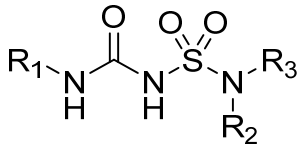
CLAIMS

1. A compound of Formula (I):



(I),

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

R_1 is C_3-C_{16} cycloalkyl, or C_5-C_{10} aryl, wherein the C_3-C_{16} cycloalkyl, or C_5-C_6 aryl is optionally substituted by one or more **R_{1S}**; wherein each **R_{1S}** is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, or halo;

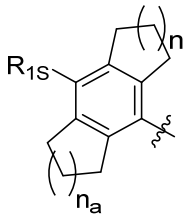
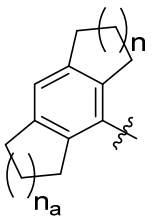
R_2 is -(CX_2X_2)$_n$-**R_{2S}**, wherein n is 0, 1, or 2, and each **X_2** is independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl is optionally substituted with one or more halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo;

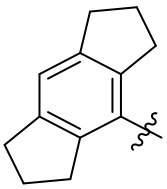
R_{2S} is 4- to 8-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo; and

R_3 is 7- to 12-membered heterocycloalkyl or 5- or 6-membered heteroaryl optionally substituted with one or more **R_{3S}**, wherein each **R_{3S}** is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, halo, or C_3-C_8 heterocycloalkyl wherein the C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, or C_3-C_8 heterocycloalkyl is optionally substituted with –O(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, halo, or -CN.

2. The compound of any one of the preceding claims, wherein **R_1** is C_9-C_{10} bicyclic cycloalkyl.

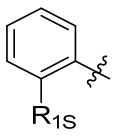
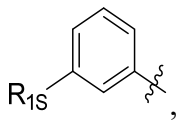
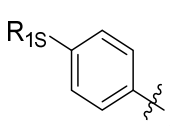
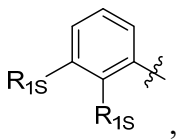
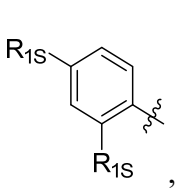
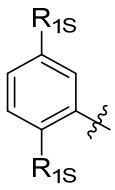
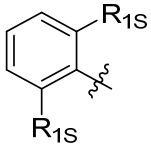
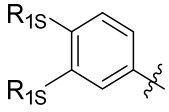
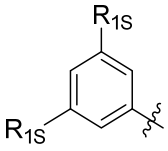
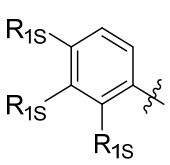
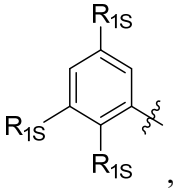
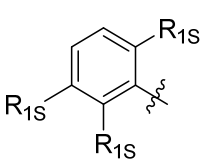
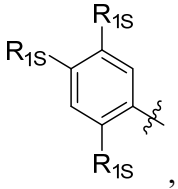
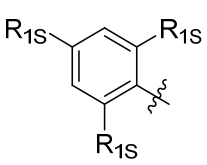
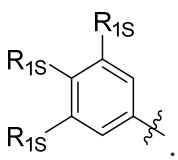
3. The compound of any one of the preceding claims, wherein **R_1** is C_{12}-C_{16} tricyclic cycloalkyl.

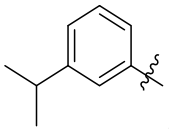
4. The compound of any one of the preceding claims, wherein $\mathbf{R_1}$ is  or , wherein n and n_a each independently are 0, 1, 2, or 3.

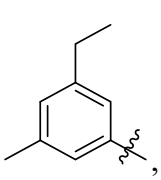
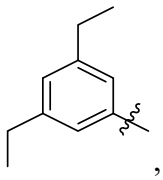
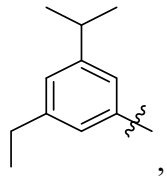
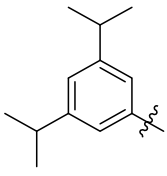
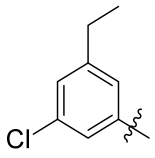
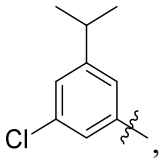
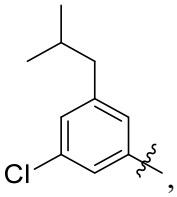
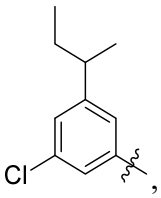
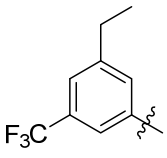
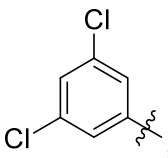
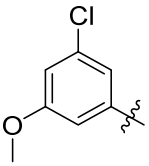
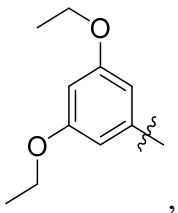
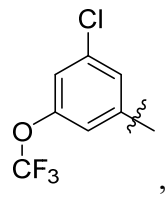
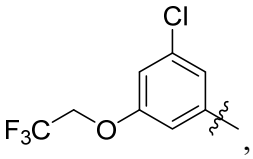
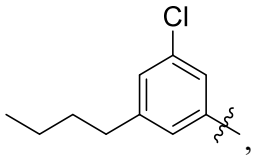
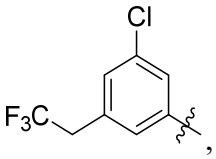
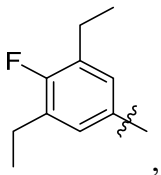
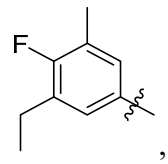
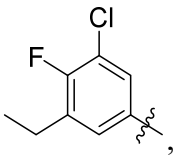
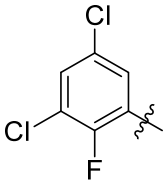
5. The compound of any one of the preceding claims, wherein $\mathbf{R_1}$ is .

6. The compound of any one of the preceding claims, wherein, $\mathbf{R_1}$ is C_5-C_{10} aryl optionally substituted by one or more $\mathbf{R_{1S}}$.

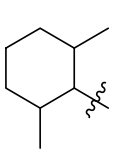
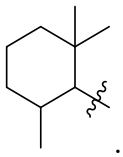
7. The compound of any one of the preceding claims, wherein $\mathbf{R_1}$ is phenyl is substituted by one, two, or three $\mathbf{R_{1S}}$.

8. The compound of any one of the preceding claims, wherein $\mathbf{R_1}$ is , , , , , , , , , , , , , , or .

9. The compound of any one of the preceding claims, wherein $\mathbf{R_1}$ is  .

, , , , , , ,
, , , , , ,
, , , , ,
, or  .

10. The compound of any one of the preceding claims, wherein $\mathbf{R_1}$ is cyclopentyl, cyclohexyl, or cycloheptyl, wherein the cyclopentyl, cyclohexyl, or cycloheptyl is optionally substituted by one or more $\mathbf{R_{1S}}$.

11. The compound of any one of the preceding claims, wherein $\mathbf{R_1}$ is  or  .

12. The compound of any one of the preceding claims, wherein at least one $\mathbf{R_{1S}}$ is methyl, ethyl, isopropyl, isobutyl, secbutyl, methoxy, ethoxy, -CF_3, -OCF_3, -OCH_2CF_3, F, or Cl.

13. The compound of any one of the preceding claims, wherein $\mathbf{R_2}$ is -$\mathbf{R_{2S}}$.

14. The compound of any one of the preceding claims, wherein $\mathbf{R_2}$ is -(C$\mathbf{X_2X_2}$)-$\mathbf{R_{2S}}$.

15. The compound of any one of the preceding claims, wherein $\mathbf{R_2}$ is -(C$\mathbf{X_2X_2}$)$_2$-$\mathbf{R_{2S}}$.

16. The compound of any one of the preceding claims, wherein each $\mathbf{X_2}$ is H.

17. The compound of any one of the preceding claims, wherein at least one $\mathbf{X_2}$ is C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl is optionally substituted with one or more halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

18. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is 4- to 8-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

19. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is 6-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

20. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is tetrahydropyranyl optionally substituted with one or more C_1-C_6 alkyl, C_1-C_6 haloalkyl, or oxo.

21. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is piperidinyl optionally substituted with one or more C_1-C_6 alkyl, C_1-C_6 haloalkyl, or oxo.

22. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is 5-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6

alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

23. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is tetrahydrofuranyl optionally substituted with one or more C_1-C_6 alkyl, C_1-C_6 haloalkyl, or oxo.

24. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is pyrrolidinyl optionally substituted with one or more C_1-C_6 alkyl, C_1-C_6 haloalkyl, or oxo.

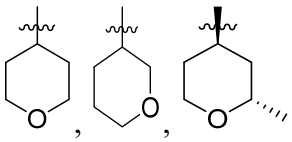
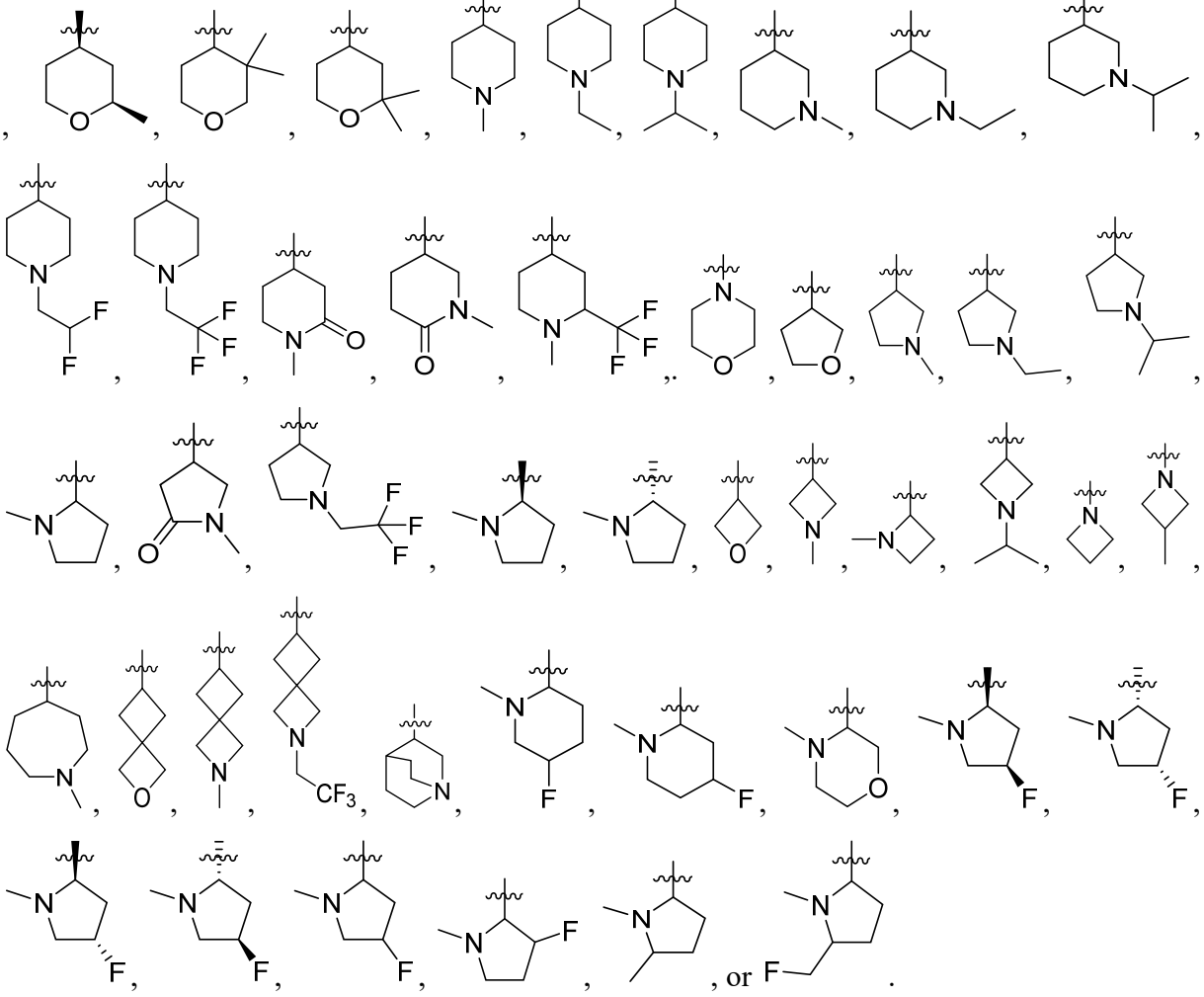
25. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is 4-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

26. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is 7-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

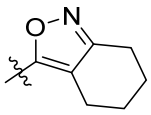
27. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is 8-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

28. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is spiro 7-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_1-C_6 haloalkyl, or oxo.

29. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is bridged heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

30. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is , .

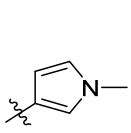
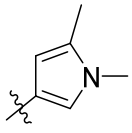
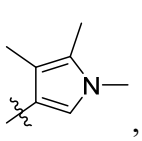
31. The compound of any one of the preceding claims, wherein $\mathbf{R_3}$ is 7- to 12-membered heterocycloalkyl optionally substituted with one or more $\mathbf{R_{3S}}$.

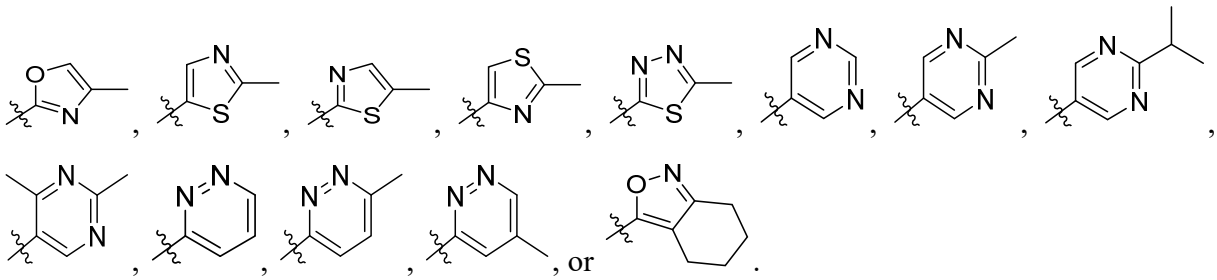
32. The compound of any one of the preceding claims, wherein $\mathbf{R_3}$ is .

33. The compound of any one of the preceding claims, wherein $\mathbf{R_3}$ is 5- or 6-membered heteroaryl optionally substituted with one or more $\mathbf{R_{3S}}$, wherein each $\mathbf{R_{3S}}$ is independently C_1-C_6

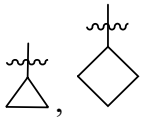
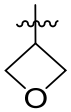
alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, halo, or C_3-C_8 heterocycloalkyl wherein the C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, or C_3-C_8 heterocycloalkyl is optionally substituted with –O(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, halo, or -CN.

34. The compound of any one of the preceding claims, wherein **R_3** is pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, isoxazolyl, furanyl, oxazolyl, isothiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl, pyridazinyl, or 4,5,6,7-tetrahydrobenzo[c]isoxazole, wherein the pyrazolyl, imidazolyl, triazolyl, tetrazolyl, isoxazolyl, furanyl, oxazolyl, isothiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl, pyridazinyl, or 4,5,6,7-tetrahydrobenzo[c]isoxazole is optionally substituted by one or more **R_{3S}**.

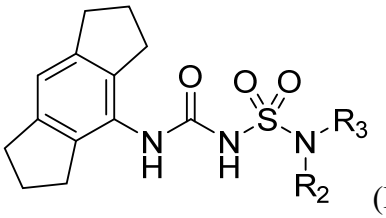
35. The compound of any one of the preceding claims, wherein **R_3** is , , ,

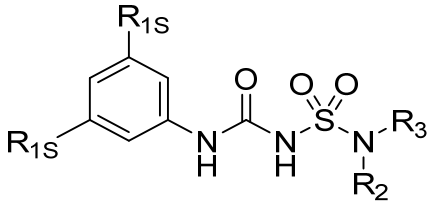


36. The compound of any one of the preceding claims, wherein at least one **R_{3S}** is C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, halo, or C_3-C_8 heterocycloalkyl wherein the C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, or C_3-C_8 heterocycloalkyl is optionally substituted with –O(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, halo, or -CN.

37. The compound of any one of the preceding claims, wherein at least one **R_{3S}** is , , methyl, ethyl, isopropyl, -CH_2OCH_3, -CH_2CF_3, -$CH_2CH_2OCH_3$, -CH_2CN, CH_2CF_2, or -$CH_2CH_2N(CH_3)_2$.

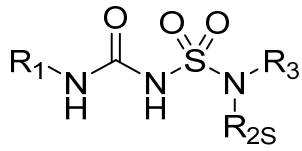
38. The compound of any one of claims 1-37, wherein the compound is of Formula (Ia-1) or (Ia-2):

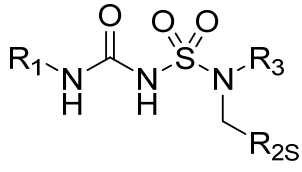

(Ia-1);

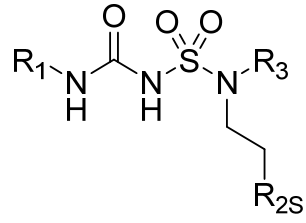

(Ia-2);

or a solvate, or pharmaceutically acceptable salt thereof.

39. The compound of any one of claims 1-37, wherein the compound is of Formula (Ib-1), (Ib-2), or (Ib-3):

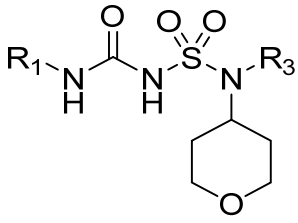

(Ib-1);

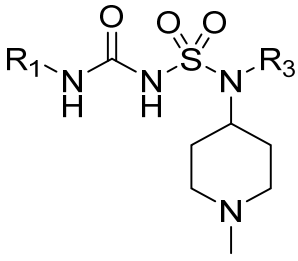

(Ib-2);

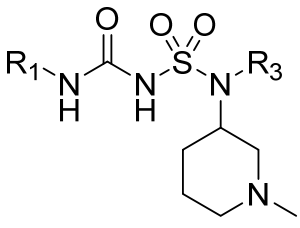

(Ib-3);

or a solvate, or pharmaceutically acceptable salt thereof.

40. The compound of any one of claims 1-37, wherein the compound is of any one of Formulae (Ib-1a), (Ib-1b), or (Ib-1c):

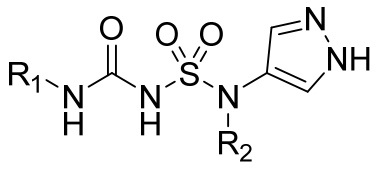

(Ib-1a);


(Ib-1b);

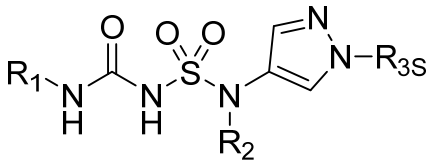

(Ib-1c);

or a solvate, or pharmaceutically acceptable salt thereof.

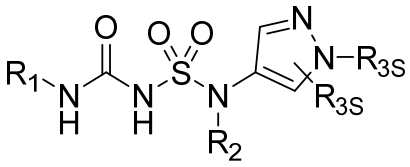
41. The compound of any one of claims 1-37, wherein the compound is of Formula (Ic-1), (Ic-2), (Ic-3), or (Ic-4):



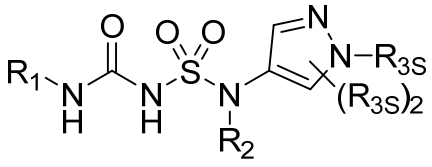
(Ic-1),



(Ic-2),



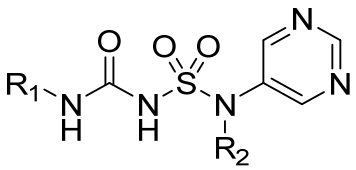
(Ic-3),



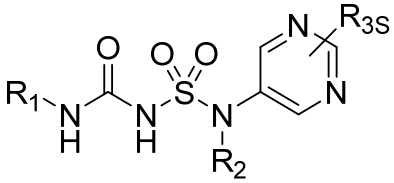
(Ic-4),

or a solvate, or pharmaceutically acceptable salt thereof.

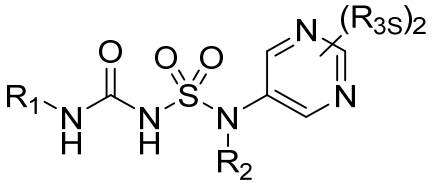
42. The compound of any one of claims 1-37, wherein the compound is of Formula (Ic-5), (Ic-6, (Ic-7), or (Ic-8):

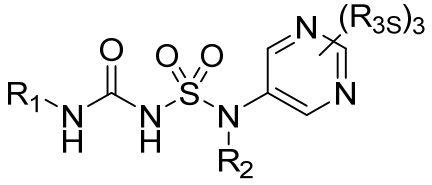


(Ic-5),



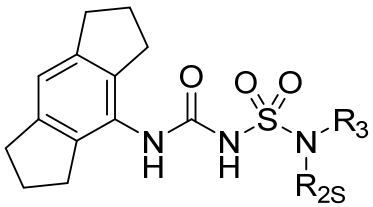
(Ic-6),

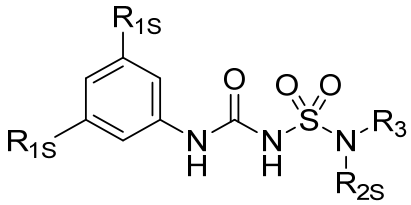

(Ic-7),


(Ic-8),

or a solvate, or pharmaceutically acceptable salt thereof.

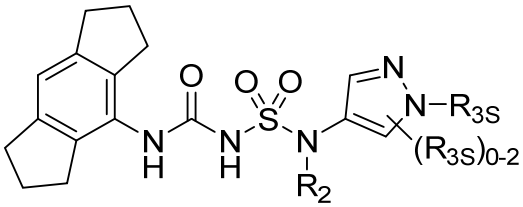
43. The compound of any one of claims 1-37, wherein the compound is of Formula (Iab-1) or (Iab-2):

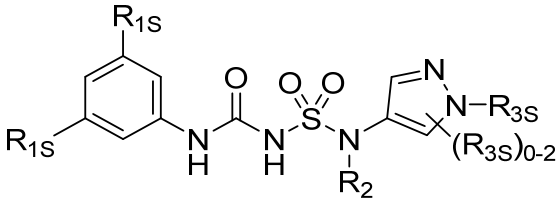

(Iab-1),


(Iab-2),

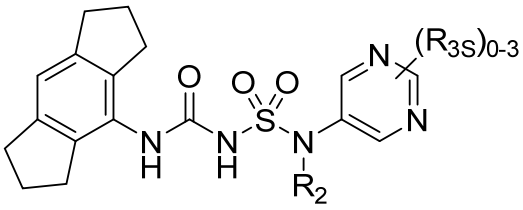
or a solvate, or pharmaceutically acceptable salt thereof.

44. The compound of any one of claims 1-37, wherein the compound is of Formula (Iac-1), (Iac-2), (Iac-3), or (Iac-4):

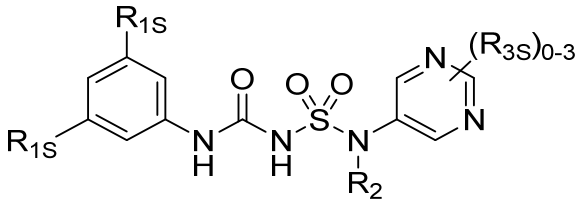

(Iac-1),



(Iac-2),



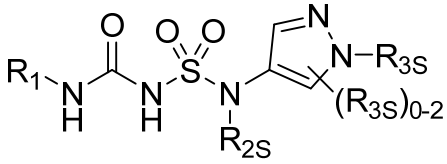
(Iac-3),



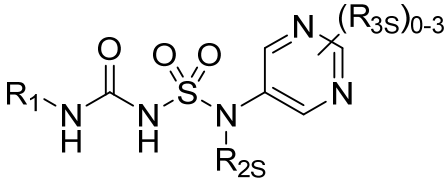
(Iac-4),

or a solvate, or pharmaceutically acceptable salt thereof.

45. The compound of any one of claims 1-37, wherein the compound is of Formula (Ibc-1) or (Ibc-2):



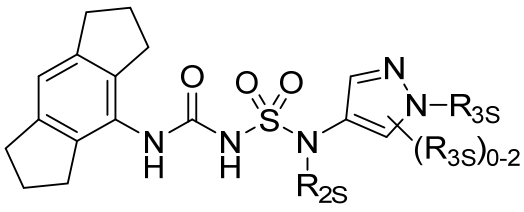
(Ibc-1),



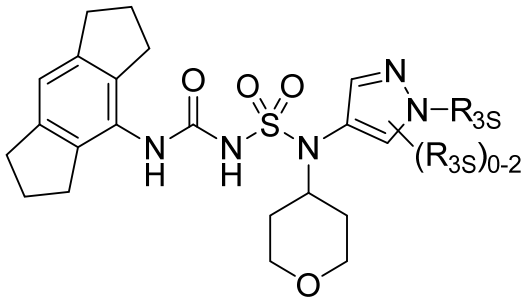
(Ibc-2),

or a solvate, or pharmaceutically acceptable salt thereof.

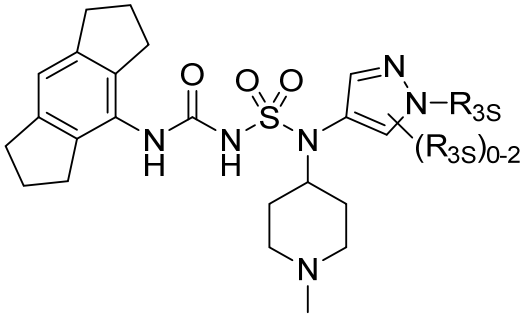
46. The compound of any one of claims 1-37, wherein the compound is of Formula (Iabc-1), (Iabc-1a), or (Iabc-1b):



(Iabc-1);



(Iabc-1a);



(Iabc-1b);

or a solvate, or pharmaceutically acceptable salt thereof.

47. The compound of any one of the preceding claims, being selected from Compound Nos. 1-166 and pharmaceutically acceptable salts thereof.

48. The compound of any one of the preceding claims, being selected from Compound Nos. 1A-166A and pharmaceutically acceptable salts thereof.

49. A compound being an isotopic derivative of the compound of any one of the preceding claims.

50. The compound of claim 49, being a deuterium labeled compound.

51. A process for preparing the compound of claim 1, which comprises one or more steps described in Schemes 1-2.

52. A pharmaceutical composition comprising the compound of any one of claims 1-48 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.

53. The pharmaceutical composition of claim 52, wherein the compound is selected from Compound Nos. 1-166.

54. The pharmaceutical composition of claim 52, wherein the compound is selected from Compound Nos. 1A-166A.

55. A compound of any one of claims 1-48 or a pharmaceutically acceptable salt thereof for use in therapy.

56. Use of compound of any one of claims 1-48 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating or preventing a disease or disorder associated with an implicated inflammasome activity.

57. The use of claim 56, wherein the disease or disorder is an inflammatory disorder, an autoinflammatory disorder, an autoimmune disorder, a neurodegenerative disease, or cancer.

58. The use of claim 56 or claim 57, wherein the disease or disorder is an inflammatory disorder, an autoinflammatory disorder or an autoimmune disorder; optionally, the disease or disorder is selected from cryopyrin-associated auto-inflammatory syndrome (CAPS; e.g., familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), chronic infantile neurological cutaneous and articular (CINCA) syndrome/ neonatal-onset multisystem inflammatory disease (NOMID)), familial Mediterranean fever (FMF), nonalcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), gout, rheumatoid arthritis, osteoarthritis, Crohn's disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), fibrosis, obesity, type 2 diabetes, multiple sclerosis, dermatological disease (e.g., acne) and neuroinflammation occurring in protein misfolding diseases (e.g., Prion diseases).

59. The use of claim 56 or claim 57, wherein the disease or disorder is a neurodegenerative disease; optionally, the disease or disorder is Parkinson's disease or Alzheimer's disease.

60. The use of claim 56 or claim 57, wherein the disease or disorder is cancer; optionally, the cancer is metastasising cancer, brain cancer, gastrointestinal cancer, skin cancer, non-small-cell lung carcinoma, head and neck squamous cell carcinoma or colorectal adenocarcinoma.