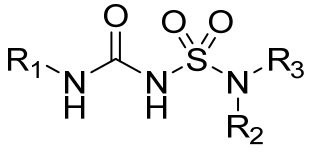
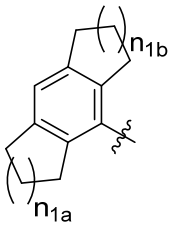
CLAIMS:

1. A compound of Formula (I):



(I),

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

$R_1$ is  , wherein $n_{1a}$ and $n_{1b}$ each independently are 0 or 1;

$R_2$ is $-(CH_2)_{n2}-R_{2S}$, wherein $n_2$ is 1 or 2;

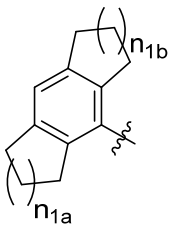
$R_{2S}$ is 4- to 8-membered heterocycloalkyl in which at least one heteroatom is O, wherein the 4- to 8-membered heterocycloalkyl is optionally substituted with one or more $R_{2SS}$;

each $R_{2SS}$ independently is $C_1$-$C_6$ 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;

$R_3$ is 5- or 6-membered heteroaryl optionally substituted with one or more $R_{3S}$; and

each $R_{3S}$ independently is halo, $C_1$-$C_6$ alkyl, or $C_1$-$C_6$ haloalkyl.

2. The compound of any one of the preceding claims, wherein:

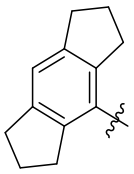
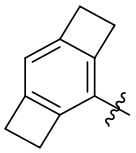
$R_1$ is  , wherein $n_{1a}$ and $n_{1b}$ each independently are 0 or 1;

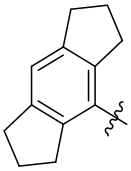
$R_2$ is $-(CH_2)_{n2}-R_{2S}$, wherein $n_2$ is 1 or 2;

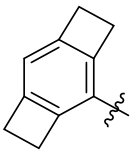
$R_{2S}$ is 4- to 8-membered heterocycloalkyl in which at least one heteroatom is O, wherein the 4- to 8-membered heterocycloalkyl is optionally substituted with one or more -OH; and

$R_3$ is 5- or 6-membered heteroaryl optionally substituted with one or more $C_1$-$C_6$ alkyl.

3. The compound of any one of the preceding claims, wherein both of $n_{1a}$ and $n_{1b}$ are 1.

4. The compound of any one of the preceding claims, wherein $R_1$ is  or .

5. The compound of any one of the preceding claims, wherein $R_1$ is .

6. The compound of any one of the preceding claims, wherein $R_1$ is .

7. The compound of any one of the preceding claims, wherein $R_2$ is $-CH_2-R_{2S}$.

8. The compound of any one of the preceding claims, wherein $R_2$ is $-CH_2-R_{2S}$; and $R_{2S}$ is tetrahydrofuranyl or tetrahydropyranyl, wherein the tetrahydrofuranyl or tetrahydropyranyl is optionally substituted with one or more -OH.

9. The compound of any one of the preceding claims, wherein $R_2$ is $-(CH_2)_2-R_{2S}$.

10. The compound of any one of the preceding claims, wherein $R_2$ is $-(CH_2)_2-R_{2S}$; and $R_{2S}$ is tetrahydrofuranyl or tetrahydropyranyl, wherein the tetrahydrofuranyl or tetrahydropyranyl is optionally substituted with one or more –OH.

11. The compound of any one of the preceding claims, wherein $R_{2S}$ is 5- to 6-membered heterocycloalkyl in which at least one heteroatom is O, wherein the 5- to 6-membered heterocycloalkyl is optionally substituted with one or more $R_{2SS}$.

12. The compound of any one of the preceding claims, wherein $R_{2S}$ is 5- to 6-membered heterocycloalkyl having one heteroatom, wherein the heteroatom is O, and wherein the 5- to 6-membered heterocycloalkyl is optionally substituted with one or more $R_{2SS}$.

13. The compound of any one of the preceding claims, wherein $R_{2S}$ is 5-membered heterocycloalkyl having one heteroatom, wherein the heteroatom is O, and wherein the 5-membered heterocycloalkyl is optionally substituted with one or more $R_{2SS}$.

14. The compound of any one of the preceding claims, wherein $R_{2S}$ is 6-membered heterocycloalkyl having one heteroatom, wherein the heteroatom is O, and wherein the 6-membered heterocycloalkyl is optionally substituted with one or more $R_{2SS}$.

15. The compound of any one of the preceding claims, wherein at least one $R_{2SS}$ is -OH.

16. The compound of any one of the preceding claims, wherein $R_{2S}$ is tetrahydrofuranyl or tetrahydropyranyl, wherein the tetrahydrofuranyl or tetrahydropyranyl is optionally substituted with one or more $R_{2SS}$.

17. The compound of any one of the preceding claims, wherein $R_{2S}$ is tetrahydrofuranyl or tetrahydropyranyl, wherein the tetrahydrofuranyl or tetrahydropyranyl is optionally substituted with one or more -OH.

18. The compound of any one of the preceding claims, wherein $R_{2S}$ is tetrahydrofuranyl optionally substituted with one or more -OH.

19. The compound of any one of the preceding claims, wherein $R_{2S}$ is tetrahydrofuranyl.

20. The compound of any one of the preceding claims, wherein $R_{2S}$ is tetrahydrofuranyl substituted with one or more -OH.

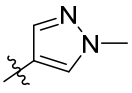
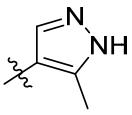
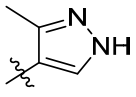
21. The compound of any one of the preceding claims, wherein $R_{2S}$ is tetrahydropyranyl.

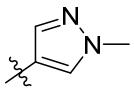
22. The compound of any one of the preceding claims, wherein $R_{2S}$ is tetrahydropyranyl substituted with one or more -OH.

23. The compound of any one of the preceding claims, wherein $R_3$ is 5- or 6-membered heteroaryl substituted with one or more $R_{3S}$.

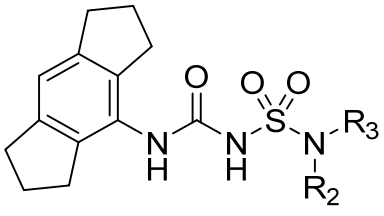
24. The compound of any one of the preceding claims, wherein $R_3$ is 5- or 6-membered heteroaryl substituted with one or more $C_1$-$C_6$ alkyl.

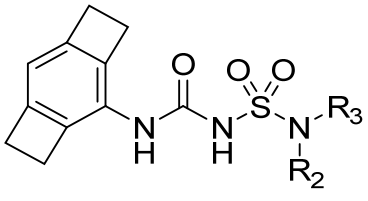
25. The compound of any one of the preceding claims, wherein $R_3$ is pyrazolyl substituted with one or more $C_1$-$C_6$ alkyl.

26. The compound of any one of the preceding claims, wherein $R_3$ is , , or .

27. The compound of any one of the preceding claims, wherein $R_3$ is .

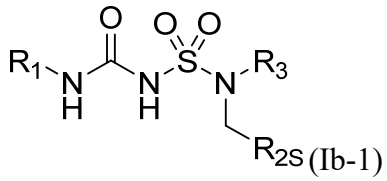
28. The compound of any one of the preceding claims, wherein the compound is of Formula (Ia-1) or (Ia-2):

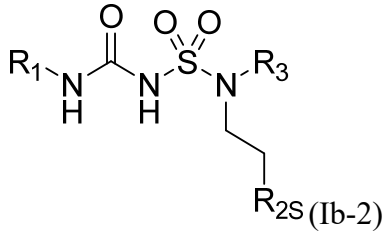

(Ia-1)


(Ia-2)

or a prodrug, solvate, or pharmaceutically acceptable salt thereof.

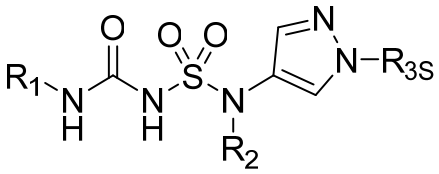
29. The compound of any one of the preceding claims, wherein the compound is of Formula (Ib-1) or (Ib-2):

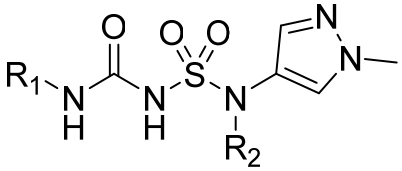

(Ib-1)

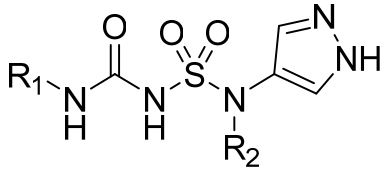

(Ib-2)

or a prodrug, solvate, or pharmaceutically acceptable salt thereof.

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

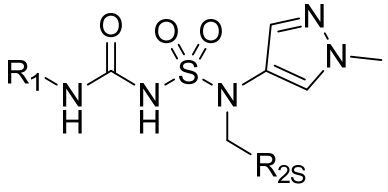

(Ic-1),

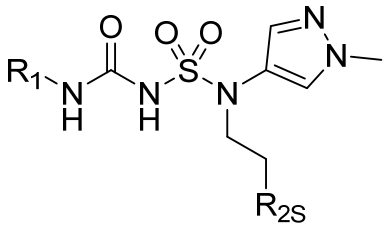

(Ic-2),


(Ic-3),

or a prodrug, solvate, or pharmaceutically acceptable salt thereof.

31. The compound of any one of the preceding claims, wherein the compound is of Formula (Id-1) or (Id-2):

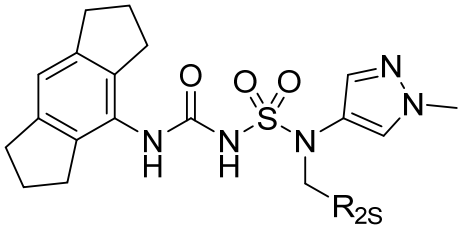

(Id-1),



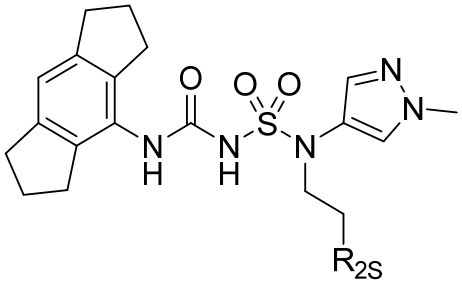
(Id-2),

or a prodrug, solvate, or pharmaceutically acceptable salt thereof.

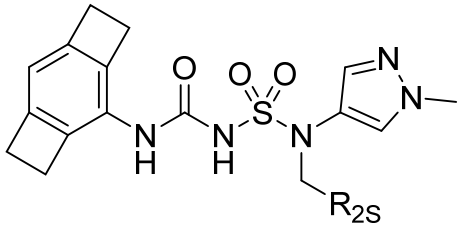
32. The compound of any one of the preceding claims, wherein the compound is of Formula (Ie-1), (Ie-2), (Ie-3), or (Ie-4):



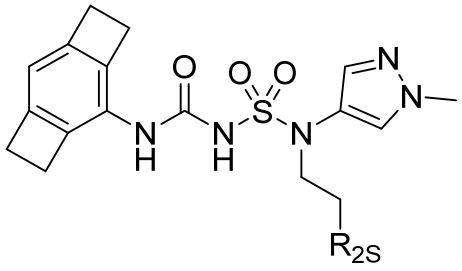
(Ie-1),



(Ie-2),



(Ie-3),



(Ie-4),

or a prodrug, solvate, or pharmaceutically acceptable salt thereof.

33. The compound of any one of the preceding claims, being selected from Compound Nos. 1, 1A, 1B, 2, 2A, 2B, 3, 3A, 3B, 4, 4A, 4B, 5, 5A, 5B, 6, 6A, 6B, 7A, 7B, 8A, and 8B, and prodrugs and pharmaceutically acceptable salts thereof.

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

35. A compound obtainable by, or obtained by, a method described herein;
optionally, the method comprises one or more steps described in Schemes 1-3.

36. An intermediate obtained by a method for preparing the compound of any one of the preceding claims;
optionally, the intermediate is selected from the intermediates described in Examples 1-12.

37. A pharmaceutical composition comprising the compound of any one of the preceding claims and a pharmaceutically acceptable diluent or carrier.

~~38. A method of inhibiting inflammasome activity, comprising contacting a cell with an effective amount of the compound of any one of the preceding claims; optionally, the inflammasome is NLRP3 inflammasome, and the activity is *in vitro* or *in vivo*.~~

~~39. A method of treating or preventing a disease or disorder in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the compound of any one of the preceding claims, or the pharmaceutical composition of any one of the preceding claims.~~

~~40.~~38. The compound of any one of claims 1-35, the intermediate of claim 36, or the pharmaceutical composition of claim 37~~anyone of the preceding claims~~, for use in inhibiting inflammasome activity; optionally, the inflammasome is NLRP3 inflammasome, and the activity is *in vitro* or *in vivo*.

~~41.~~39. The compound of any one of claims 1-35, the intermediate of claim 36, or the pharmaceutical composition of claim 37~~anyone of the preceding claims~~, for use in treating or preventing a disease or disorder.

~~42.~~40. Use of the compound of any one of claims 1-35, the intermediate of claim 36, or the pharmaceutical composition of claim 37~~the preceding claims~~ in the manufacture of a medicament for inhibiting inflammasome activity; optionally, the inflammasome is NLRP3 inflammasome, and the activity is *in vitro* or *in vivo*.

~~43.~~41. Use of the compound of any one of claims 1-35, the intermediate of claim 36, or the pharmaceutical composition of claim 37~~the preceding claims~~ in the manufacture of a medicament for treating or preventing a disease or disorder associated with an implicated inflammasome activity; optionally, the disease or disorder is a disease or disorder in which inflammasome activity is implicated.

~~44. The method, compound, pharmaceutical composition, or use of any one of the preceding claims, wherein the disease or disorder is associated with an implicated inflammasome activity; optionally, the disease or disorder is a disease or disorder in which inflammasome activity is implicated.~~

~~45.~~42. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~ claim 41, wherein the disease or disorder is an inflammatory disorder, an autoinflammatory disorder, an autoimmune disorder, a neurodegenerative disease, or cancer.

~~46.~~43. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 41 or 42, 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).

~~47.~~44. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 41 or 42, wherein the disease or disorder is a neurodegenerative disease; optionally, the disease or disorder is Parkinson's disease or Alzheimer's disease.

~~48.~~45. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 41 or 42, 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.

~~49.~~46. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 41 or 42, wherein the disease or disorder is an inflammatory disease.

~~50.~~47. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 46, wherein the inflammatory disease is associated with an infection.

~~51.~~48. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 47, wherein the infection is a viral infection.

~~52.~~49. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 48, wherein the viral infection is caused by a single stranded RNA virus.

~~53.~~50. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 49, wherein the single stranded RNA virus is a coronavirus.

~~54.~~51. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 50, wherein the coronavirus is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV 2).

~~55.~~52. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 46, wherein the inflammatory disease is associated with an infection by SARS-CoV 2 leading to 2019 novel coronavirus disease(COVID-19).

~~56.~~53. The ~~method, compound, pharmaceutical composition or~~ use of ~~any one of the preceding claims~~claim 46, wherein the inflammatory disease comprises cytokine release syndrome (CRS).

~~57.~~54. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 53, wherein the CRS is associated with COVID-19.

~~58.~~55. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 53, wherein the CRS is associated with an adoptive cell therapy.

~~59.~~56. The ~~method, compound, pharmaceutical composition, or~~ use of ~~any one of the preceding claims~~claim 55, wherein the adoptive cell therapy comprises chimeric antigen receptor T cell (CAR-T) therapy.