treatment of CAPS, and these biologic agents have been used in clinical trials for other IL-1β-associated diseases.

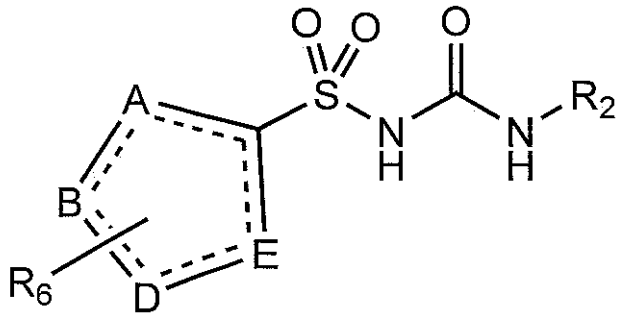
[0013] Several small molecules have been shown to inhibit the NLRP3 inflammasome. Glyburide inhibits IL-1β production at micromolar concentrations in response to the activation of NLRP3 but not NLRC4 or NLRP1.Other previously characterised NLRP3 inhibitors include parthenolide, 3,4-methylenedioxy-β-nitrostyrene and dimethyl sulfoxide (DMSO), although these agents have limited potency and are nonspecific.

[0014] Certain diarylsulfonylurea-containing compounds have been identified as cytokine release inhibitory drugs (CRIDs) (Perregaux et al.; J. Pharmacol. Exp. Ther. 299, 187-197, 2001). CRIDs are a class of diarylsulfonylurea containing compounds that inhibit the post-translational processing of IL-1β. Post-translational processing of IL-1β is accompanied by activation of caspase-1 and cell death. CRIDs arrest activated monocytes so that caspase-1 remains inactive and plasma membrane latency is preserved.

[0015] There is a need to provide compounds with improved pharmacological and/or physiological and or physicochemical properties and/or those that provide a useful alternative to known compounds.

SUMMARY

[0016] In one aspect, the present invention refers to a compound of formula (II), or a pharmaceutically acceptable salt or solvate thereof:



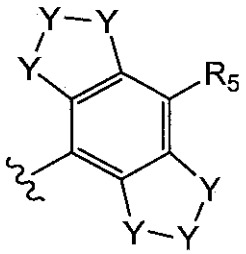
Formula (II)

wherein A, B, D and E are independently selected from C, N, O, S and Se, but at least one thereof is C and at least one thereof is N;

each dashed line may represent a bond;

each incidence of R_6 is independently selected from the group consisting of hydrogen, halide, cyano, C_1-C_6 alkyl, C_1-C_6 alkylamino, C_1-C_6 alkylhydroxy, C_3-C_6 cycloalkyl, alkylphenyl, phenyl, benzyl, C_1-C_6 ester, C_2-C_6 alkenyl, C_1-C_6 trifluoroalkyl and C_1-C_6 alkoxy, each of which may be optionally substituted, as appropriate, or R_6 may be a fluorescent group; and

R_2 is selected from a 2,6-dialkylphenyl, a 2,6-dialkyl-4-halophenyl, a 2,6-dicycloalkylphenyl, a 2,6-dicycloalkyl-4-halophenyl, and:



wherein each incidence of Y is independently selected from C, N, S and O, which may be optionally substituted as appropriate; and

R_5 is selected from the group consisting of hydrogen, halo, cyano, amide, sulphonamide, acyl, hydroxyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_5

cycloalkyl, C_1-C_6 alkoxy all of which groups may be optionally substituted, as appropriate, with halo, cyano or C_1-C_6 alkoxy.

[0016a] In another aspect, the present invention refers to a pharmaceutical composition comprising a compound of the present invention, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier, diluent and/or excipient.

[0016b] In yet another aspect, the present invention refers to the use of the compound or the pharmaceutically effective salt or solvate of the present invention, or use of the pharmaceutical composition of the present invention, in the manufacture of a medicament for the treatment, prevention or diagnosis of:

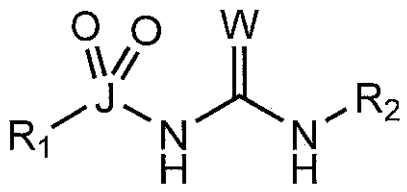
(a) an inflammatory disease, disorder or condition or an autoimmune disease, disorder or condition; and/or

(b) a cancer, tumour or other malignancy; and/or

(c) a disease, disorder or condition selected from the group consisting of constitutive inflammation including the cryopyrin-associated periodic syndromes (CAPS): Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS) and neonatal-onset multisystem inflammatory disease (NOMID); including autoinflammatory diseases: familial Mediterranean fever (FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D and periodic fever syndrome (HIDS), deficiency of interleukin 1 receptor (DIRA) antagonist, 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, and developmental delay (SIFD); Sweet's syndrome, chronic nonbacterial osteomyelitis (CNO), chronic recurrent multifocal osteomyelitis

(CRMO) and synovitis, acne, pustulosis, hyperostosis, osteitis syndrome (SAPHO); autoimmune diseases including multiple sclerosis (MS), type-1 diabetes, psoriasis, rheumatoid arthritis, Behcet's disease, Sjogren's syndrome and Schnitzler syndrome; respiratory diseases including chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis and cystic fibrosis; central nervous system diseases including Parkinson's disease, Alzheimer's disease, motor neuron disease, Huntington's disease, cerebral malaria and brain injury from pneumococcal meningitis; metabolic diseases including Type 2 diabetes, atherosclerosis, obesity, gout, pseudo-gout; ocular diseases including those of the ocular epithelium, age-related macular degeneration (AMD), corneal infection, uveitis and dry eye; kidney disease including chronic kidney disease, oxalate nephropathy and diabetic nephropathy; liver disease including non-alcoholic steatohepatitis and alcoholic liver disease; inflammatory reactions in skin including contact hypersensitivity and sunburn; inflammatory reactions in the joints including osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis; viral infections including alpha virus including Chikungunya and Ross River, and flavivirus including Dengue and Zika viruses, flu, HIV; hidradenitis suppurativa (HS) and other cyst-causing skin diseases; cancers including lung cancer metastasis, pancreatic cancers, gastric cancers, myelodisplastic syndrome, leukemia; polymyositis; stroke; myocardial infarction; Graft versus Host Disease; hypertension; colitis; helminth infection; bacterial infection; abdominal aortic aneurism; wound healing; depression, psychological stress; pericarditis including Dressler's syndrome, ischaemia reperfusion injury and any disease where an individual has been determined to carry a germline or somatic non-silent mutation in NLRP3.

[0016c] According to a first example of thedisclosure, there is provided a compound of formula (I), or a pharmaceutically acceptable salt, solvate or prodrug thereof:



Formula (I)

wherein, W is selected from O, S and Se;

J is selected from S and Se;

R_1 is selected from the group consisting of cycloalkyl, aryl, heteroaryl and heterocyclyl, all of which may be optionally substituted;

R_2 is selected from the group consisting of cycloalkyl, aryl, heteroaryl and heterocyclyl, all of which may be optionally substituted; and

both R_1 is directly bonded to J and R_2 is directly bonded to the adjacent nitrogen, via a carbon atom.

[0017] According to a second example of the disclosure there is provided a pharmaceutical composition comprising a compound of the first example, or a pharmaceutically acceptable salt, solvate or prodrug thereof, and a pharmaceutically acceptable carrier, diluent and/or excipient.

[0018] A third example of the disclosure resides in 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 first example, or a pharmaceutically effective salt, solvate or prodrug thereof, or the pharmaceutical composition of the second example to thereby treat or prevent the disease disorder or condition.

[0019] A fourth example of the disclosure provides for a compound of the first example, or a pharmaceutically effective salt, solvate or prodrug thereof, or the pharmaceutical composition of the second example for use in the treatment or prevention of a disease, disorder or condition.

[0020] A fifth example of the disclosure provides for use of a compound of the first example, or a pharmaceutically effective salt, solvate or prodrug thereof, in the manufacture of a medicament for the treatment or prevention of a disease, disorder or condition.

[0021] In one example, the disease, disorder or condition is responsive to inhibition of activation of the NLRP3 inflammasome.

[0022] In particular non-limiting examples of the above examples, the disease, disorder or condition is a disease, disorder or condition of the immune system, the cardiovascular system, the endocrine system, the gastrointestinal tract, the renal system, the respiratory system, the central nervous system, is a cancer or other malignancy and/or is caused by or associated with a pathogen.

[0023] In a sixth example of the disclosure there is provided a method of diagnosing a disease, disorder or condition in a mammal including the step of administering a labelled compound of formula (I), (Ia), (Ib), (Ic) or (II), or a pharmaceutically effective salt, solvate or prodrug thereof, to the mammal or to a biological sample obtained from the mammal to facilitate diagnosis of the disease disorder or condition in the mammal.

[0024] A seventh example of the disclosure resides in a method of modulating the activity of a biological target comprising the step of exposing the biological target to a compound of the first example, or a pharmaceutically acceptable salt thereof.

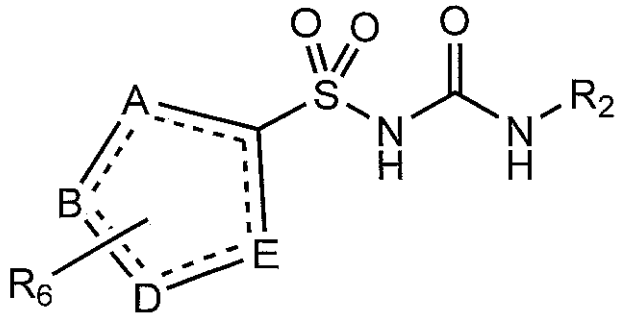
[0025] The biological target may be selected from the group consisting of the NLRP3 inflammasome, IL-1β, IL-17, IL-18, IL-1α, IL-37, IL-33 and Th17 cells.

[0026] The various features and embodiments of the present invention, referred to in individual sections above apply, as appropriate, to other sections, *mutatis mutandis*. Consequently features specified in one section may be combined with features specified in other sections as appropriate.

[0027] Further features and advantages of the present invention will become apparent from the following detailed description.

CLAIMS

1. A compound of formula (II), or a pharmaceutically acceptable salt or solvate thereof:



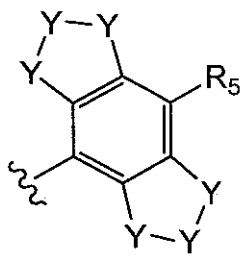
Formula (II)

wherein A, B, D and E are independently selected from C, N, O, S and Se, but at least one thereof is C and at least one thereof is N;

each dashed line may represent a bond;

each incidence of R_6 is independently selected from the group consisting of hydrogen, halide, cyano, C_1-C_6 alkyl, C_1-C_6 alkylamino, C_1-C_6 alkylhydroxy, C_3-C_6 cycloalkyl, alkylphenyl, phenyl, benzyl, C_1-C_6 ester, C_2-C_6 alkenyl, C_1-C_6 trifluoroalkyl and C_1-C_6 alkoxy, each of which may be optionally substituted, as appropriate, or R_6 may be a fluorescent group; and

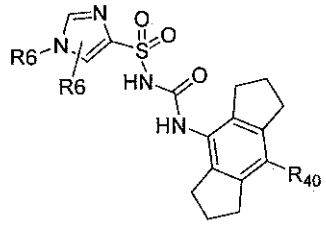
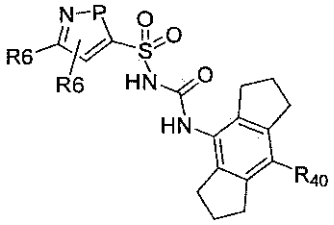
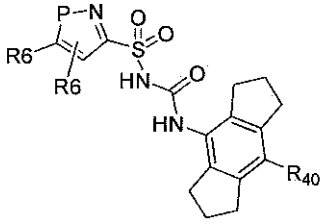
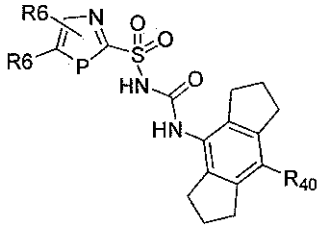
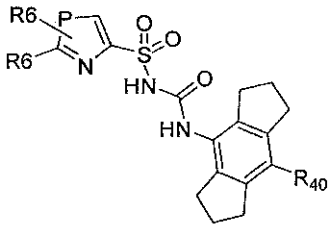
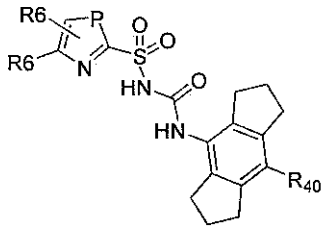
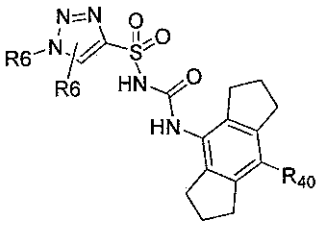
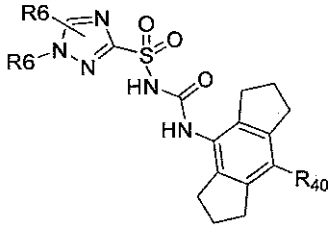
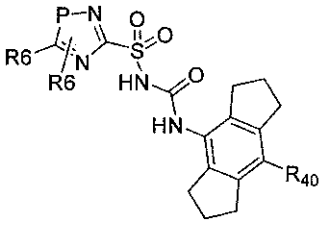
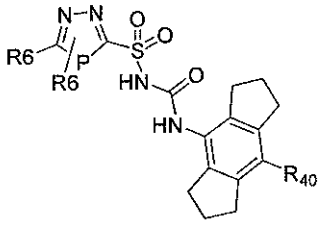
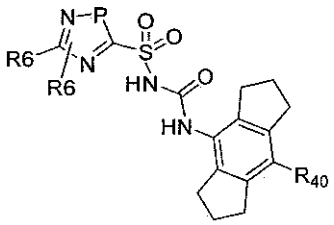
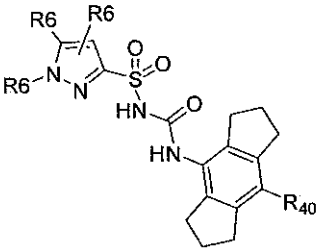
R_2 is selected from a 2,6-dialkylphenyl, a 2,6-dialkyl-4-halophenyl, a 2,6-dicycloalkylphenyl, a 2,6-dicycloalkyl-4-halophenyl, and:

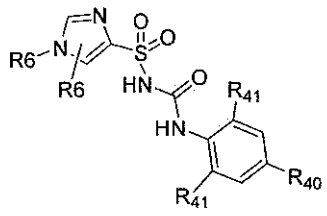
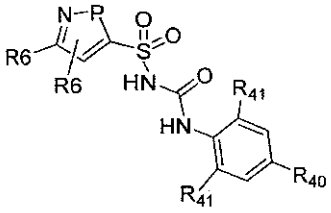
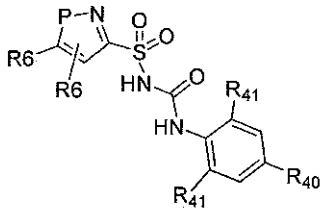
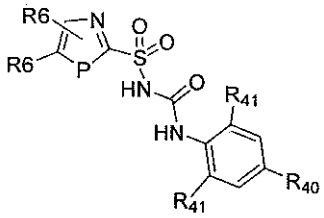
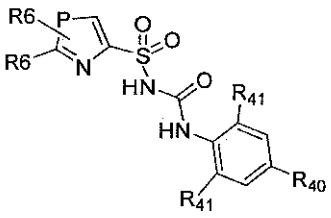
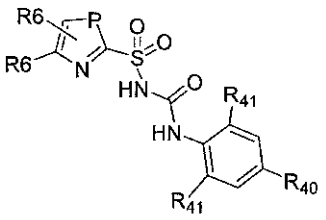
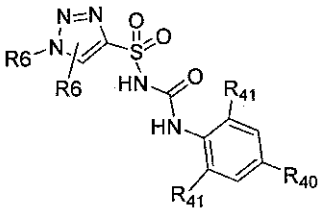
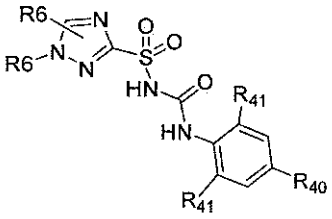
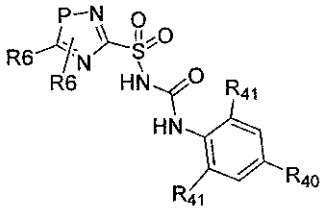
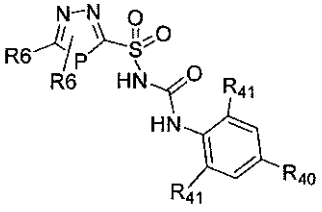
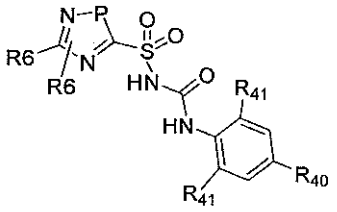
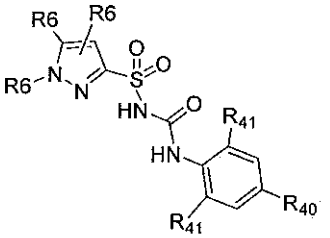


wherein each incidence of Y is independently selected from C, N, S and O, which may be optionally substituted as appropriate; and

R_5 is selected from the group consisting of hydrogen, halo, cyano, amide, sulphonamide, acyl, hydroxyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_5 cycloalkyl, C_1-C_6 alkoxy all of which groups may be optionally substituted, as appropriate, with halo, cyano or C_1-C_6 alkoxy.

2. The compound of claim 1, wherein the compound of formula (II) is selected from the group consisting of:

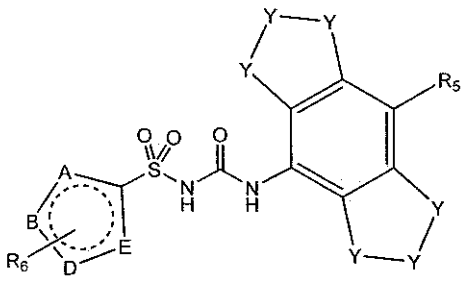
wherein R_{40} is selected from H, alkyl and halo;

R_{41} is selected from H, alkyl and cycloalkyl;

each incidence of P is independently selected from C, O or S; and

each incidence of R_6, when present, is independently selected from those groups defined in claim 1.

3. The compound of any one of the preceding claims, wherein the compound is a compound of formula (IIb), or a pharmaceutically acceptable salt or solvate thereof:



Formula (IIb)

wherein Y and R_5 are as defined in claim 1 or claim 2;

A, B, D and E are selected from N and C and at least two of A, B, D and E are N;

each incidence of R_6 is independently selected from the group consisting of hydrogen, halide, cyano, C_1-C_6 alkyl, C_1-C_6 alkylamino, C_1-C_6 alkylhydroxy, C_3-C_6 cycloalkyl, alkylphenyl, phenyl, benzyl, C_1-C_6 ester, C_2-C_6 alkenyl, C_1-C_6 trifluoroalkyl and C_1-C_6 alkoxy, each of which may be optionally substituted.

4. The compound of any one of the preceding claims, wherein at least two of A, B, D and E are N.

5. The compound of any one of the preceding claims, wherein A, B, D and E are selected from N and C.

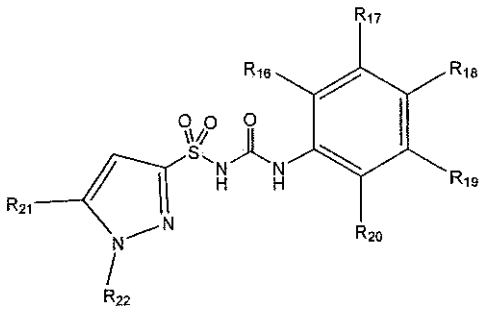
6. The compound of any one of the preceding claims, wherein A is C and at least two of B, D and E are N.

7. The compound of any one of the preceding claims, wherein A, B, D and E form a ring selected from a pyrazole, an imidazole, a triazole, and a tetrazole.

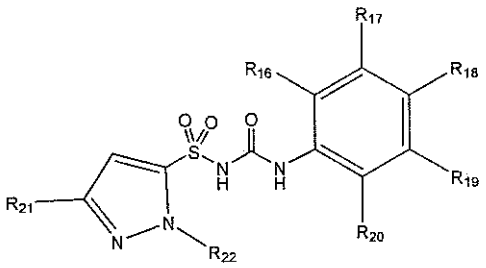
8. The compound of any one of the preceding claims, wherein A, B, D and E form a ring selected from a pyrazole and an imidazole ring.

9. The compound of any one of the preceding claims, wherein A, B, D and E form a pyrazole ring.

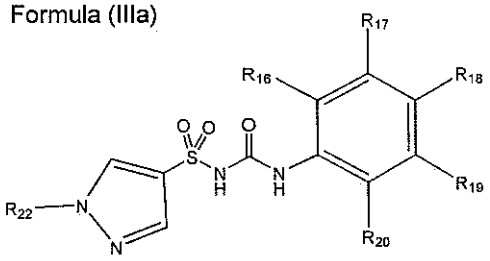
10. The compound of any one of the preceding claims, wherein the compound is a compound of formula (IIIa), (IIIb) or (IIIc), or a pharmaceutically acceptable salt or solvate thereof:



Formula (IIIa)



Formula (IIIb)



Formula (IIIc)

either wherein:

R_{21} is selected from H, alkyl, perhaloalkyl or hydroxylalkyl;

R_{22} is selected from H, alkyl, perhaloalkyl, C_3-C_6 cycloalkyl, phenyl or benzyl;

R_{16} and R_{17}, together with the atoms to which they are attached, form a cyclopentyl ring;

R_{19} and R_{20}, together with the atoms to which they are attached, form a cyclopentyl ring;

R_{18} is H or halogen; and

provided that R_{21} and R_{22} are not both H;

or wherein:

R_{21} is selected from H, alkyl, perhaloalkyl or hydroxylalkyl;

R_{22} is selected from H, alkyl, perhaloalkyl, C_3-C_6 cycloalkyl, phenyl and benzyl;

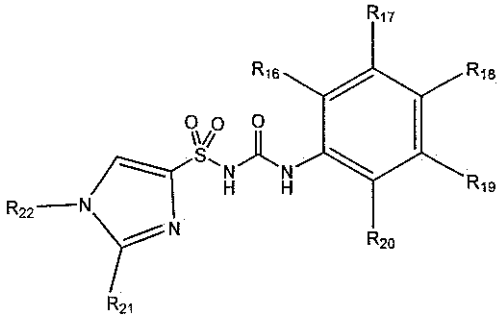
R_{16} and R_{20} are C_{1-6} alkyl or C_{3-5} cycloalkyl;

R_{17} and R_{19} are H;

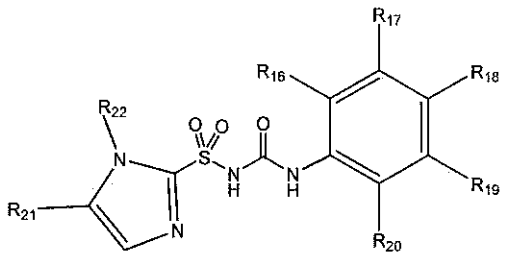
R_{18} is H or halogen; and

provided that R_{21} and R_{22} are not both H.

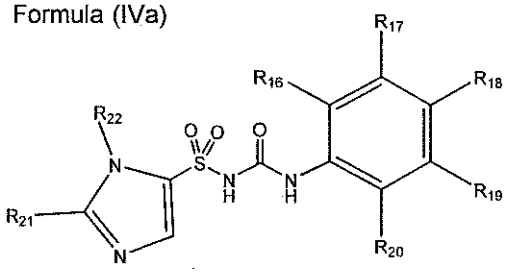
11. The compound of any one of claim 1 to claim 8, wherein the compound is a compound of formula (IVa), (IVb) or (IVc), or a pharmaceutically acceptable salt or solvate thereof:



Formula (IVa)



Formula (IVb)



Formula (IVc)

either wherein:

R_{21} and R_{22} are selected from H, alkyl, perhaloalkyl, hydroxylalkyl, C_3-C_6 cycloalkyl, phenyl and benzyl;

R_{16} and R_{17}, together with the atoms to which they are attached, form a cyclopentyl ring;

R_{19} and R_{20}, together with the atoms to which they are attached, form a cyclopentyl ring;

R_{18} is H or halogen; and

provided that R_{21} and R_{22} are not both H;

or wherein:

R_{21} and R_{22} are selected from H, alkyl, perhaloalkyl, hydroxylalkyl, C_3-C_6 cycloalkyl, phenyl and benzyl; preferably wherein the perhaloalkyl and hydroxylalkyl are C_{1-6} perhaloalkyl and hydroxylalkyl;

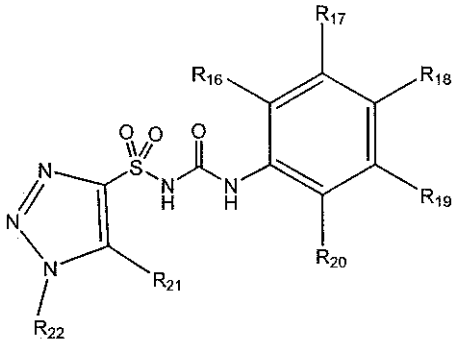
R_{16} and R_{20} are C_{1-6} alkyl or C_{3-5} cycloalkyl;

R_{17} and R_{19} are H;

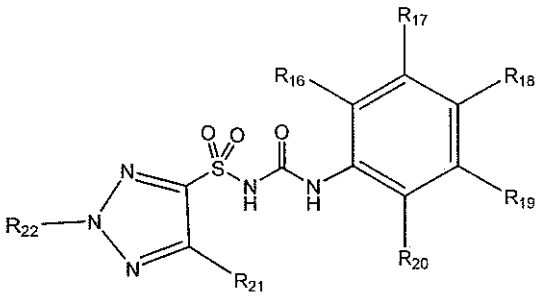
R_{18} is H or halogen; and

provided that R_{21} and R_{22} are not both H.

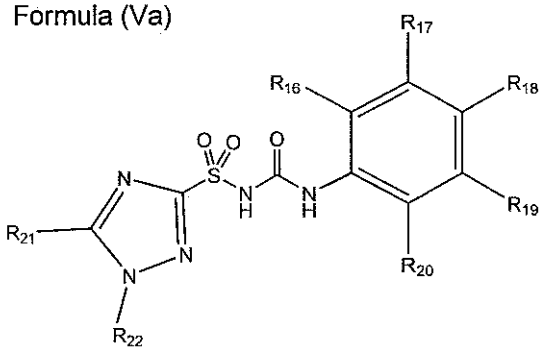
12. The compound of any one of claim 1 to claim 7, wherein the compound is a compound of formula (Va), (Vb) or (Vc), or a pharmaceutically acceptable salt or solvate thereof:



Formula (Va)



Formula (Vb)



Formula (Vc)

either wherein:

R_{21} and R_{22} are selected from H, alkyl, perhaloalkyl, hydroxylalkyl, C_3-C_6 cycloalkyl, phenyl and benzyl;

R_{16} and R_{17}, together with the atoms to which they are attached, form a cyclopentyl ring;

R_{19} and R_{20}, together with the atoms to which they are attached, form a cyclopentyl ring;

R_{18} is H or halogen; and

provided that R_{21} and R_{22} are not both H;

or wherein:

R_{21} and R_{22} are selected from H, alkyl, perhaloalkyl, hydroxylalkyl, C_3-C_6 cycloalkyl, phenyl and benzyl;

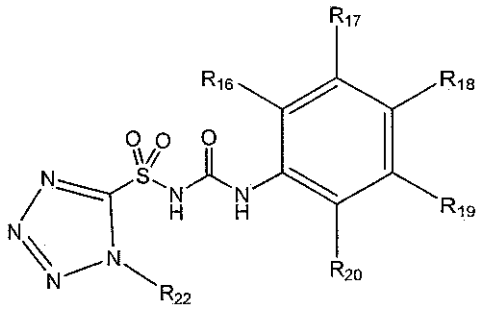
R_{16} and R_{20} are C_{1-6} alkyl or C_{3-5} cycloalkyl;

R_{17} and R_{19} are H;

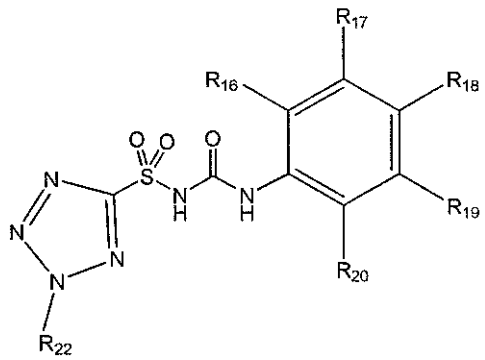
R_{18} is H or halogen; and

provided that R_{21} and R_{22} are not both H.

13. The compound of any one of claim 1 to claim 7, wherein the compound is a compound of formula (VIa) or (VIb), or a pharmaceutically acceptable salt or solvate thereof:



Formula (VIa)



Formula (VIb)

either wherein:

R_{22} is selected from alkyl, perhaloalkyl, hydroxylalkyl, C_3-C_6 cycloalkyl, phenyl and benzyl;

R_{16} and R_{17}, together with the atoms to which they are attached, form a cyclopentyl ring;

R_{19} and R_{20}, together with the atoms to which they are attached, form a cyclopentyl ring; and

R_{18} is H or halogen;

or wherein:

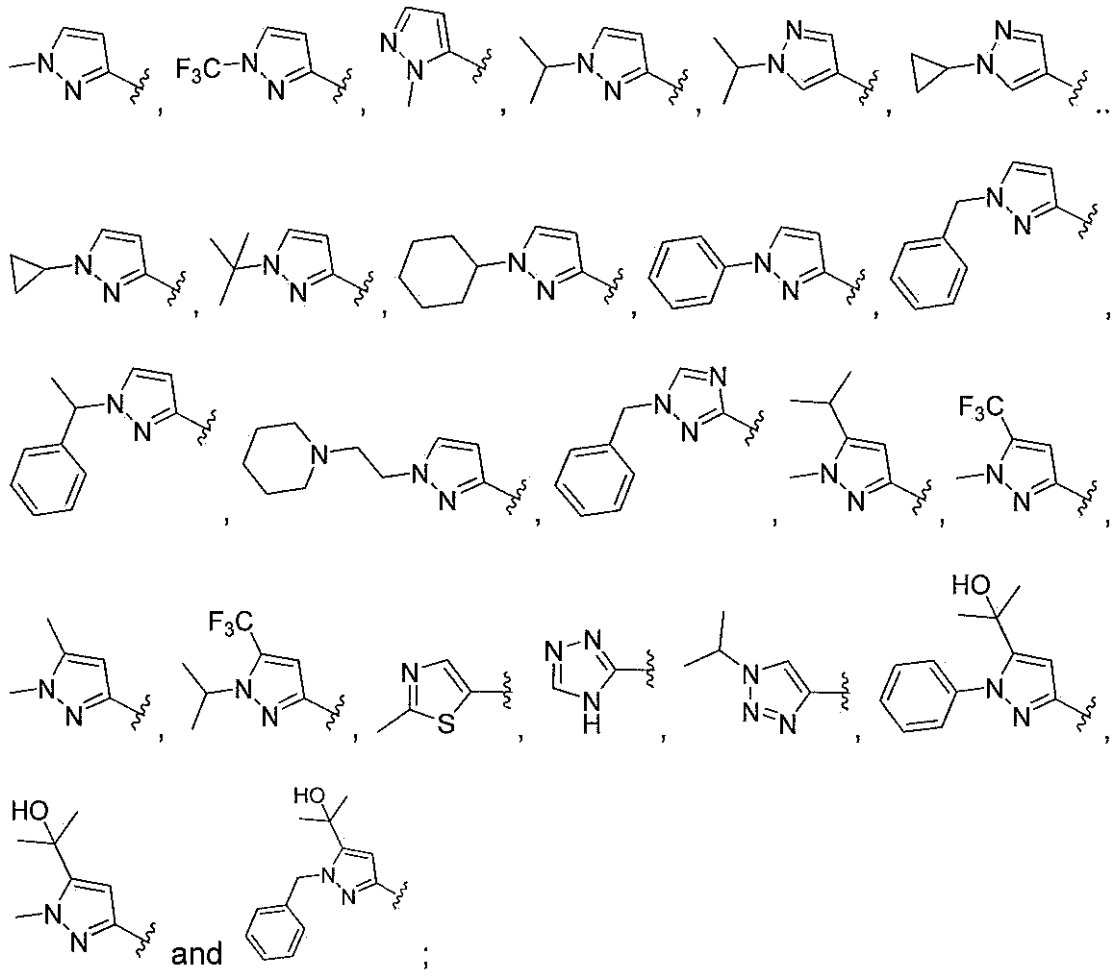
R_{22} is selected from alkyl, perhaloalkyl, hydroxylalkyl, C_3-C_6 cycloalkyl, phenyl and benzyl;

R_{16} and R_{20} are C_{1-6} alkyl or C_{3-5} cycloalkyl, preferably isopropyl or cyclopentyl;

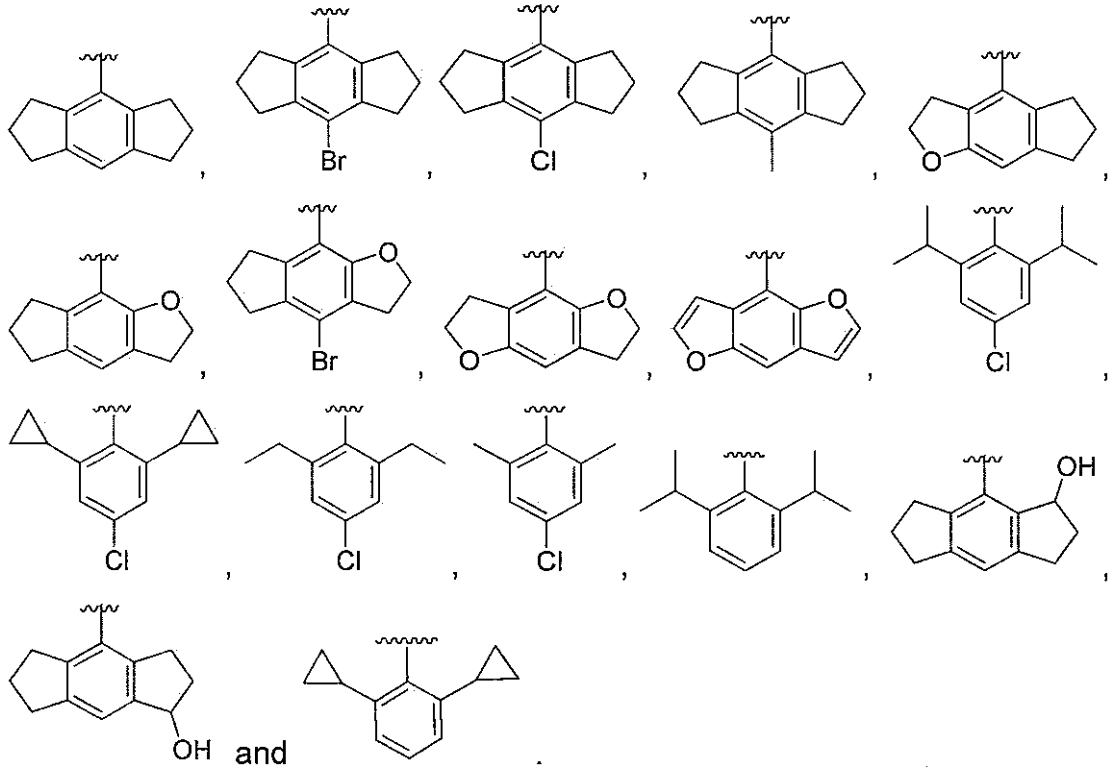
R_{17} and R_{19} are H; and

R_{18} is H or halogen.

14. The compound of any one of claim 1 to claim 9, wherein R_1 is selected from the group consisting of:

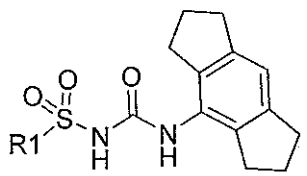


and in combination with each such R_1 group, R_2 may be independently selected from the group consisting of:

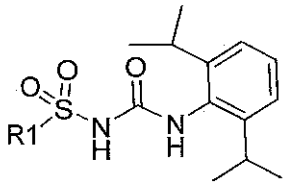


15. The compound of any one of the preceding claims, wherein R_2 is selected from hexahydroindacene, 2,6-diisopropylphenyl, 2,6-diisopropyl-4-chlorophenyl, 2,6-dicyclopropylphenyl and 2,6-dicyclopropyl-4-chlorophenyl.

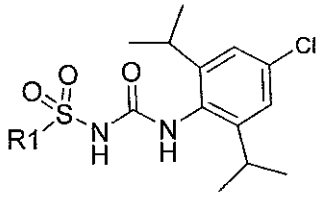
16. The compound of any one of the preceding claims, wherein the compound is a compound of formula (Ia), (Ib) or (Ic), or a pharmaceutically acceptable salt or solvate thereof:



formula (Ia)



formula (Ib)

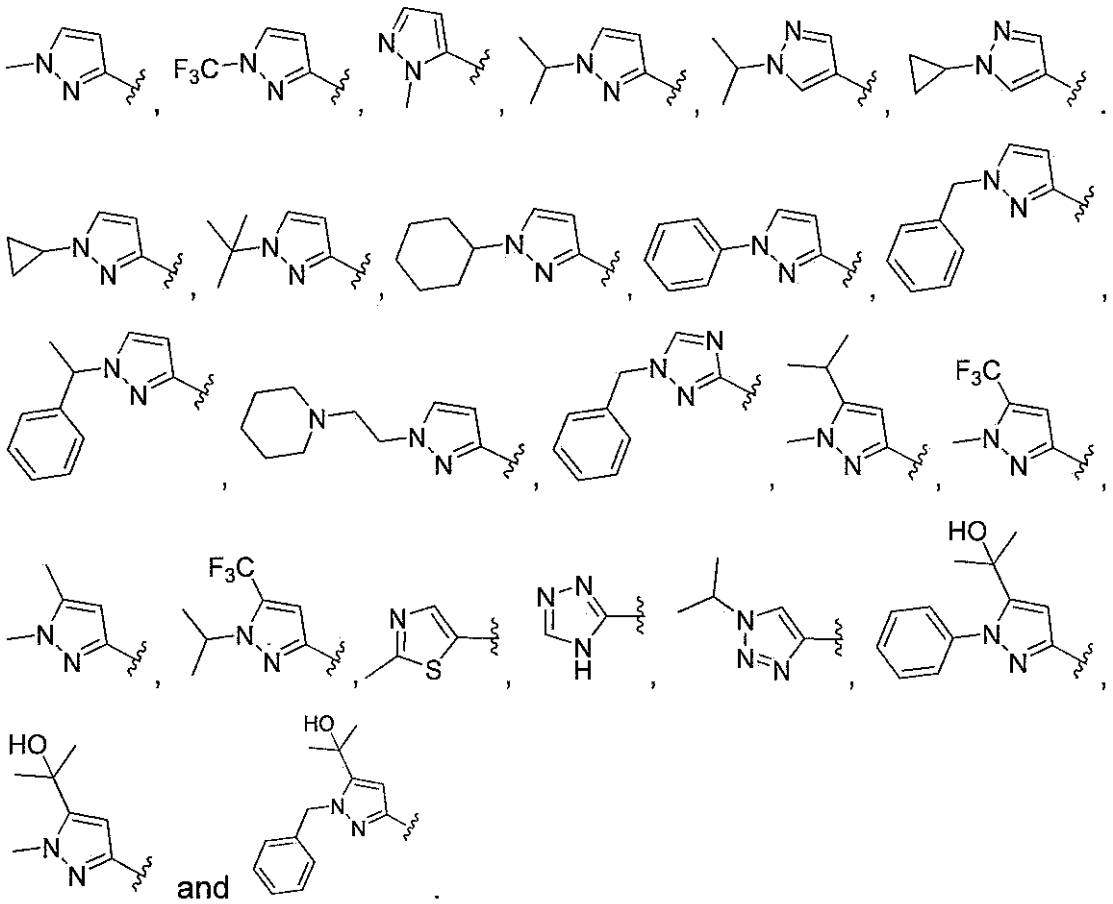


formula (Ic)

wherein R_1 is as defined in any one of the preceding claims.

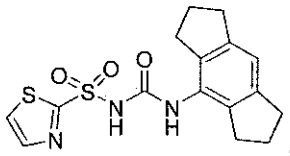
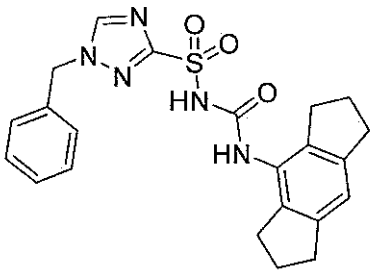
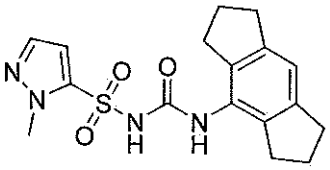
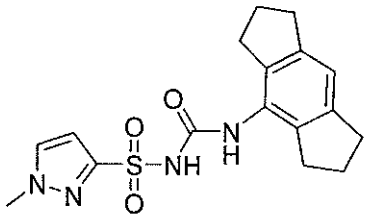
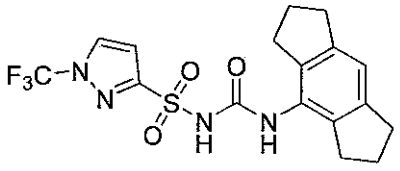
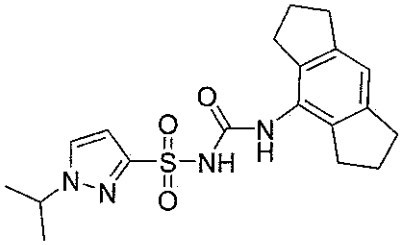
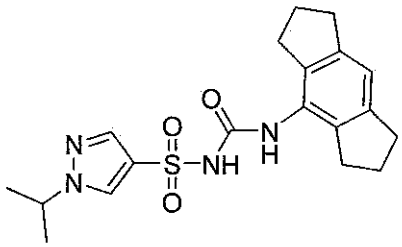
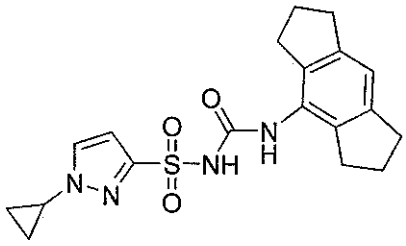
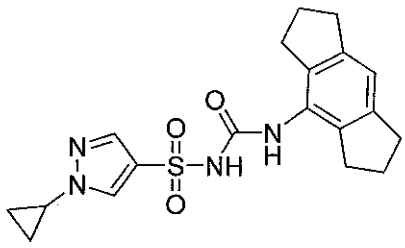
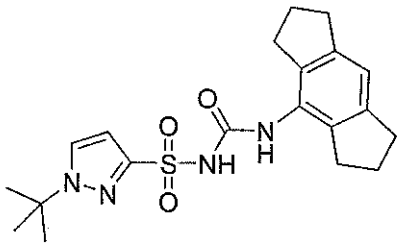
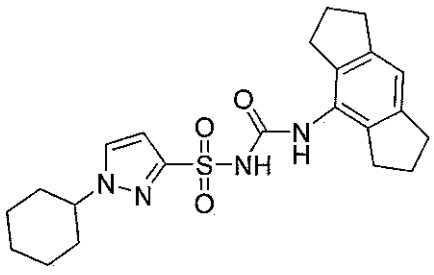
17. The compound of claim 16, wherein R_1 is selected from the group consisting of pyrazole, pyrrolidine, pyrrole, triazole, tetrazole and imidazole, all of which may be optionally substituted as appropriate.

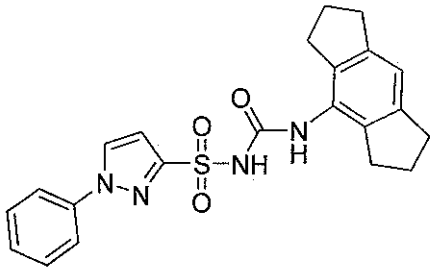
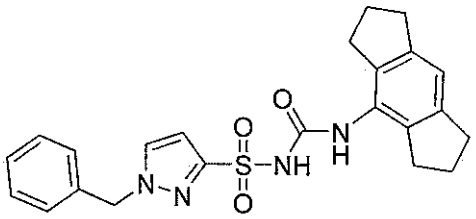
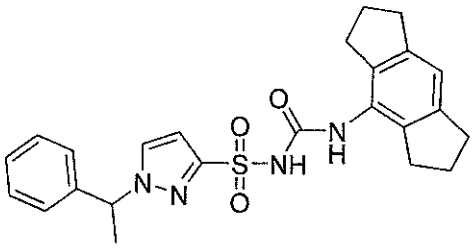
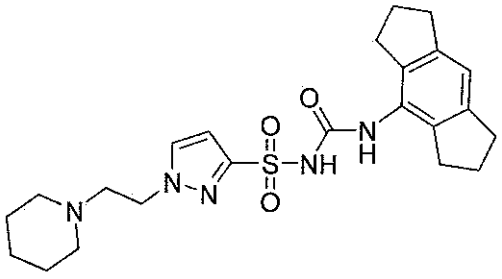
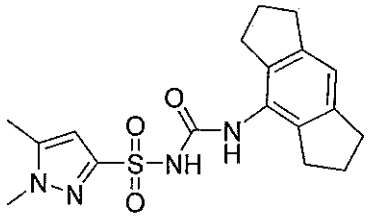
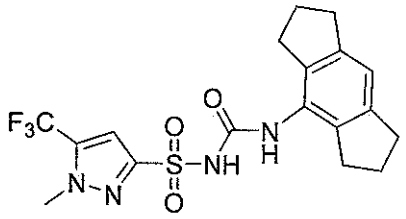
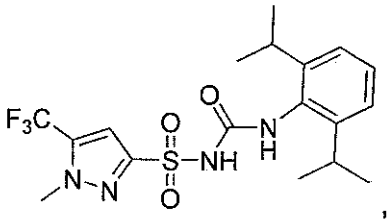
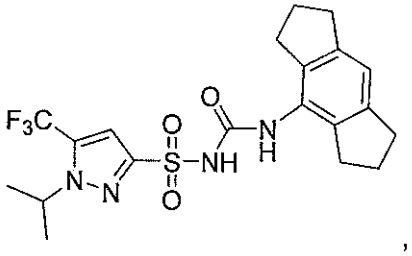
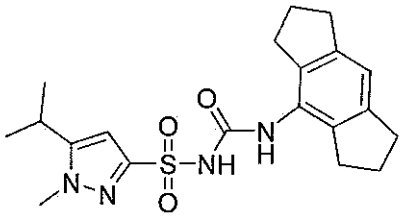
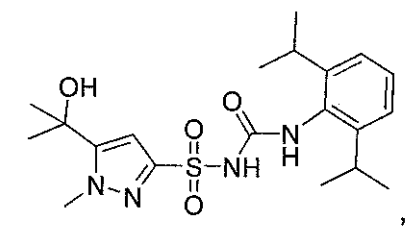
18. The compound of claim 16 or claim 17, wherein R_1 is selected from the group consisting of:



19. The compound of any one of the preceding claims, wherein any optional substituent is independently selected from the group consisting of C1-10 alkyl; C3-6 cycloalkyl; hydroxyalkyl; C1-10 alkoxy; C2-10 alkenyl; C2-10 alkynyl; C6-C12 aryl; aryloxy; heteroaryl; optionally substituted heterocyclyl; halo; hydroxyl; halogenated alkyl; amino; alkylamino; arylamino; acyl; amido; CN; NO_2; N_3; CH_2OH; $CONH_2$; $CONR_{24}R_{25}$; CO_2R_{24}; CH_2OR_{24}; $NHCOR_{24}$; $NHCO_2R_{24}$; C1-3 alkylthio; sulfate; sulfonic acid; sulfonate esters; phosphonic acid; phosphate; phosphonate; mono-, di-, or triphosphate esters; trityl; monomethoxytrityl; $R_{24}SO$; $R_{24}SO_2$; CF_3S; CF_3SO_2; and trialkylsilyl; wherein R_{24} and R_{25} are each independently selected from H or C1-10 alkyl.

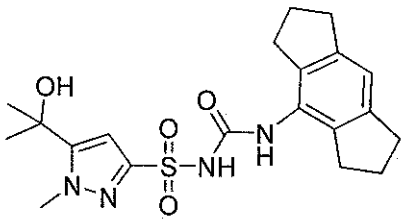
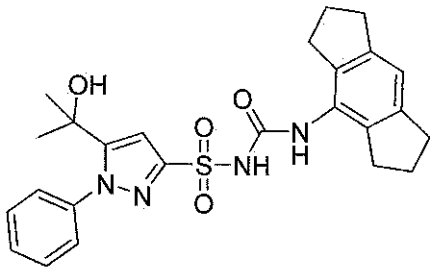
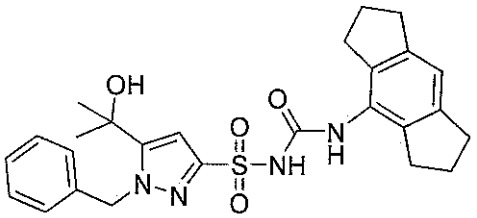
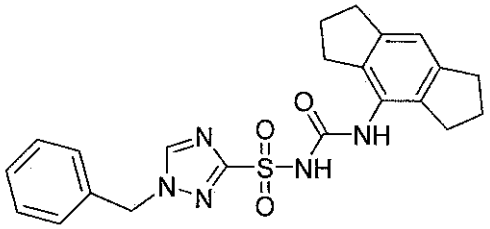
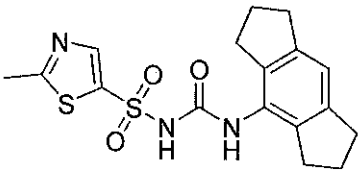
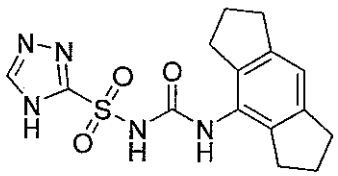
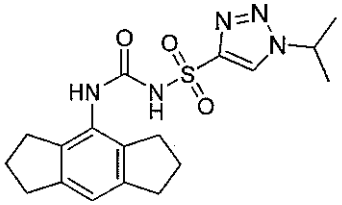
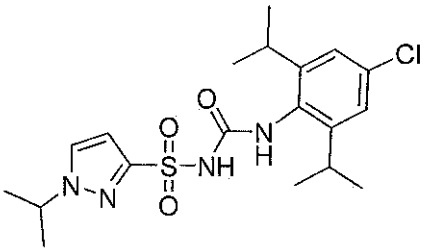
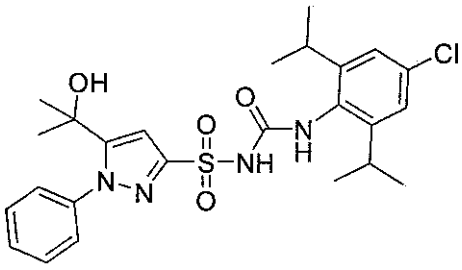
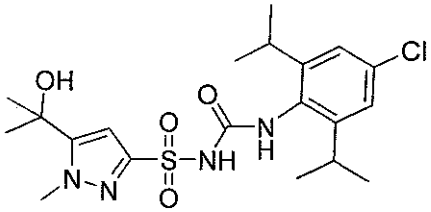
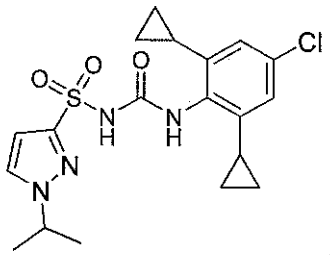
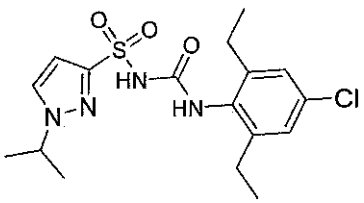
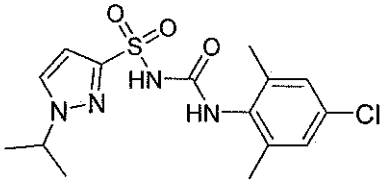
20. The compound of any one of the preceding claims, wherein the compound is selected from the group consisting of:


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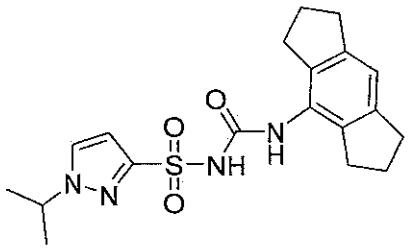
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and

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and pharmaceutically acceptable salts and solvates thereof.

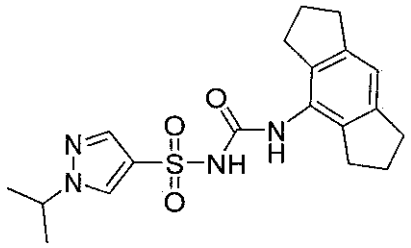
21. The compound of any one of claims 1 to 20, wherein the compound is



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or a pharmaceutically acceptable salt or solvate thereof.

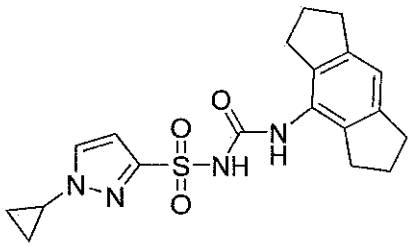
22. The compound of any one of claims 1 to 20, wherein the compound is



,

or a pharmaceutically acceptable salt or solvate thereof.

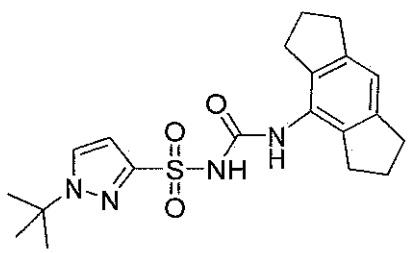
23. The compound of any one of claims 1 to 20, wherein the compound is



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or a pharmaceutically acceptable salt or solvate thereof.

24. The compound of any one of claims 1 to 20, wherein the compound is



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or a pharmaceutically acceptable salt or solvate thereof.

25. The compound or the pharmaceutically effective salt or solvate of any one of the preceding claims, wherein the compound, or the pharmaceutically effective salt or solvate thereof, is an inhibitor of the NLRP3 inflammasome.

26. A pharmaceutical composition comprising a compound of any one of claim 1 to claim 25, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier, diluent and/or excipient.

27. The compound or the pharmaceutically effective salt or solvate of any one of claim 1 to claim 25, wherein the compound, or the pharmaceutically effective salt or solvate thereof, is for use in:

(a) medicine; and/or

(b) the treatment or prevention of a disease, disorder or condition; and/or

(c) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is one which is responsive to inhibition of activation of the NLRP3 inflammasome; and/or

(d) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is responsive to modulation of one or more of IL-1β, IL-17, IL-18, IL-1α, IL-37, IL-33 and Th17 cells; and/or

(e) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a disease, disorder or condition of the immune system; and/or

(f) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is an inflammatory disease, disorder or condition or an autoimmune disease, disorder or condition; and/or

(g) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a disease, disorder or condition of the skin; and/or

(h) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a disease, disorder or condition of the cardiovascular system; and/or

(i) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a cancer, tumour or other malignancy; and/or

(j) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a disease, disorder or condition of the renal system; and/or

(k) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a disease, disorder or condition of the gastro-intestinal tract; and/or

(l) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a disease, disorder or condition of the respiratory system; and/or

(m) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a disease, disorder or condition of the endocrine system; and/or

(n) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is a disease, disorder or condition of the central nervous system (CNS); and/or

(o) the treatment or prevention of a disease, disorder or condition, wherein the disease, disorder or condition is selected from the group consisting of constitutive inflammation including the cryopyrin-associated periodic syndromes (CAPS): Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS) and neonatal-onset multisystem inflammatory disease (NOMID); including autoinflammatory diseases: familial Mediterranean fever (FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D and periodic fever

syndrome (HIDS), deficiency of interleukin 1 receptor (DIRA) antagonist, 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, and developmental delay (SIFD); Sweet's syndrome, chronic nonbacterial osteomyelitis (CNO), chronic recurrent multifocal osteomyelitis (CRMO) and synovitis, acne, pustulosis, hyperostosis, osteitis syndrome (SAPHO); autoimmune diseases including multiple sclerosis (MS), type-1 diabetes, psoriasis, rheumatoid arthritis, Behcet's disease, Sjogren's syndrome and Schnitzler syndrome; respiratory diseases including chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis and cystic fibrosis; central nervous system diseases including Parkinson's disease, Alzheimer's disease, motor neuron disease, Huntington's disease, cerebral malaria and brain injury from pneumococcal meningitis; metabolic diseases including Type 2 diabetes, atherosclerosis, obesity, gout, pseudo-gout; ocular diseases including those of the ocular epithelium, age-related macular degeneration (AMD), corneal infection, uveitis and dry eye; kidney disease including chronic kidney disease, oxalate nephropathy and diabetic nephropathy; liver disease including non-alcoholic steatohepatitis and alcoholic liver disease; inflammatory reactions in skin including contact hypersensitivity and sunburn; inflammatory reactions in the joints including osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis; viral infections including alpha virus including Chikungunya and Ross River, and flavivirus including Dengue and Zika viruses, flu, HIV; hidradenitis suppurativa (HS) and other cyst-causing skin diseases; cancers including lung cancer metastasis, pancreatic cancers, gastric cancers, myelodisplastic syndrome, leukemia; polymyositis; stroke; myocardial infarction; Graft versus Host Disease; hypertension; colitis; helminth infection; bacterial infection; abdominal aortic aneurism; wound healing; depression, psychological

stress; pericarditis including Dressler's syndrome, ischaemia reperfusion injury and any disease where an individual has been determined to carry a germline or somatic non-silent mutation in NLRP3; and/or

(p) diagnosing a disease, disorder or condition in a mammal including that a labelled compound of any one of claim 1 to claim 25, or a pharmaceutically effective salt or solvate thereof, or metal ion chelate complex thereof, is to be administered to the mammal or to a biological sample obtained from the mammal to facilitate diagnosis of the disease, disorder or condition in the mammal; and/or

(q) modulating the activity of a biological target comprising that the biological target is to be exposed to a compound of any one of claim 1 to claim 25, or a pharmaceutically effective salt or solvate thereof; and/or

(r) modulating the activity of a biological target comprising that the biological target is to be exposed to a compound of any one of claim 1 to claim 25, or a pharmaceutically effective salt or solvate thereof, wherein the biological target may be selected from the group consisting of the NLRP3 inflammasome, IL-1β, IL-17, IL-18, IL-1α, IL-37, IL-33 and Th17 cells.

28. Use of the compound or the pharmaceutically effective salt or solvate of any one of claim 1 to claim 25, or use of the pharmaceutical composition of claim 26, in the manufacture of a medicament for the treatment, prevention or diagnosis of:

(a) an inflammatory disease, disorder or condition or an autoimmune disease, disorder or condition; and/or

(b) a cancer, tumour or other malignancy; and/or

(c) a disease, disorder or condition selected from the group consisting of constitutive inflammation including the cryopyrin-associated periodic syndromes (CAPS): Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS) and neonatal-onset multisystem inflammatory disease (NOMID); including autoinflammatory diseases: familial Mediterranean fever

(FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D and periodic fever syndrome (HIDS), deficiency of interleukin 1 receptor (DIRA) antagonist, 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, and developmental delay (SIFD); Sweet's syndrome, chronic nonbacterial osteomyelitis (CNO), chronic recurrent multifocal osteomyelitis (CRMO) and synovitis, acne, pustulosis, hyperostosis, osteitis syndrome (SAPHO); autoimmune diseases including multiple sclerosis (MS), type-1 diabetes, psoriasis, rheumatoid arthritis, Behcet's disease, Sjogren's syndrome and Schnitzler syndrome; respiratory diseases including chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis and cystic fibrosis; central nervous system diseases including Parkinson's disease, Alzheimer's disease, motor neuron disease, Huntington's disease, cerebral malaria and brain injury from pneumococcal meningitis; metabolic diseases including Type 2 diabetes, atherosclerosis, obesity, gout, pseudo-gout; ocular diseases including those of the ocular epithelium, age-related macular degeneration (AMD), corneal infection, uveitis and dry eye; kidney disease including chronic kidney disease, oxalate nephropathy and diabetic nephropathy; liver disease including non-alcoholic steatohepatitis and alcoholic liver disease; inflammatory reactions in skin including contact hypersensitivity and sunburn; inflammatory reactions in the joints including osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis; viral infections including alpha virus including Chikungunya and Ross River, and flavivirus including Dengue and Zika viruses, flu, HIV; hidradenitis suppurativa (HS) and other cyst-causing skin diseases; cancers including lung cancer metastasis, pancreatic cancers, gastric cancers, myelodisplastic syndrome, leukemia; polymyositis; stroke; myocardial infarction;

Graft versus Host Disease; hypertension; colitis; helminth infection; bacterial infection; abdominal aortic aneurism; wound healing; depression, psychological stress; pericarditis including Dressler's syndrome, ischaemia reperfusion injury and any disease where an individual has been determined to carry a germline or somatic non-silent mutation in NLRP3.