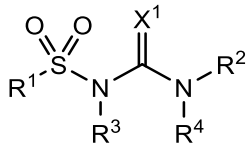
each R^{5b} is independently H, D, halogen, OH, CN, –SR^6, –OR^6, –NHR^6, –NR^6R^7, or C_1-C_6alkyl; wherein the C_1-C_6alkyl is optionally substituted with D, halogen, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$;

R^6 and R^7 are independently, at each occurrence H, D, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, C_3-C_8cycloalkyl, or heterocyclyl; wherein the heterocyclyl contains 1-5 heteroatoms selected from the group consisting of N, S, P and O; wherein the C_1-C_6alkyl, C_2-C_8alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, or heterocyclyl is optionally substituted with D, halogen, C_1-C_6alkyl,-OH, -O-C_1-C_6alkyl, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or

R^6 and R^7 together with the atom to which they are attached can form heterocyclyl containing 1-3 heteroatoms selected from the group consisting of N, S, P and O; and

n is an integer from 0 to 5.

2. The compound of claim 1, wherein the compound is of formula (I):

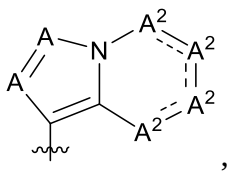


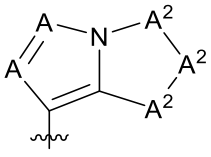
(I),

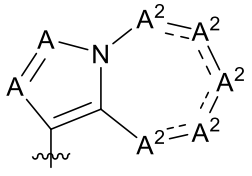
or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein:

X^1 is O;

R^1 is selected from the group consisting of:



,


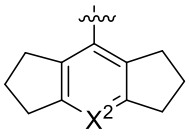
, and


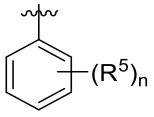
;

wherein ⎓ represents a single bond;

each A is independently CR^5 or N;

each A^2 is independently C(R^5)$_2$, NR_5, or O; wherein at least one A^2 is NR^5 or O;

R^2 is


or


;

X^2 is N or CR^5;

R^3 and R^4 are H;

each R^5 is independently H, D, halogen, OH, CN, $–SR^6$, $–OR^6$, $–NHR^6$, $–NR^6R^7$, or C_1-C_6alkyl; or

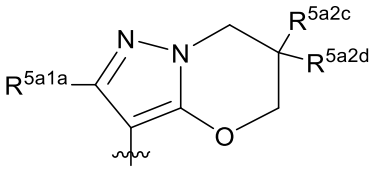
R^6 and R^7 are independently, at each occurrence H, D, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, C_3-C_8cycloalkyl, or heterocyclyl; wherein the heterocyclyl contains 1-5 heteroatoms selected from the group consisting of N, S, P and O; or

R^6 and R^7 together with the atom to which they are attached can form heterocyclyl containing 1-3 heteroatoms selected from the group consisting of N, S, P and O; and

n is an integer from 0 to 5.

3. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein one A is CR^{5a} and the other A is N.

4. The compound of claim 1 or 3, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein each R^{5a} is independently H, $-NHR^6$, $-NR^6R^7$, C_1-C_6alkyl, or heterocyclyl containing N, wherein the C_1-C_6alkyl is substituted with $-NH_2$, $-NH(C_1$-C_6alkyl), or $-N(C_1$-C_6alkyl)$_2$, and wherein the heterocyclyl is optionally substituted with D, halogen, C_1-C_6alkyl, $-OR^6$, $-NH_2$, $-NH(C_1$-C_6alkyl), or $-N(C_1$-C_6alkyl)$_2$.

5. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^1 is 

, wherein:

R^{5a1a} is H;

R^{5a2c} and R^{5a2d} are each independently H, D, halogen, -OH, -CN, $-SR^6$, $-OR^6$, $-NHR^6$, $-NR^6R^7$, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, or $-CH_2$-C_3-C_8cycloalkyl; wherein the C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, and $-CH_2$-C_3-C_8cycloalkyl are optionally substituted with D, halogen, C_1-C_6alkyl, $-OR^6$, $-NH_2$, $-NH(C_1$-C_6alkyl), or $-N(C_1$-C_6alkyl)$_2$; or

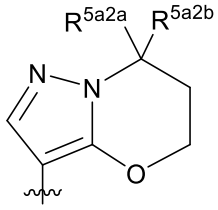
R^{5a2c} and R^{5a2d} together with the atoms to which they are attached can form C_3-C_8cycloalkyl or heterocyclyl; wherein the heterocyclyl contains 1-3 heteroatoms selected from the group consisting of N, S, P and O; wherein the C_3-C_8cycloalkyl and heterocyclyl are

optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or

R^{5a2c} and R^{5a2d} can form an oxo group.

6. The compound of claim 5, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein each R^{5a2c} and R^{5a2d} is independently H, halogen, -OH, –OR^6, -NR^6R^7, C_1-C_6alkyl, C_3-C_8cycloalkyl, heterocyclyl, or -CH_2-C_3-C_8cycloalkyl.

7. The compound of claim 5, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^{5a2c} and R^{5a2d} together with the atoms to which they are attached form C_3-C_8cycloalkyl or heterocyclyl.

8. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^1 is 

, wherein:

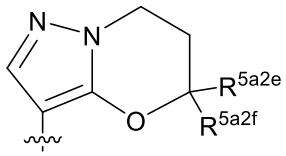
R^{5a2a} and R^{5a2b} are each independently H, D, halogen, -OH, -CN, -SR^6, -OR^6, -NHR^6, -NR^6R^7, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, or -CH_2-C_3-C_8cycloalkyl; wherein the C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, and -CH_2-C_3-C_8cycloalkyl are optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or

R^{5a2a} and R^{5a2b} together with the atoms to which they are attached can form C_3-C_8cycloalkyl or heterocyclyl; wherein the heterocyclyl contains 1-3 heteroatoms selected from the group consisting of N, S, P and O; wherein the C_3-C_8cycloalkyl and heterocyclyl are optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or

R^{5a2a} and R^{5a2b} can form an oxo group.

9. The compound of claim 8, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein each R^{5a2a} and R^{5a2b} is independently H, halogen, -OH, –OR^6, -NR^6R^7, C_1-C_6alkyl, C_3-C_8cycloalkyl, heterocyclyl, or -CH_2-C_3-C_8cycloalkyl.

10. The compound of claim 8, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^{5a2a} and R^{5a2b} together with the atoms to which they are attached form C_3-C_8cycloalkyl or heterocyclyl.

11. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^1 is , wherein:

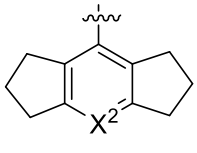
R^{5a2e} and R^{5a2f} are each independently H, D, halogen, -OH, -CN, -SR^6, -OR^6, -NHR^6, -NR^6R^7, C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, or -CH_2-C_3-C_8cycloalkyl; wherein the C_1-C_6alkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, C_3-C_8cycloalkyl, heterocyclyl, and -CH_2-C_3-C_8cycloalkyl are optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or

R^{5a2e} and R^{5a2f} together with the atoms to which they are attached can form C_3-C_8cycloalkyl or heterocyclyl; wherein the heterocyclyl contains 1-3 heteroatoms selected from the group consisting of N, S, P and O; wherein the C_3-C_8cycloalkyl and heterocyclyl are optionally substituted with D, halogen, C_1-C_6alkyl, -OR^6, -NH_2, -NH(C_1-C_6alkyl), or -N(C_1-C_6alkyl)$_2$; or

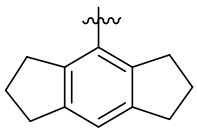
R^{5a2e} and R^{5a2f} can form an oxo group.

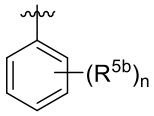
12. The compound of claim 11, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein each R^{5a2e} and R^{5a2f} is independently H, halogen, -OH, –OR^6, -NR^6R^7, C_1-C_6alkyl, C_3-C_8cycloalkyl, heterocyclyl, or -CH_2-C_3-C_8cycloalkyl.

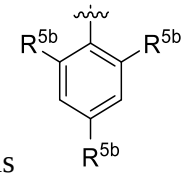
13. The compound of claim 12, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^{5a2e} and R^{5a2f} together with the atoms to which they are attached form C_3-C_8cycloalkyl or heterocyclyl.

14. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^2 is .

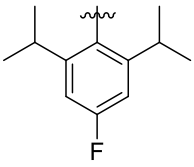
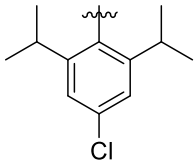
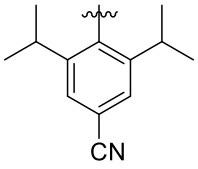
15. The compound of claim 14, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein X^2 is CR^{5b} and R^{5b} is H, fluoro, chloro, or methyl.

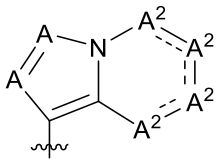
16. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^2 is .

17. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^2 is .

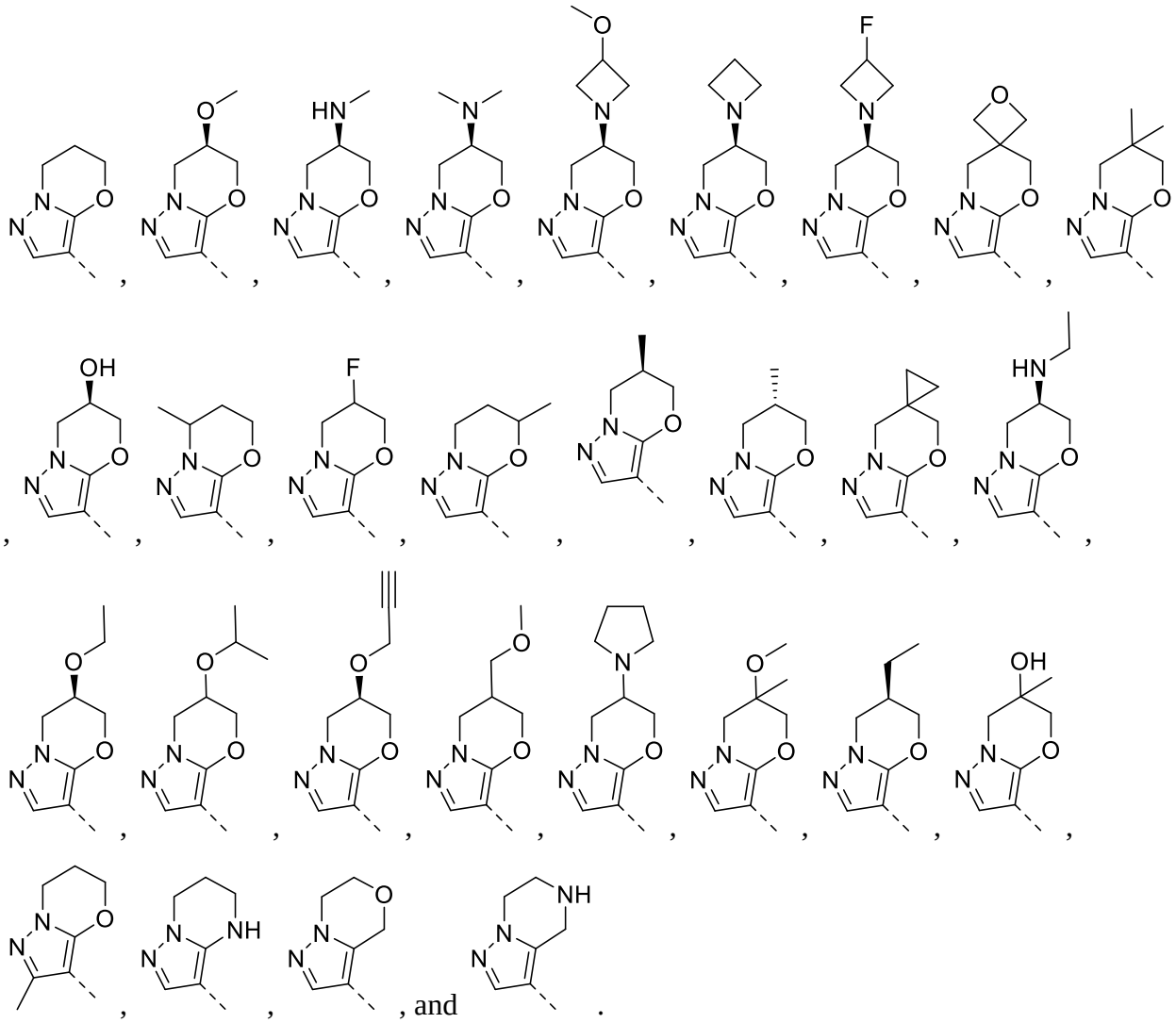
18. The compound of claim 17, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^2 is .

19. The compound of claim 1, 17 or 18, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein each R^{5b} is independently selected from the group consisting of H, halogen, -OH, -CN, $–NO_2$, $–OR^6$, C_1-C_6alkyl, C_2-C_6alkenyl, and C_4-C_8cycloalkenyl.

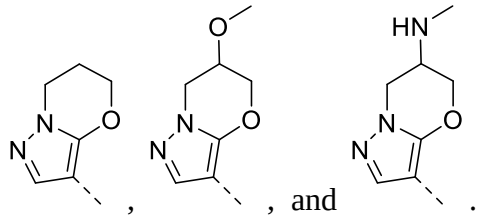
20. The compound of claim 18, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^2 is selected from the group consisting of , , and .

21. The compound of any one of claims 1 to 4 or 14 to 20, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^1 is .

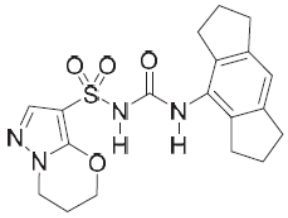
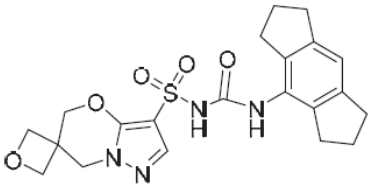
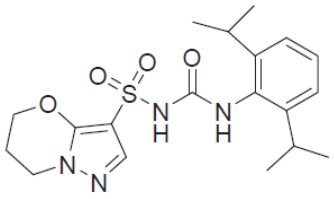
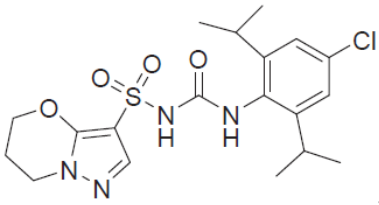
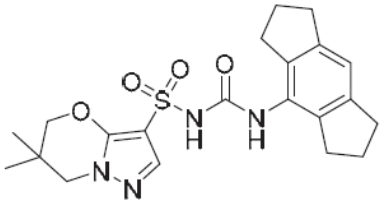
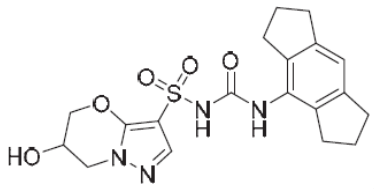
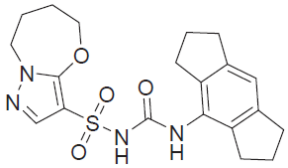
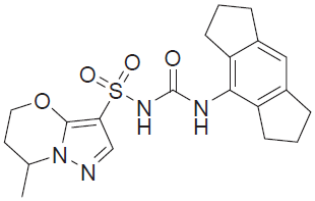
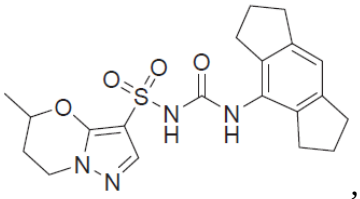
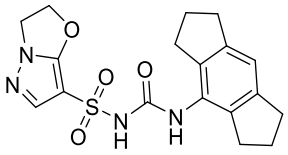
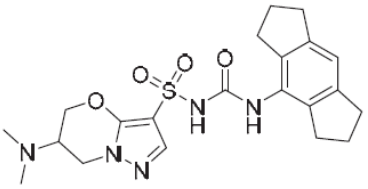
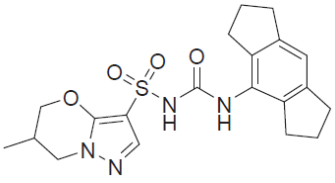
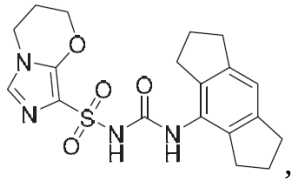
22. The compound of any one of claims 1 or 14 to 21, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^1 is selected from the group consisting of



23. The compound of any one of claims 1 or 14 to 21, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, wherein R^1 is selected from the group consisting of

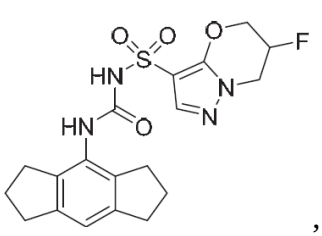
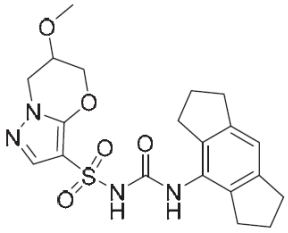
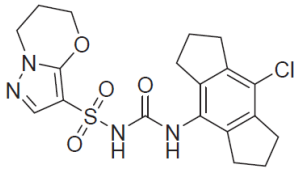


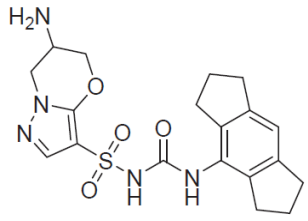
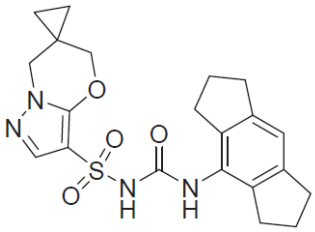
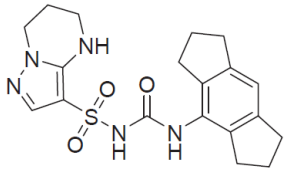
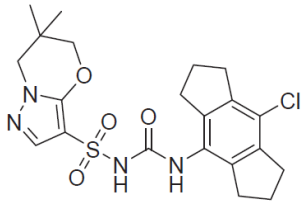
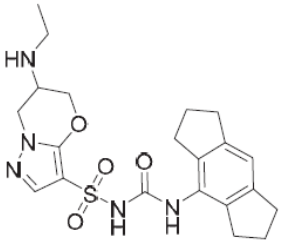
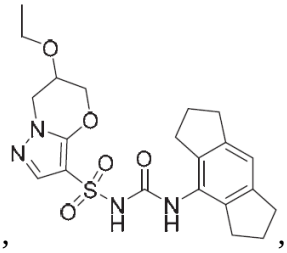
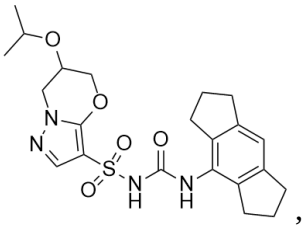
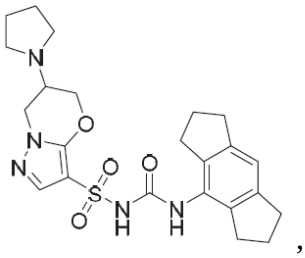
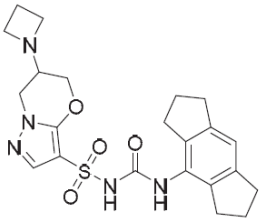
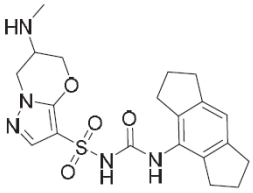
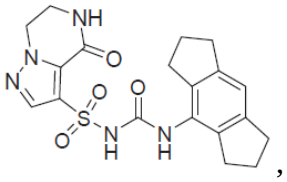
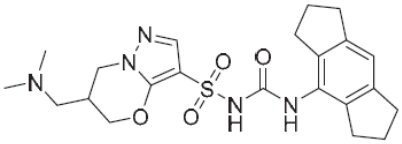
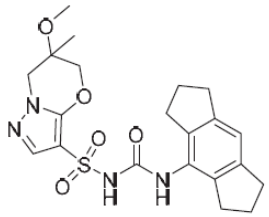
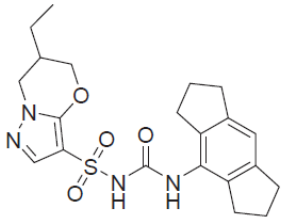
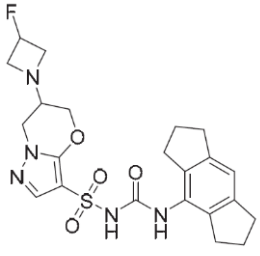
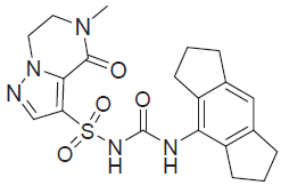
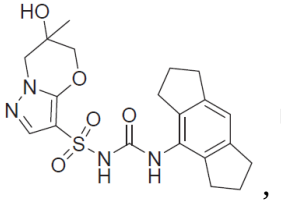
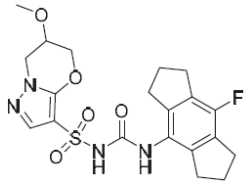
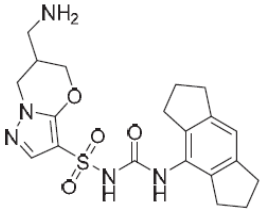
24. The compound of claim 1, wherein the compound is:


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or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

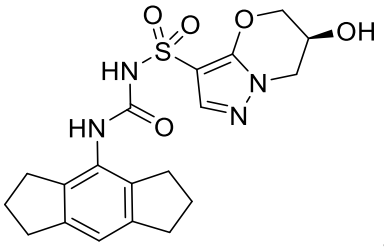
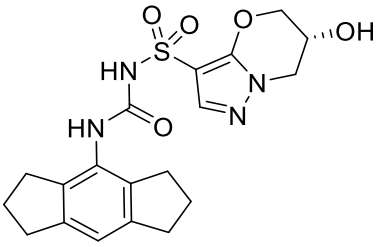
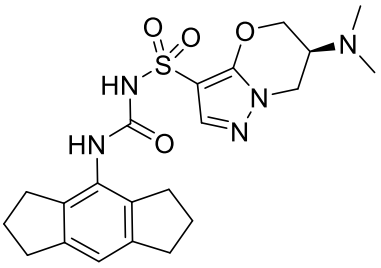
25. The compound of claim 1, wherein the compound is:

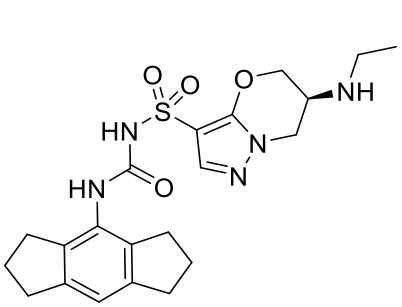
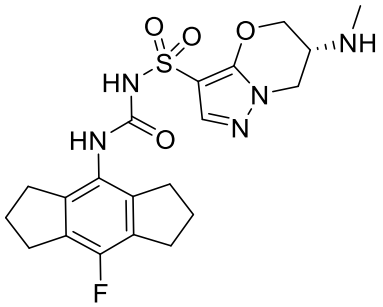
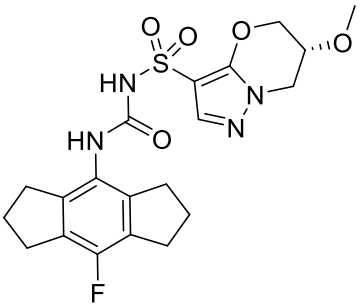
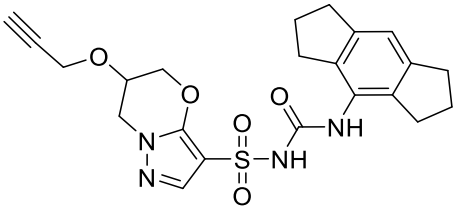
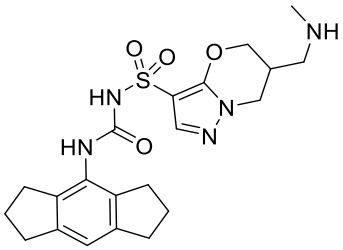
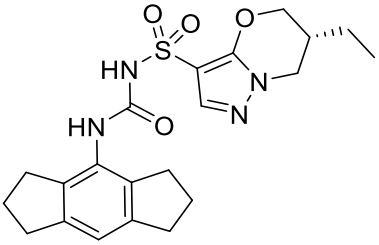
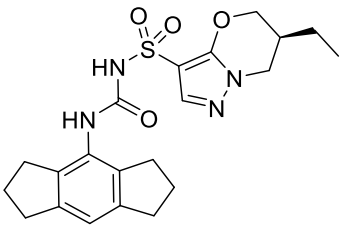
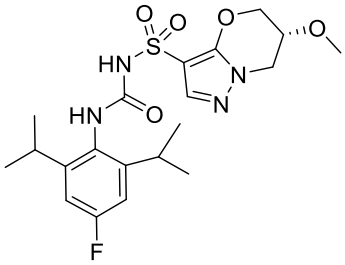
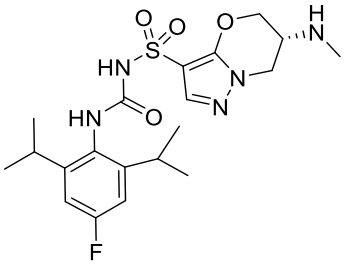
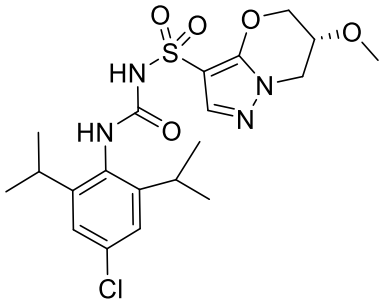
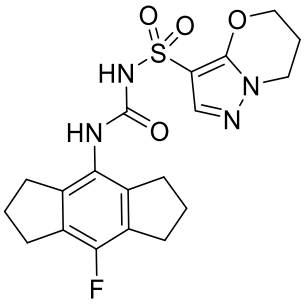
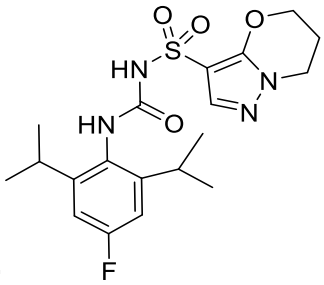

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or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

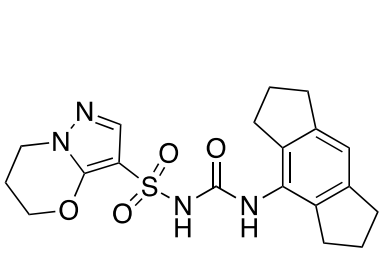
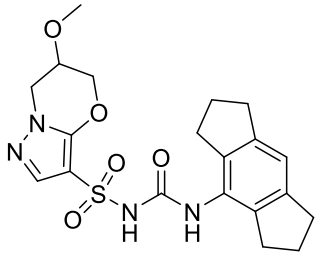
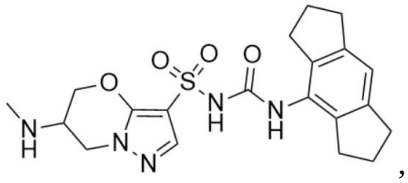
26. The compound of claim 1, wherein the compound is:

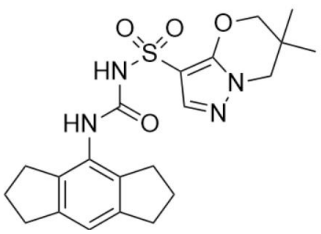
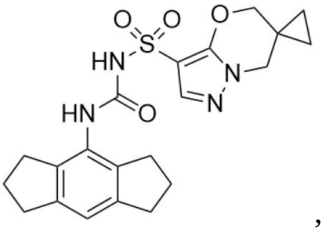
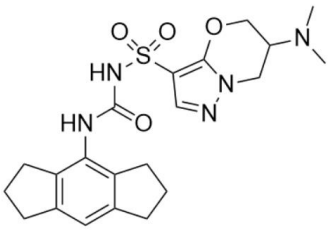

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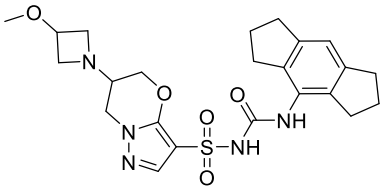
or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

27. The compound of claim 1, wherein the compound is:

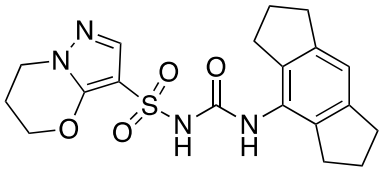

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, or , or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

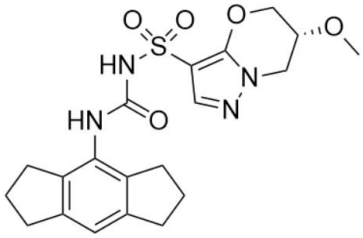
28. The compound of claim 1, wherein the compound is:

, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

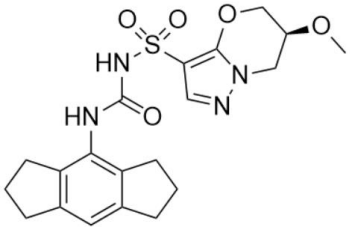
29. The compound of claim 1, wherein the compound is:

, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

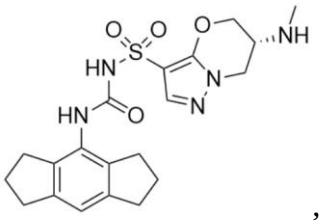
30. The compound of claim 1, wherein the compound is:

, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

31. The compound of claim 1, wherein the compound is:

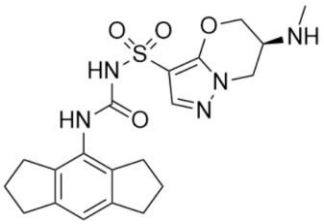
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

32. The compound of claim 1, wherein the compound is:



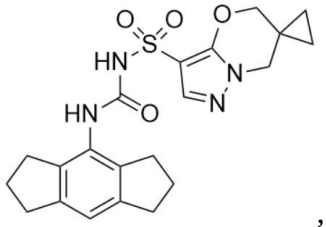
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

33. The compound of claim 1, wherein the compound is:



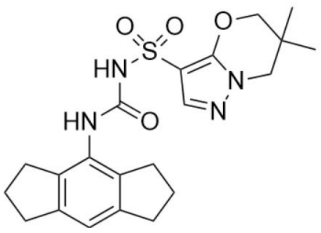
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

34. The compound of claim 1, wherein the compound is:



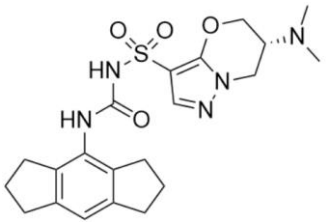
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

35. The compound of claim 1, wherein the compound is:



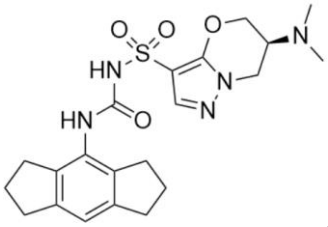
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

36. The compound of claim 1, wherein the compound is:



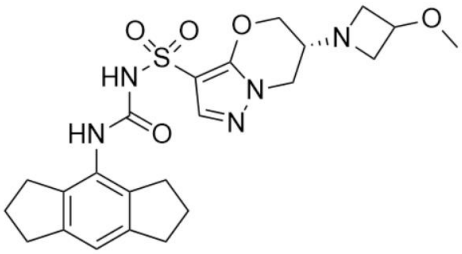
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

37. The compound of claim 1, wherein the compound is:



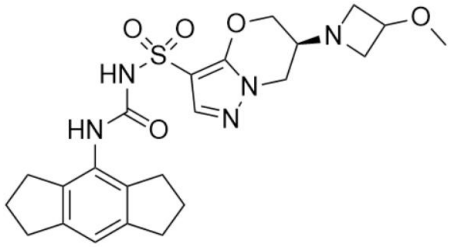
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

38. The compound of claim 1, wherein the compound is:



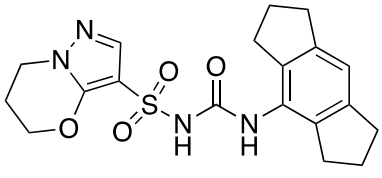
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

39. The compound of claim 1, wherein the compound is:



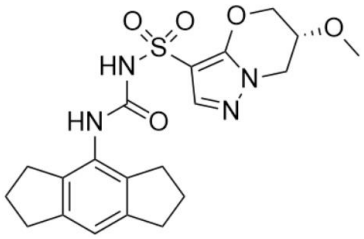
, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof.

40. The compound of claim 1, wherein the compound is



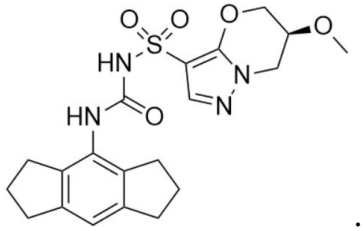
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41. The compound of claim 1, wherein the compound is



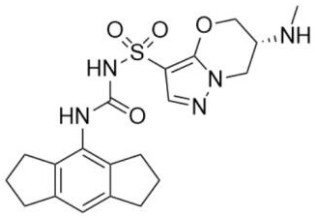
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42. The compound of claim 1, wherein the compound is



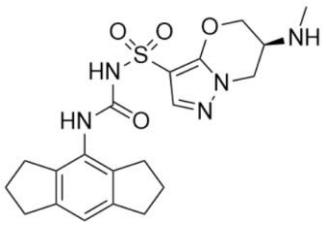
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43. The compound of claim 1, wherein the compound is



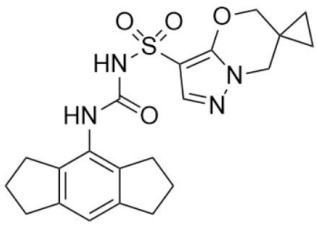
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44. The compound of claim 1, wherein the compound is



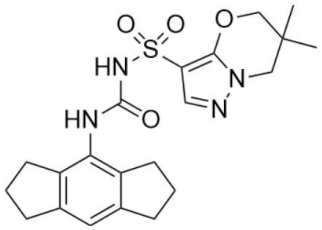
.

45. The compound of claim 1, wherein the compound is

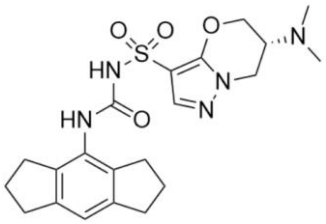


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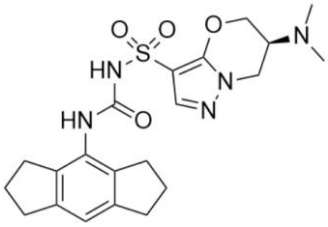
46. The compound of claim 1, wherein the compound is



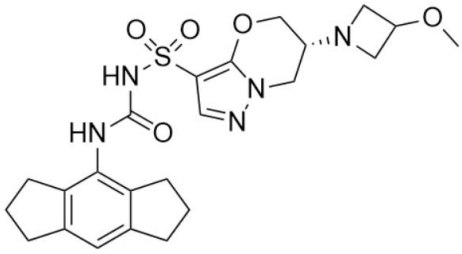
47. The compound of claim 1, wherein the compound is



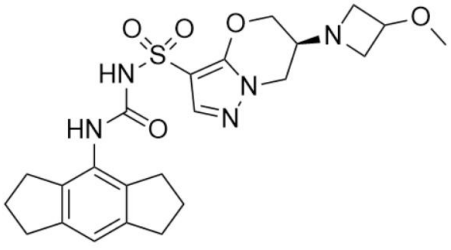
48. The compound of claim 1, wherein the compound is



49. The compound of claim 1, wherein the compound is



50. The compound of claim 1, wherein the compound is



51. A pharmaceutical composition comprising a compound of any one of claims 1 to 39, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, and a pharmaceutically acceptable carrier.

52. A pharmaceutical composition comprising a compound of any one of claims 40 to 50, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, and a pharmaceutically acceptable carrier.

53. A compound of any one of claims 1 to 39, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, or a compound of any one of claims 40 to 50, for use in therapy.

54. Use of a compound of any one of claims 1 to 39, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, or a compound of any one of claims 40 to 50, in the manufacture of a medicament for the treatment of a disease, disorder, or condition that is of the immune system, the cardiovascular system, the endocrine system, the gastrointestinal tract, the renal system, the respiratory system, the central nervous system, or that is a cancer or other malignancy.

55. Use of a compound of any one of claims 1 to 39, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, or a compound of any one of claims 40 to 50, in the manufacture of a medicament for the treatment of an inflammatory or autoimmune disease, disorder, or condition.

56. Use of a compound of any one of claims 1 to 39, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, or a compound of any one of claims 40 to 50, in the manufacture of a medicament for the treatment of a disease, disorder, or condition selected from the group consisting of constitutive inflammation, the cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), neonatal-onset multisystem inflammatory disease (NOMID), familial Mediterranean fever (FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D, periodic fever syndrome (HIDS), Majeed syndrome, pyogenic arthritis, pyoderma gangrenosum and acne (PAPA), haploinsufficiency of A20 (HA20), pediatric granulomatous arthritis (PGA), PLCG2-associated antibody deficiency and immune dysregulation (PLAID), PLCG2-associated autoinflammation, antibody deficiency and immune dysregulation (APLAID), sideroblastic anemia with B-cell immunodeficiency, periodic fevers, developmental delay (SIFD), Sweet's syndrome, chronic nonbacterial osteomyelitis (CNO), chronic recurrent multifocal osteomyelitis (CRMO) and synovitis, acne, pustulosis, hyperostosis, osteitis syndrome (SAPHO), multiple sclerosis (MS), type-1 diabetes, psoriasis,

rheumatoid arthritis, Behcet's disease, Sjogren's syndrome, Schnitzler syndrome, idiopathic pulmonary fibrosis (IPF), chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis, cystic fibrosis, Parkinson's disease, Alzheimer's disease, motor neuron disease, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis, Type 2 diabetes, atherosclerosis, obesity, gout, pseudo-gout, disease of the ocular epithelium, age-related macular degeneration (AMD), corneal infection, uveitis, dry eye, kidney disease, chronic kidney disease, oxalate nephropathy, diabetic nephropathy, non-alcoholic steatohepatitis, alcoholic liver disease, inflammatory reactions in skin, contact hypersensitivity, sunburn, osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis, cyst-causing skin diseases, cancers, lung cancer metastasis, pancreatic cancers, gastric cancers, myelodisplastic syndrome, leukemia, polymyositis, stroke, myocardial infarction, Graft versus Host Disease, hypertension, colitis, bacterial infection, abdominal aortic aneurism, wound healing, pericarditis, Dressler's syndrome, and ischaemia reperfusion injury.

57. Use of a compound of any one of claims 1 to 39, or a pharmaceutically acceptable salt, solvate, stereoisomer, or tautomer thereof, or a compound of any one of claims 40 to 50, in the manufacture of a medicament for the treatment of a disease, disorder, or condition selected from the group consisting of cryopyrin-associated periodic syndromes (CAPS), atherosclerosis, gout, pseudo-gout, rheumatoid arthritis, systemic juvenile idiopathic arthritis, non-alcoholic steatohepatitis, myocardial infarction, Parkinson's disease, Alzheimer's disease, multiple sclerosis, and type-1 diabetes.