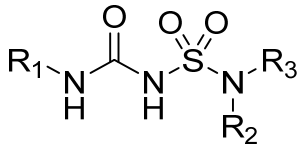
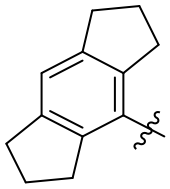
CLAIMS

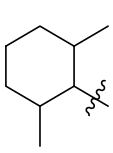
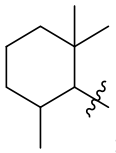
1. A compound of Formula (I):



(I),

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

R_1 is  ; or

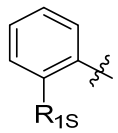
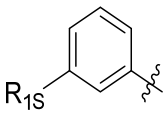
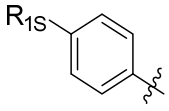
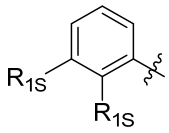
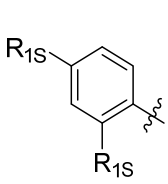
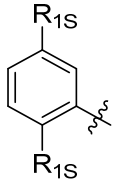
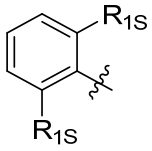
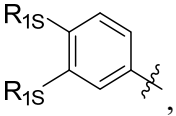
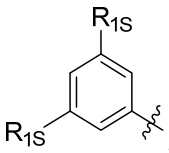
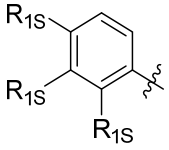
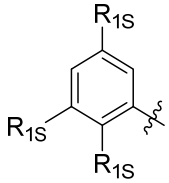
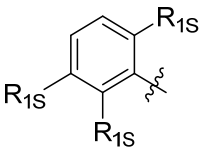
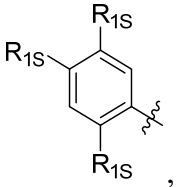
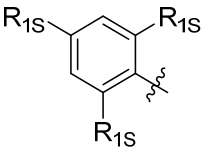
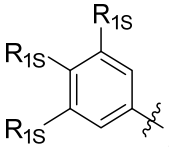
R_1 is  or  : or

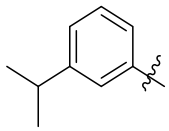
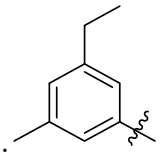
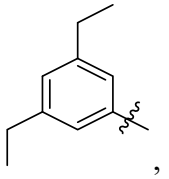
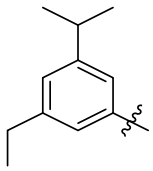
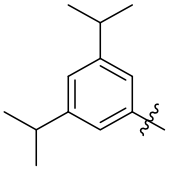
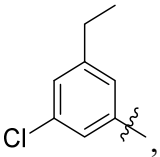
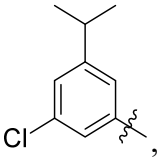
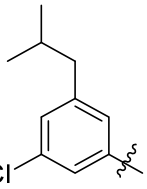
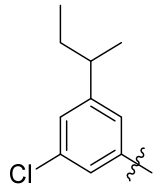
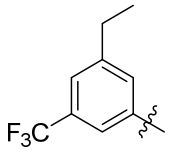
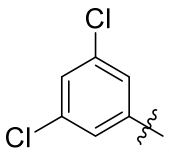
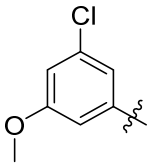
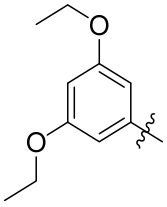
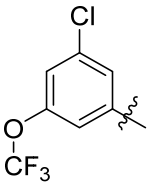
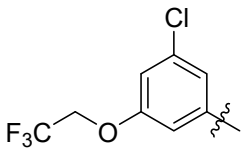
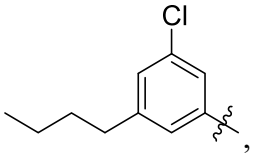
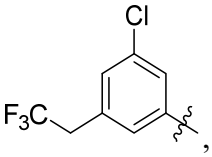
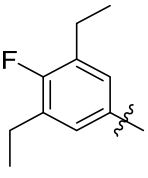
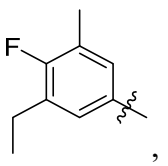
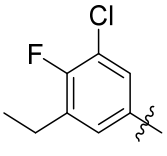
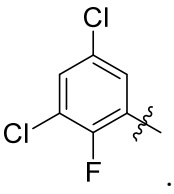
R_1 is phenyl is substituted by one, two, or three **R_{1S}**; wherein each **R_{1S}** is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, or halo;

R_2 is -**R_{2S}**, -(CH_2)-**R_{2S}** or -$(CH_2)_2$-**R_{2S}**;

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 claim 1, wherein $\mathbf{R_1}$ is , , , , , , , , , , , , , , or .

3. The compound of claim 1 or claim 2, wherein $\mathbf{R_1}$ is . , , , , , , , , , , , , , , , , , , , or .

4. 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.

5. 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.

6. 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.

7. 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.

8. 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.

9. 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.

10. 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.

11. 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.

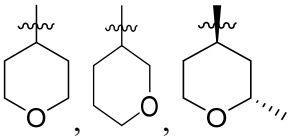
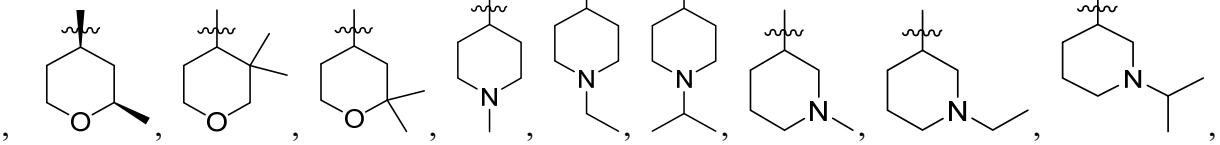
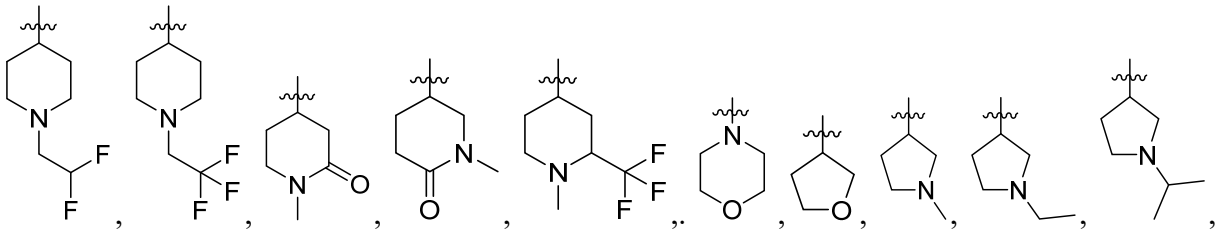
12. The compound of any one of the preceding claims, wherein $\mathbf{R_{2S}}$ is 4-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$,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

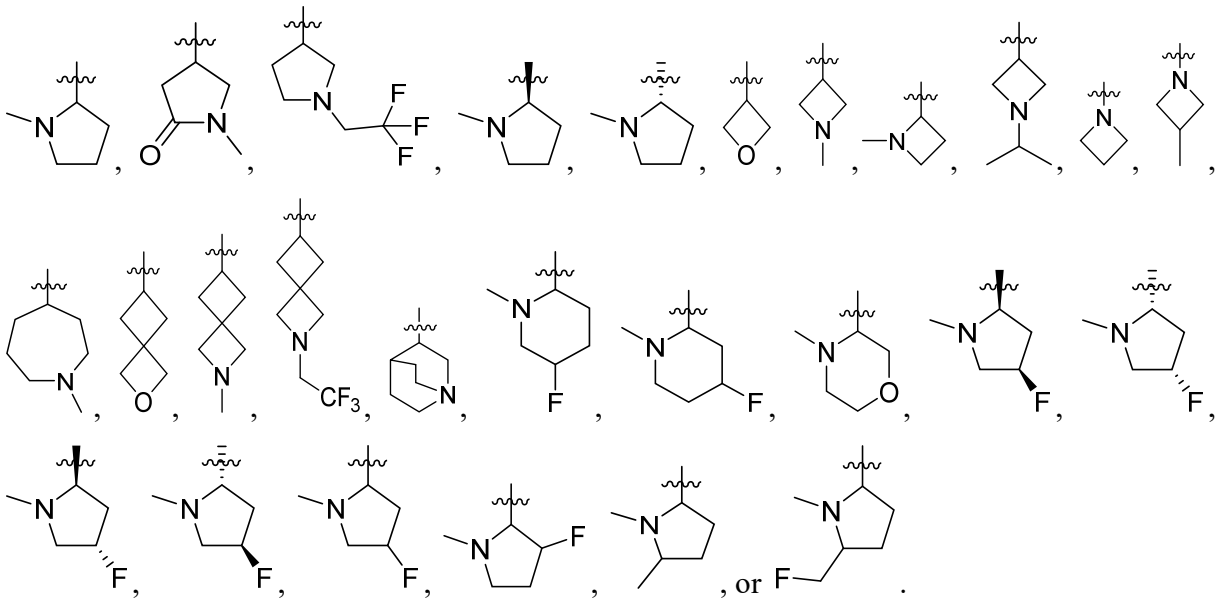
13. The compound of any one of the preceding claims, wherein **R_{2S}** is 7-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, halo, -CN, -OH, -O(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, or oxo.

14. The compound of any one of the preceding claims, wherein **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.

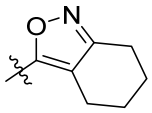
15. The compound of any one of the preceding claims, wherein **R_{2S}** is spiro 7-membered heterocycloalkyl optionally substituted with one or more C_1-C_6 alkyl, C_1-C_6 haloalkyl, or oxo.

16. The compound of any one of the preceding claims, wherein **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.

17. The compound of any one of the preceding claims, wherein **R_{2S}** is 



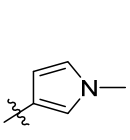
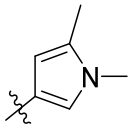
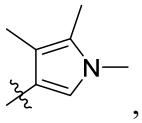


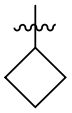
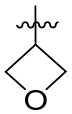
18. The compound of any one of the preceding claims, wherein $\mathbf{R_3}$ is 7- to 12-membered heterocycloalkyl optionally substituted with one or more $\mathbf{R_{3S}}$.

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

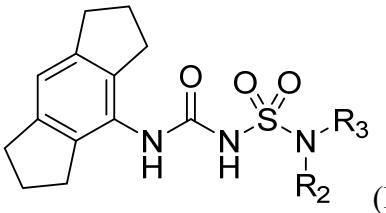
20. The compound of any one of the preceding claims, wherein $\mathbf{R_3}$ is 5- or 6-membered heteroaryl optionally substituted with one or more $\mathbf{R_{3S}}$, wherein each $\mathbf{R_{3S}}$ is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, halo, or C_3-C_8 heterocycloalkyl 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.

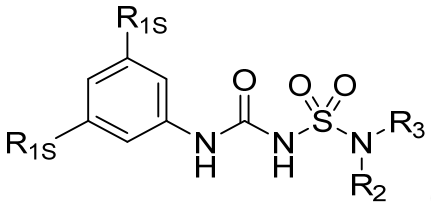
21. The compound of any one of the preceding claims, wherein $\mathbf{R_3}$ is pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, isoxazolyl, furanyl, oxazolyl, isothiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl, pyridazinyl, or 4,5,6,7-tetrahydrobenzo[c]isoxazole, wherein the pyrazolyl, imidazolyl,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

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

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

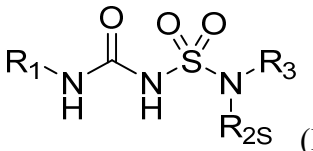
25. The compound of any one of claims 1-24, wherein the compound is of Formula (Ia-1) or (Ia-2):

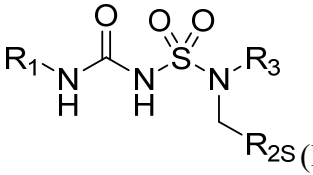
 (Ia-1);

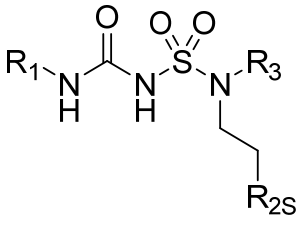
 (Ia-2);

or a solvate, or pharmaceutically acceptable salt thereof.

26. The compound of any one of claims 1-24, wherein the compound is of Formula (Ib-1), (Ib-2), or (Ib-3):

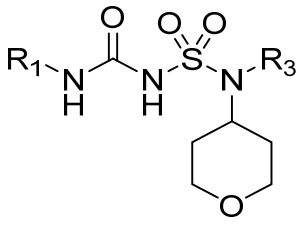
 (Ib-1);

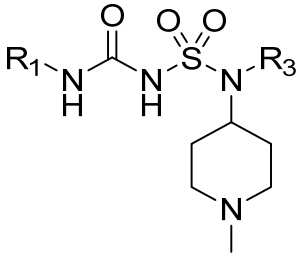
 (Ib-2);

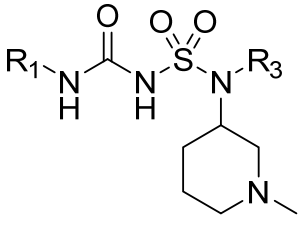

(Ib-3);

or a solvate, or pharmaceutically acceptable salt thereof.

27. The compound of any one of claims 1-24, wherein the compound is of any one of Formulae (Ib-1a), (Ib-1b), or (Ib-1c):

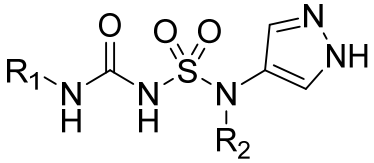

(Ib-1a);

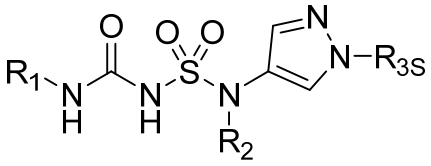

(Ib-1b);


(Ib-1c);

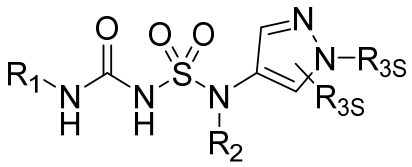
or a solvate, or pharmaceutically acceptable salt thereof.

28. The compound of any one of claims 1-24, wherein the compound is of Formula (Ic-1), (Ic-2), (Ic-3), or (Ic-4):

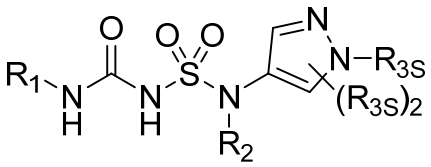

(Ic-1),



(Ic-2),



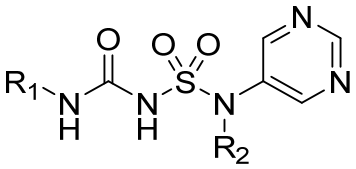
(Ic-3),



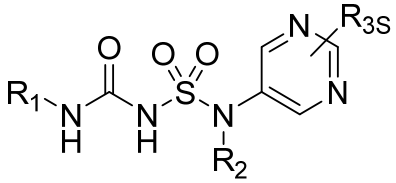
(Ic-4),

or a solvate, or pharmaceutically acceptable salt thereof.

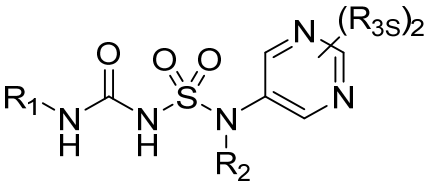
29. The compound of any one of claims 1-24, wherein the compound is of Formula (Ic-5), (Ic-6, (Ic-7), or (Ic-8):



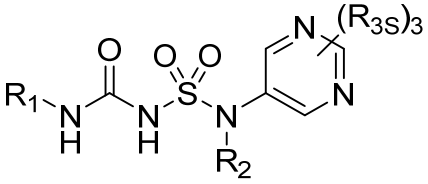
(Ic-5),



(Ic-6),



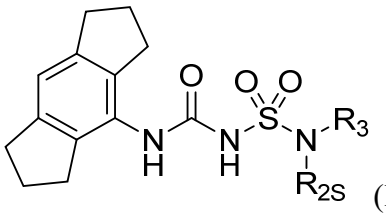
(Ic-7),

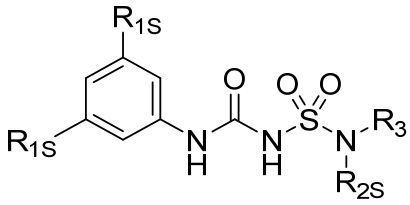


(Ic-8),

or a solvate, or pharmaceutically acceptable salt thereof.

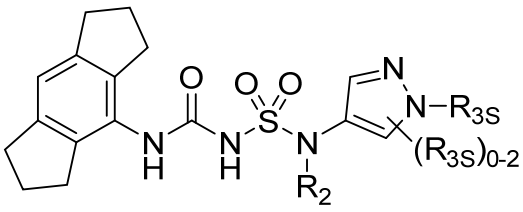
30. The compound of any one of claims 1-24, wherein the compound is of Formula (Iab-1) or (Iab-2):

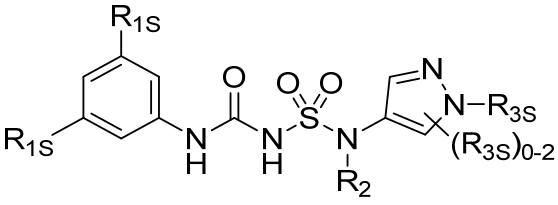

(Iab-1),

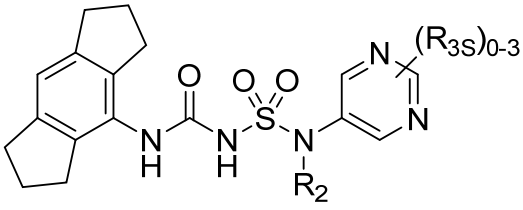

(Iab-2),

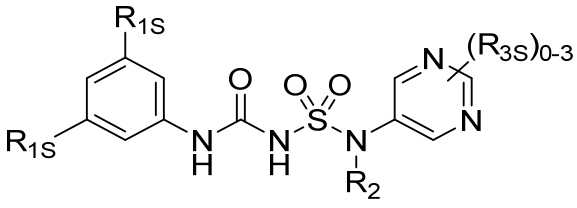
or a solvate, or pharmaceutically acceptable salt thereof.

31. The compound of any one of claims 1-24, wherein the compound is of Formula (Iac-1), (Iac-2), (Iac-3), or (Iac-4):


(Iac-1),

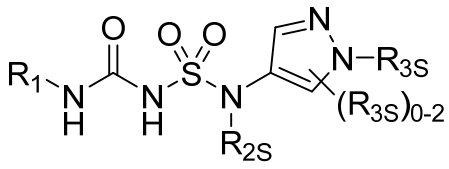

(Iac-2),


(Iac-3),

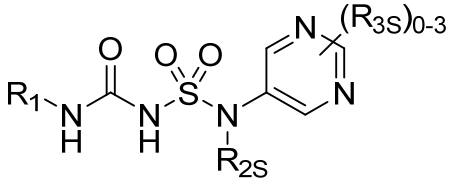

(Iac-4),

or a solvate, or pharmaceutically acceptable salt thereof.

32. The compound of any one of claims 1-24, wherein the compound is of Formula (Ibc-1) or (Ibc-2):



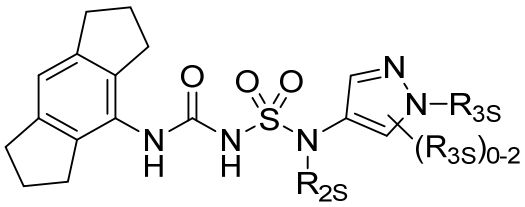
(Ibc-1),



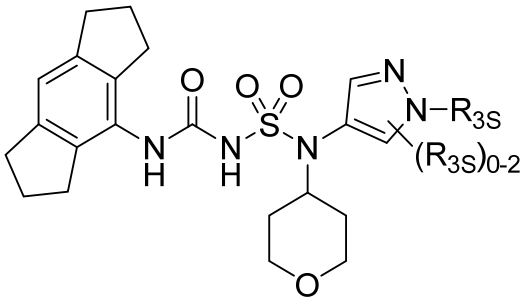
(Ibc-2),

or a solvate, or pharmaceutically acceptable salt thereof.

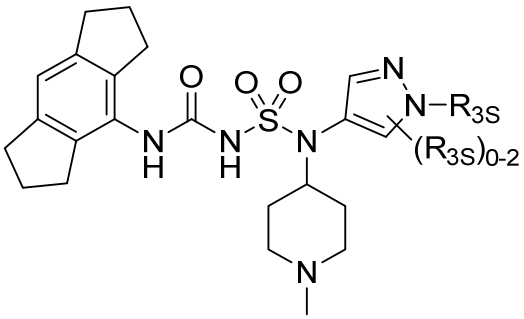
33. The compound of any one of claims 1-24, wherein the compound is of Formula (Iabc-1), (Iabc-1a), or (Iabc-1b):



(Iabc-1);



(Iabc-1a);



(Iabc-1b);

or a solvate, or pharmaceutically acceptable salt thereof.

34. A compound selected from Compound Nos. 1-166 and pharmaceutically acceptable salts thereof.

35. A compound selected from Compound Nos. 1A-166A and pharmaceutically acceptable salts thereof.

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

37. The compound of claim 36, being a deuterium labeled compound.

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

39. A pharmaceutical composition comprising the compound of any one of claims 1-35 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.

40. The pharmaceutical composition of claim 39, wherein the compound is selected from Compound Nos. 1-166.

41. The pharmaceutical composition of claim 39, wherein the compound is selected from Compound Nos. 1A-166A.

42. A compound of any one of claims 1-35 or a pharmaceutically acceptable salt thereof for use in therapy.

43. Use of compound of any one of claims 1-35 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating or preventing a disease or disorder which is an inflammatory disorder, an autoinflammatory disorder, an autoimmune disorder, a neurodegenerative disease, or cancer.

44. The use of claim 43, 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).

45. The use of claim 43, wherein the disease or disorder is a neurodegenerative disease; optionally, the disease or disorder is Parkinson's disease or Alzheimer's disease.

46. The use of claim 43, 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.