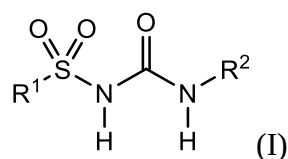


[0011] There is a need to provide compounds and pharmaceutical compositions with improved pharmacological and/or physiological and/or physicochemical properties and/or those that provide a useful alternative to known compounds and pharmaceutical compositions.

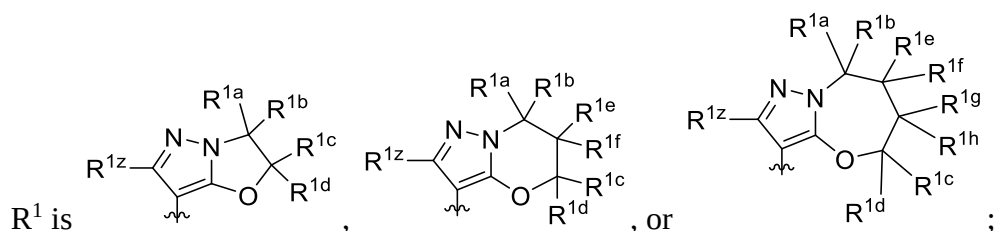
SUMMARY

[0012] The present disclosure provides compounds and pharmaceutical compositions that may be useful for inhibiting an inflammasome, such as the NLRP3 inflammasome. The compounds and pharmaceutical compositions are also useful in modulating interleukins. The disclosed compounds have desirable molecular weights, physico-chemical properties, and lipophilicity, which are features that help with achieving therapeutic efficacy and decreasing unintended liabilities.

[0013] The present disclosure, in one aspect, provides a compound having the structure of Formula (I),



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



R^{1z} is H, D, halogen, $-\text{CN}$, $-\text{NO}_2$, $-\text{SR}^{7a}$, $-\text{OR}^{7a}$, $-\text{C(O)R}^{7b}$, $-\text{P(O)R}^{7b}\text{R}^{8b}$, $-\text{S(O)}_2\text{R}^{7b}$, $-\text{S(O)R}^{7b}$, $-\text{NR}^{7a}\text{R}^{8a}$, $-\text{NR}^{7a}\text{C(O)R}^{8a}$, $-\text{NR}^{7a}\text{C(O)OR}^{8a}$, $-\text{NR}^{7a}\text{C(O)NR}^{8a}$, $-\text{NR}^{7a}\text{S(O)}_2\text{R}^{8a}$, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_2\text{-C}_6\text{alkenyl}$, $\text{C}_4\text{-C}_8\text{cycloalkenyl}$, $\text{C}_2\text{-C}_6\text{alkynyl}$, $\text{C}_3\text{-C}_{10}\text{cycloalkyl}$, C_6aryl , 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_2\text{-C}_6\text{alkenyl}$, $\text{C}_4\text{-C}_8\text{cycloalkenyl}$, $\text{C}_2\text{-C}_6\text{alkynyl}$, $\text{C}_3\text{-C}_{10}\text{cycloalkyl}$, C_6aryl , 3-7-membered heterocyclyl, and 5-6 membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, $-\text{CN}$, halogen, $\text{C}_1\text{-C}_6\text{alkyl}$, $-\text{OR}^{7a}$, $-\text{C(O)R}^{7b}$, $-\text{P(O)R}^{7b}\text{R}^{8b}$, $-\text{S(O)}_2\text{R}^{7b}$, $-\text{S(O)R}^{7b}$, $-\text{NR}^{7a}\text{R}^{8a}$, $-\text{NR}^{7a}\text{C(O)R}^{8a}$, $-\text{NR}^{7a}\text{C(O)OR}^{8a}$, $-\text{NR}^{7a}\text{C(O)NR}^{8a}$, $-\text{NR}^{7a}\text{S(O)}_2\text{R}^{8a}$, $\text{C}_3\text{-C}_{10}\text{cycloalkyl}$, C_6aryl , 3-7-membered heterocyclyl, and 5-6 membered heteroaryl;

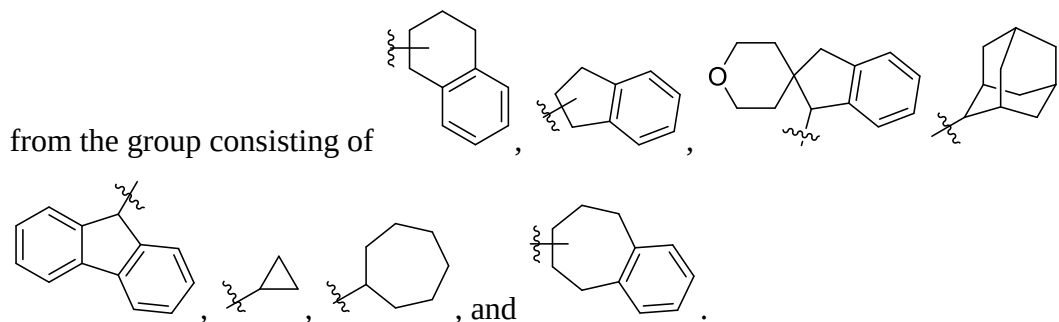
each R^{1a} , R^{1b} , R^{1c} , R^{1d} , R^{1e} , R^{1f} , R^{1g} , and R^{1h} is independently selected from H, D, halogen, $-\text{CN}$, $-\text{NO}_2$, $-\text{SR}^{11a}$, $-\text{OR}^{11a}$, $-\text{C(O)R}^{11b}$, $-\text{P(O)R}^{11b}\text{R}^{12b}$, $-\text{S(O)}_2\text{R}^{11b}$, $-\text{S(O)R}^{11b}$,

D, -CN, halogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₂-C₆alkenyl, oxo, -OR^{21a}, -C(O)R^{21b}, -P(O)R^{21b}R^{22b}, -S(O)₂R^{21b}, -S(O)R^{21b}, -NR^{21a}R^{22a}, -NR^{21a}C(O)R^{22a}, -NR^{21a}C(O)OR^{22a}, -NR^{21a}C(O)NR^{22a}, -NR^{21a}S(O)₂R^{22a}, -(CH₂)₁₋₄C₃-C₁₀cycloalkyl, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl;

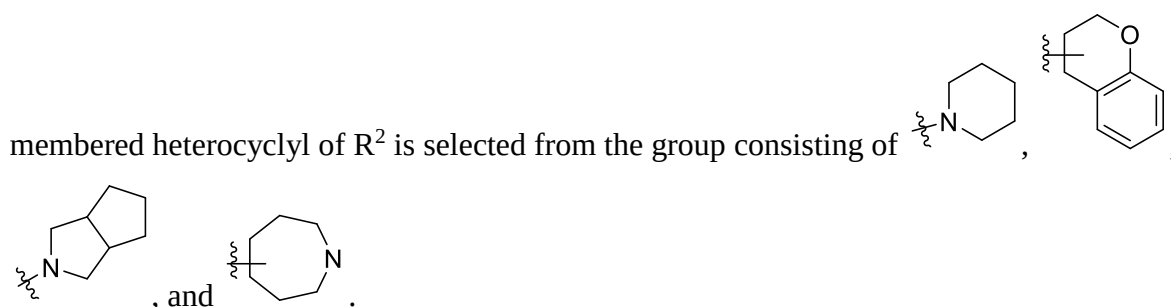
R^{7a}, R^{8a}, R^{11a}, R^{12a}, R^{13a}, R^{14a}, R^{21a}, R^{22a}, R^{23a}, and R^{24a} are independently, at each occurrence, H, D, C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, -OH, -O-C₁-C₆alkyl, -NH₂, -NH(C₁-C₆alkyl), -N(C₁-C₆alkyl)₂, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl; and

R^{7b}, R^{8b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, R^{21b}, R^{22b}, R^{23b}, and R^{24b} are independently, at each occurrence, H, D, -OH, -O(C₁-C₆alkyl), -NH₂, -NH(C₁-C₆alkyl), -N(C₁-C₆alkyl)₂, -NHS(O)₂CH₃, C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, -OH, -O-C₁-C₆alkyl, -NH₂, -NH(C₁-C₆alkyl), -N(C₁-C₆alkyl)₂, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl.

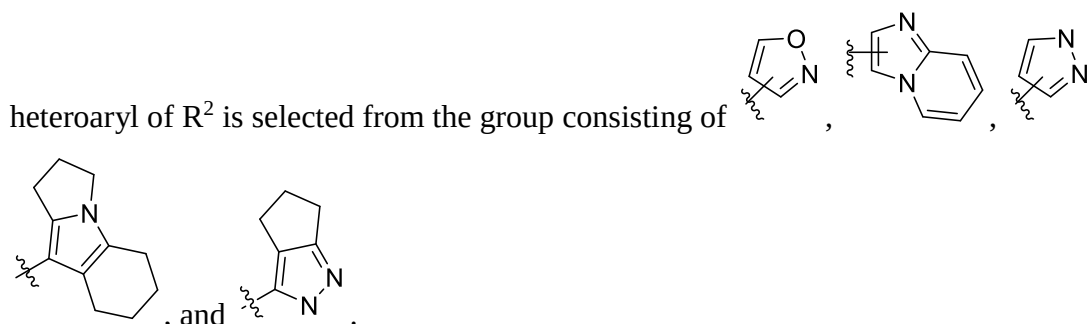
[0015] In some examples of the compound of formula (I), or a pharmaceutically acceptable salt, solvate, isomer, prodrug, or tautomer thereof, wherein R² is C₁-C₆alkyl, which is unsubstituted or substituted with one or more C₆aryl. In some of these examples, R² is C₃-C₁₀cycloalkyl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of C₁-C₆alkyl and C₆aryl. In some of these examples, R² is C₅cycloalkyl, C₆cycloalkyl, or C₇cycloalkyl, each of which is independently unsubstituted or substituted with one or more substituents selected from the group consisting of C₁-C₆alkyl and C₆aryl. In some of these examples, the C₃-C₁₀cycloalkyl of R² is cyclohexyl, cycloheptyl, 2-adamantyl, 2,3-dihydro-1H-inden-2-yl, or 9-fluorenyl, each of which is independently unsubstituted or substituted with one or more substituents selected from the group consisting of C₁-C₆alkyl and C₆aryl. In some of these examples, the C₃-C₁₀cycloalkyl of R² is selected



[0016] In some examples of the compound of formula (I), or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R^2 is 5-7-membered heterocyclyl, which is unsubstituted or substituted with one or more C_1 - C_6 alkyl. In some of these examples, the 5-7-

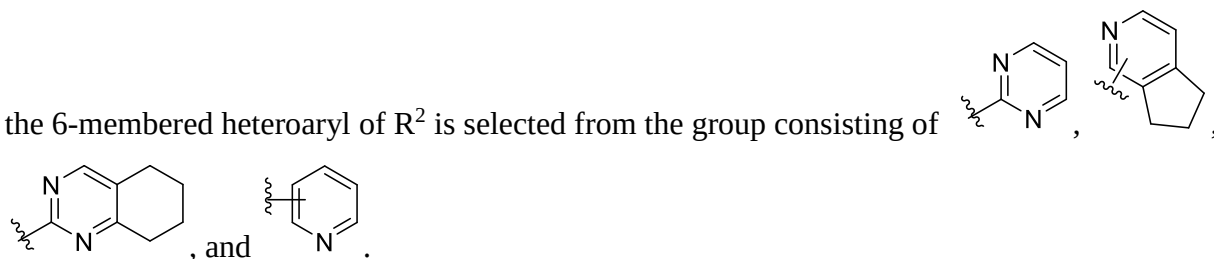


[0017] In some examples of the compound of formula (I), or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R^2 is 5-membered heteroaryl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of C_1 - C_6 alkyl, C_6 aryl, oxo, and $-(CH_2)_{1-4}C_3$ - C_{10} cycloalkyl. In some of these examples, the 5-membered heteroaryl contains 2 nitrogens. In some of these examples, the 5-membered



[0018] In some examples of the compound of formula (I), or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R^2 is 6-membered heteroaryl containing 6-11 annular atoms, which is unsubstituted or substituted with one or more substituents selected from the group consisting of halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_6 aryl, $-OR^{23a}$, C_3 - C_{10} cycloalkyl, C_2 - C_6 alkenyl, $-CN$, and $-NR^{23a}R^{24a}$. In some of these examples, R^2 is the 6-membered heteroaryl containing 6-11 annular atoms contains 2 nitrogens. In some of these examples,

the 6-membered heteroaryl of R² is selected from the group consisting of



[0019] The present disclosure provides pharmaceutical compositions comprising one or more compounds of the present disclosure, *e.g.*, a compound of Formula (I) or any variations detailed herein or one or more of Compound Nos. 1-82 in Table 1, and pharmaceutically acceptable salts, solvates (*e.g.*, hydrates), isomers, prodrugs, and tautomers thereof, and a pharmaceutically acceptable carrier. In another aspect, the present disclosure provides a pharmaceutical composition comprising a compound of the present disclosure, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, and a pharmaceutically acceptable carrier.

[0020] The present disclosure provides methods of treating disorders including the step of administering an effective amount of one or more compounds of the present disclosure, *e.g.*, a compound of Formula (I) or any variations detailed herein or one or more of Compound Nos. 1-82 in Table 1, and pharmaceutically acceptable salts, solvates (*e.g.*, hydrates), isomers, prodrugs, and tautomers thereof, to thereby treat the disorder in a subject in need thereof.

[0021] The present disclosure provides a methods of treating disorders including the step of administering an effective amount of one or more pharmaceutical compositions of the present disclosure to thereby treat the disorder in a subject in need thereof.

[0022] The present disclosure provides one or more compounds of the present disclosure, *e.g.*, a compound of Formula (I) or any variations detailed herein or one or more of Compound Nos. 1-82 in Table 1, and pharmaceutically acceptable salts, solvates (*e.g.*, hydrates), isomers, prodrugs, and tautomers thereof, or one or more pharmaceutical compositions of the present disclosure for use in the treatment of a disorder in a subject in need thereof. In another aspect, the present disclosure provides a compound of the present disclosure, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, or a pharmaceutical composition of the present disclosure, for use as a medicament. In another aspect, the present disclosure provides a compound of the present disclosure, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, or a pharmaceutical composition of the present disclosure, for use in treating a disorder that is responsive to inhibition of inflammasome.

[0023] The present disclosure provides for the use of one or more compounds of the present disclosure, *e.g.*, a compound of Formula (I) or any variations detailed herein or one or more of Compound Nos. 1-82 in Table 1, and pharmaceutically acceptable salts, solvates (*e.g.*, hydrates), isomers, prodrugs, and tautomers thereof, for the treatment of a disorder in a subject in need thereof.

[0024] The present disclosure provides for the use of one or more pharmaceutical compositions of the present disclosure for the treatment of a disorder in a subject in need thereof.

[0025] The present disclosure provides for the use of one or more compounds of the present disclosure, *e.g.*, a compound of Formula (I) or any variations detailed herein or one or more of

Compound Nos. 1-82 in Table 1, and pharmaceutically acceptable salts, solvates (e.g., hydrates), isomers, prodrugs, and tautomers thereof, in the manufacture of a medicament for the treatment of a disorder.

[0026] The present disclosure provides for the use of one or more pharmaceutical compositions of the present disclosure in the manufacture of a medicament for the treatment of a disorder. In another aspect, the present disclosure provides use of a compound of the present disclosure, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, or a pharmaceutical composition of the present disclosure, in the manufacture of a medicament for treating a disorder that is responsive to inhibition of inflammasome.

[0027] In some examples, the disorder is responsive to inflammasome inhibition.

[0028] In some examples, the disorder is responsive to inhibition of activation of the NLRP3 inflammasome.

[0029] In some examples, the disorder is a disorder of the immune system, the liver, the lung, the skin, the cardiovascular system, the renal system, the gastrointestinal tract, the respiratory system, the endocrine system, the central nervous system, or is a cancer or other malignancy, or is caused by or associated with a pathogen.

[0030] The present disclosure provides methods of modulating the activity of a biological target comprising the step of exposing the biological target to one or more compounds of the present disclosure, *e.g.*, a compound of Formula (I) or any variations detailed herein or one or more of Compound Nos. 1-82 in Table 1, and pharmaceutically acceptable salts, solvates (e.g., hydrates), isomers, prodrugs, and tautomers thereof.

[0031] The present disclosure provides methods of modulating the activity of a biological target comprising the step of exposing the biological target to one or more pharmaceutical compositions of the present disclosure.

[0032] The biological target may be selected from a group consisting of the NLRP3 inflammasome, IL-6, IL-1 β , IL-17, IL-18, IL-1 α , IL-37, IL-22, IL-33 and Th17 cells.

DETAILED DESCRIPTION

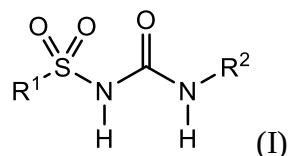
Definitions

[0033] As used throughout this disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings. If a term is missing, the conventional term as known to one skilled in the art controls.

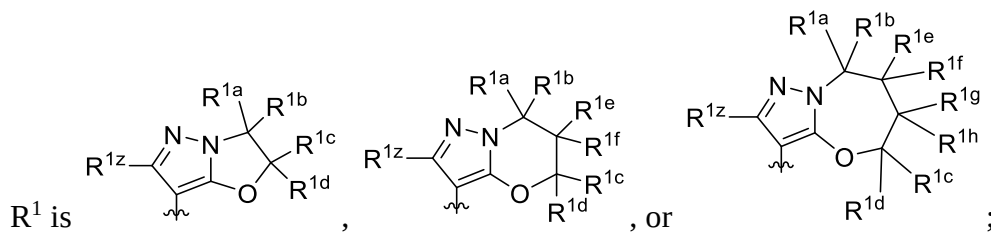
[0034] It should also be noted that any carbon as well as any heteroatom with unsatisfied valences in the text, schemes, examples and Tables herein is assumed to have the sufficient number of hydrogen atom(s) to satisfy the valences.

CLAIMS

1. A compound having the structure of Formula (I),



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



R^{1z} is H, D, halogen, -CN, $-\text{NO}_2$, $-\text{SR}^{7a}$, $-\text{OR}^{7a}$, $-\text{C}(\text{O})\text{R}^{7b}$, $-\text{P}(\text{O})\text{R}^{7b}\text{R}^{8b}$, $-\text{S}(\text{O})_2\text{R}^{7b}$, $-\text{S}(\text{O})\text{R}^{7b}$, $-\text{NR}^{7a}\text{R}^{8a}$, $-\text{NR}^{7a}\text{C}(\text{O})\text{R}^{8a}$, $-\text{NR}^{7a}\text{C}(\text{O})\text{OR}^{8a}$, $-\text{NR}^{7a}\text{C}(\text{O})\text{NR}^{8a}$, $-\text{NR}^{7a}\text{S}(\text{O})_2\text{R}^{8a}$, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_4 - C_8 cycloalkenyl, C_2 - C_6 alkynyl, C_3 - C_{10} cycloalkyl, C_6 aryl, 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_4 - C_8 cycloalkenyl, C_2 - C_6 alkynyl, C_3 - C_{10} cycloalkyl, C_6 aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C_1 - C_6 alkyl, $-\text{OR}^{7a}$, $-\text{C}(\text{O})\text{R}^{7b}$, $-\text{P}(\text{O})\text{R}^{7b}\text{R}^{8b}$, $-\text{S}(\text{O})_2\text{R}^{7b}$, $-\text{S}(\text{O})\text{R}^{7b}$, $-\text{NR}^{7a}\text{R}^{8a}$, $-\text{NR}^{7a}\text{C}(\text{O})\text{R}^{8a}$, $-\text{NR}^{7a}\text{C}(\text{O})\text{OR}^{8a}$, $-\text{NR}^{7a}\text{C}(\text{O})\text{NR}^{8a}$, $-\text{NR}^{7a}\text{S}(\text{O})_2\text{R}^{8a}$, C_3 - C_{10} cycloalkyl, C_6 aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl;

each R^{1a} , R^{1b} , R^{1c} , R^{1d} , R^{1e} , R^{1f} , R^{1g} , and R^{1h} is independently selected from H, D, halogen, -CN, $-\text{NO}_2$, $-\text{SR}^{11a}$, $-\text{OR}^{11a}$, $-\text{C}(\text{O})\text{R}^{11b}$, $-\text{P}(\text{O})\text{R}^{11b}\text{R}^{12b}$, $-\text{S}(\text{O})_2\text{R}^{11b}$, $-\text{S}(\text{O})\text{R}^{11b}$, $-\text{NR}^{11a}\text{R}^{12a}$, $-\text{NR}^{11a}\text{C}(\text{O})\text{R}^{12a}$, $-\text{NR}^{11a}\text{C}(\text{O})\text{OR}^{12a}$, $-\text{NR}^{11a}\text{C}(\text{O})\text{NR}^{12a}$, $-\text{NR}^{11a}\text{S}(\text{O})_2\text{R}^{12a}$, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_4 - C_8 cycloalkenyl, C_2 - C_6 alkynyl, C_3 - C_{10} cycloalkyl, C_6 aryl, 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_4 - C_8 cycloalkenyl, C_2 - C_6 alkynyl, C_3 - C_{10} cycloalkyl, C_6 aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C_1 - C_6 alkyl, $-\text{OR}^{11a}$, $-\text{C}(\text{O})\text{R}^{11b}$, $-\text{P}(\text{O})\text{R}^{11b}\text{R}^{12b}$, $-\text{S}(\text{O})_2\text{R}^{11b}$, $-\text{S}(\text{O})\text{R}^{11b}$, $-\text{NR}^{11a}\text{R}^{12a}$, $-\text{NR}^{11a}\text{C}(\text{O})\text{R}^{12a}$, $-\text{NR}^{11a}\text{C}(\text{O})\text{OR}^{12a}$, $-\text{NR}^{11a}\text{C}(\text{O})\text{NR}^{12a}$, $-\text{NR}^{11a}\text{S}(\text{O})_2\text{R}^{12a}$, C_3 - C_{10} cycloalkyl, C_6 aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl; or

two of the following groups, R^{1a} , R^{1b} , R^{1c} , R^{1d} , R^{1e} , R^{1f} , R^{1g} , and R^{1h} , when present, together with the atoms to which they are attached can form a C₃-C₁₀cycloalkyl or a 3-7-membered heterocyclyl; wherein the C₃-C₁₀cycloalkyl and 3-7-membered heterocyclyl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, -OR^{13a}, -C(O)R^{13b}, -P(O)R^{13b}R^{14b}, -S(O)₂R^{13b}, -S(O)R^{13b}, -NR^{13a}R^{14a}, -NR^{13a}C(O)R^{14a}, -NR^{13a}C(O)OR^{14a}, -NR^{13a}C(O)NR^{14a}, and -NR^{13a}S(O)₂R^{14a}; or

two geminal groups R^{1a} and R^{1b} ; R^{1c} and R^{1d} ; R^{1e} and R^{1f} ; or R^{1g} and R^{1h} , when present, can form an oxo group;

R^2 is selected from the group consisting of C₁-C₆alkyl, C₃-C₁₀cycloalkyl, 5-7-membered heterocyclyl, 5-membered heteroaryl, 6-membered heteroaryl containing 6-11 annular atoms, or -NR^{2g}R^{2h}; wherein the C₁-C₆alkyl, C₃-C₁₀cycloalkyl, 5-7-membered heterocyclyl, 5-membered heteroaryl, and 6-membered heteroaryl containing 6-11 annular atoms are independently unsubstituted or substituted with one or more substituents, or optionally two of the substituents when present, together with the atoms to which they are attached can form a ring;

each R^{2g} and R^{2h} is independently H, D, C₁-C₆alkyl, C₃-C₁₀cycloalkyl, C₆aryl, 3-7 membered heterocyclyl, or 5-6 membered heteroaryl, wherein the C₁-C₆alkyl, C₃-C₁₀cycloalkyl, C₆aryl, 3-7 membered heterocyclyl, and 5-6 membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₂-C₆alkenyl, oxo, -OR^{21a}, -C(O)R^{21b}, -P(O)R^{21b}R^{22b}, -S(O)₂R^{21b}, -S(O)R^{21b}, -NR^{21a}R^{22a}, -NR^{21a}C(O)R^{22a}, -NR^{21a}C(O)OR^{22a}, -NR^{21a}C(O)NR^{22a}, -NR^{21a}S(O)₂R^{22a}, -(CH₂)₁₋₄C₃-C₁₀cycloalkyl, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl;

R^{7a} , R^{8a} , R^{11a} , R^{12a} , R^{13a} , R^{14a} , R^{21a} , and R^{22a} are independently, at each occurrence, H, D, C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, -OH, -O-C₁-C₆alkyl, -NH₂, -NH(C₁-C₆alkyl), -N(C₁-C₆alkyl)₂, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl; and

R^{7b} , R^{8b} , R^{11b} , R^{12b} , R^{13b} , R^{14b} , R^{21b} , and R^{22b} are independently, at each occurrence, H, D, -OH, -O(C₁-C₆alkyl), -NH₂, -NH(C₁-C₆alkyl), -N(C₁-C₆alkyl)₂, -NHS(O)₂CH₃, C₁-

C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, -OH, -O-C₁-C₆alkyl, -NH₂, -NH(C₁-C₆alkyl), -N(C₁-C₆alkyl)₂, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl.

2. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein:

R² is selected from the group consisting of C₁-C₆alkyl, C₃-C₁₀cycloalkyl, 5-7-membered heterocyclyl, 5-membered heteroaryl, 6-membered heteroaryl containing 6-11 annular atoms, or -NR^{2g}R^{2h}; wherein the C₁-C₆alkyl, C₃-C₁₀cycloalkyl, 5-7-membered heterocyclyl, 5-membered heteroaryl, and 6-membered heteroaryl containing 6-11 annular atoms are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₂-C₆alkenyl, oxo, -OR^{23a}, -C(O)R^{23b}, -P(O)R^{23b}R^{24b}, -S(O)₂R^{23b}, -S(O)R^{23b}, -NR^{23a}R^{24a}, -NR^{23a}C(O)R^{24a}, -NR^{23a}C(O)OR^{24a}, -NR^{23a}C(O)NR^{24a}, -NR^{23a}S(O)₂R^{24a}, -(CH₂)₁₋₄C₃-C₁₀cycloalkyl, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl;

R^{23a}, and R^{24a} are independently, at each occurrence, H, D, C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, -OH, -O-C₁-C₆alkyl, -NH₂, -NH(C₁-C₆alkyl), -N(C₁-C₆alkyl)₂, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl; and

R^{23b}, and R^{24b} are independently, at each occurrence, H, D, -OH, -O(C₁-C₆alkyl), -NH₂, -NH(C₁-C₆alkyl), -N(C₁-C₆alkyl)₂, -NHS(O)₂CH₃, C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, or 5-6-membered heteroaryl; wherein the C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₃-C₁₀cycloalkyl, C₄-C₈cycloalkenyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6-membered heteroaryl are independently unsubstituted or substituted with one or more substituents selected from the group consisting of D, -CN, halogen, C₁-C₆alkyl, -OH, -O-C₁-C₆alkyl, -NH₂, -NH(C₁-

C₆alkyl), -N(C₁-C₆alkyl)₂, C₃-C₁₀cycloalkyl, C₆aryl, 3-7-membered heterocyclyl, and 5-6 membered heteroaryl.

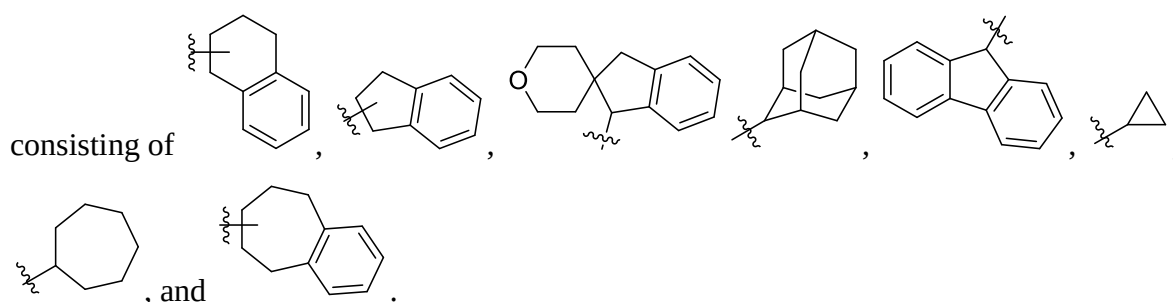
3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R² is C₁-C₆alkyl, which is unsubstituted or substituted with one or more C₆aryl.

4. The compound of claim 1 or 2, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R² is C₃-C₁₀cycloalkyl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of C₁-C₆alkyl and C₆aryl.

5. The compound of claim 4, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R² is C₅cycloalkyl, C₆cycloalkyl, or C₇cycloalkyl, each of which is independently unsubstituted or substituted with one or more substituents selected from the group consisting of C₁-C₆alkyl and C₆aryl.

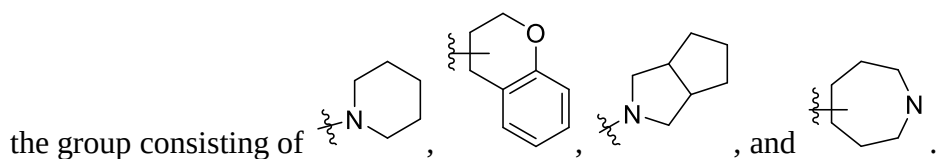
6. The compound of claim 4 or 5, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein the C₃-C₁₀cycloalkyl of R² is cyclohexyl, cycloheptyl, 2-adamantyl, 2,3-dihydro-1H-inden-2-yl, or 9-fluorenyl, each of which is independently unsubstituted or substituted with one or more substituents selected from the group consisting of C₁-C₆alkyl and C₆aryl.

7. The compound of claim 4 or 5, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein the C₃-C₁₀cycloalkyl of R² is selected from the group



8. The compound of claim 1 or 2, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R² is 5-7-membered heterocyclyl, which is unsubstituted or substituted with one or more C₁-C₆alkyl.

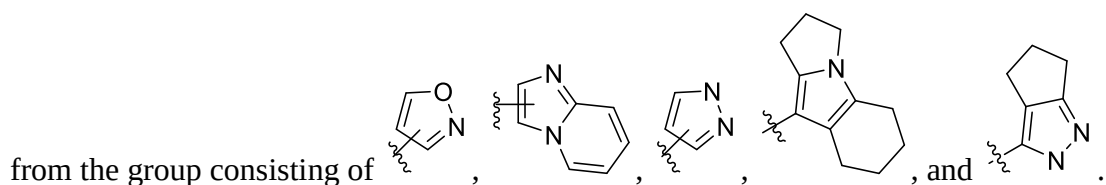
9. The compound of claim 8, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein the 5-7-membered heterocyclyl of R² is selected from



10. The compound of claim 1 or 2, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R² is 5-membered heteroaryl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of C₁-C₆alkyl, C₆aryl, oxo, and -(CH₂)₁₋₄C₃-C₁₀cycloalkyl.

11. The compound of claim 10, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein the 5-membered heteroaryl contains 2 nitrogens.

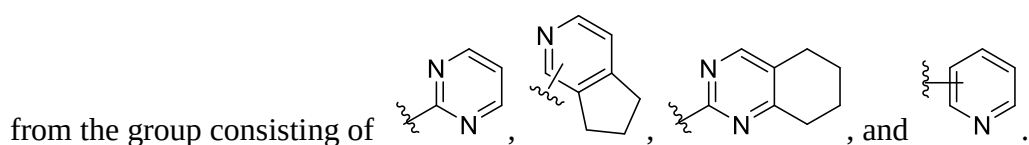
12. The compound of claim 10 or 11, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein the 5-membered heteroaryl of R² is selected



13. The compound of claim 1 or 2, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R² is 6-membered heteroaryl containing 6-11 annular atoms, which is unsubstituted or substituted with one or more substituents selected from the group consisting of halogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₆aryl, -OR^{23a}, C₃-C₁₀cycloalkyl, C₂-C₆alkenyl, -CN, and -NR^{23a}R^{24a}.

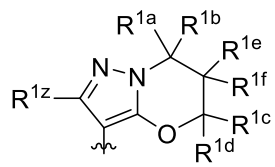
14. The compound of claim 13, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R² is the 6-membered heteroaryl containing 6-11 annular atoms contains 2 nitrogens.

15. The compound of claim 13 or 14, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein the 6-membered heteroaryl of R² is selected



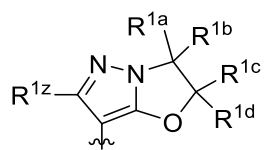
16. The compound of claim 1 or 2, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R^2 is $-NR^{2g}R^{2h}$.

17. The compound of any one of claims 1 to 16, or a pharmaceutically acceptable



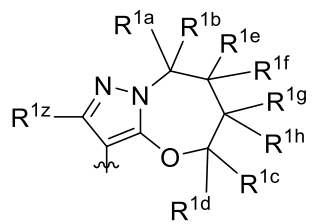
salt, solvate, isomer, or tautomer thereof, wherein R^1 is

18. The compound of any one of claims 1 to 16, or a pharmaceutically acceptable



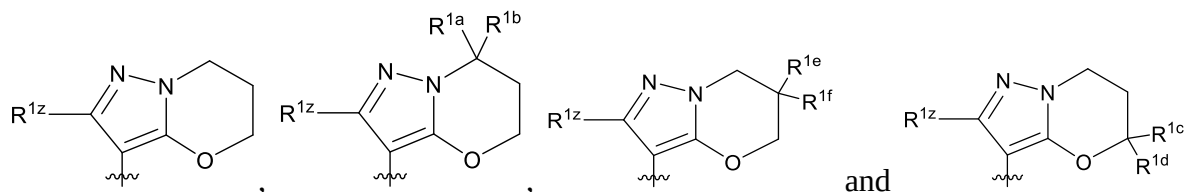
salt, solvate, isomer, or tautomer thereof, wherein R^1 is

19. The compound of any one of claims 1 to 16, or a pharmaceutically acceptable

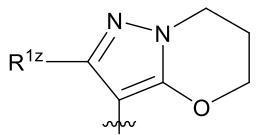


salt, solvate, isomer, or tautomer thereof, wherein R^1 is

20. The compound of claim 17, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R^1 is selected from the group consisting of

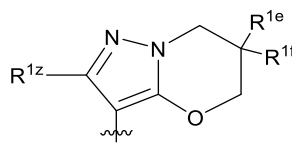


21. The compound of claim 17, or a pharmaceutically acceptable salt, solvate,



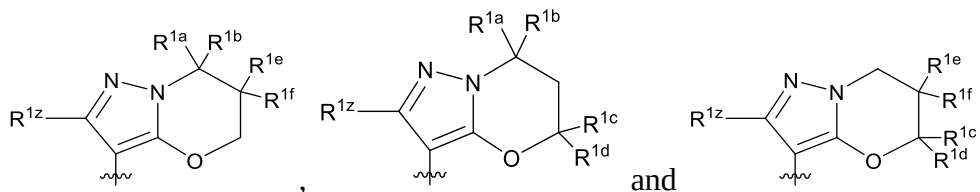
isomer, or tautomer thereof, wherein R^1 is

22. The compound of claim 17, or a pharmaceutically acceptable salt, solvate,



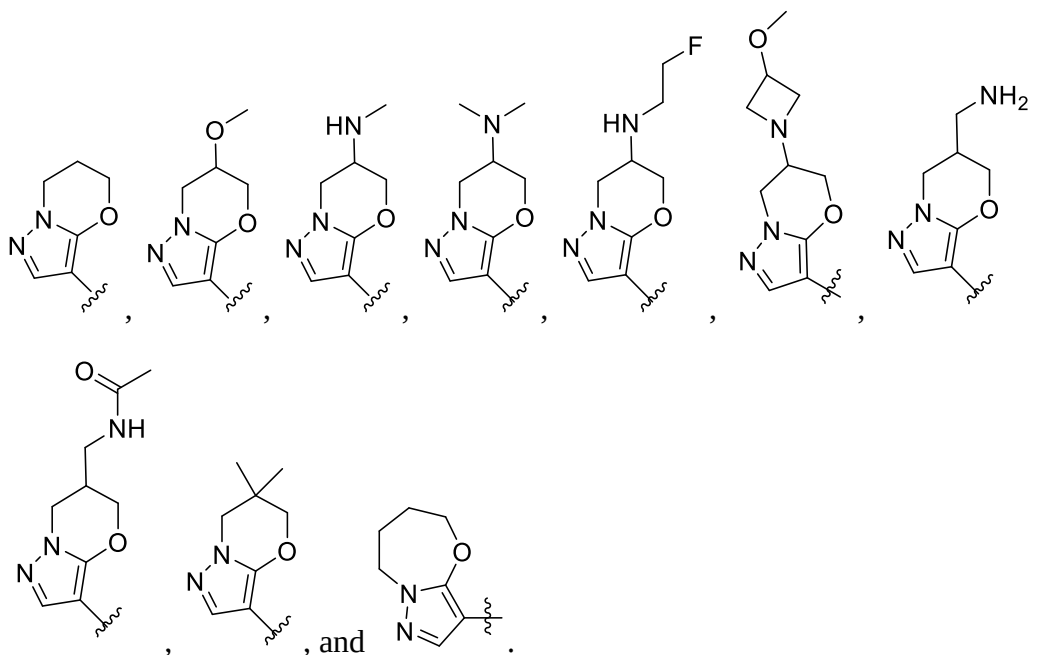
isomer, or tautomer thereof, wherein R^1 is

23. The compound of claim 17, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R^1 is selected from the group consisting of

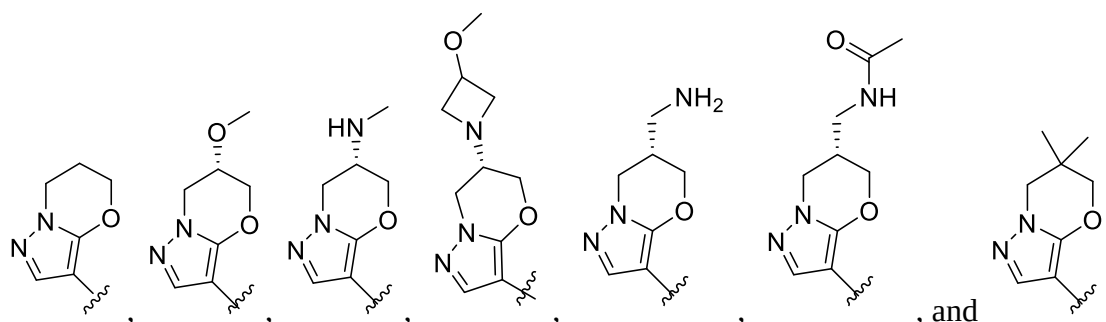


24. The compound of any one of claims 1 to 23, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R^{1z} is H.

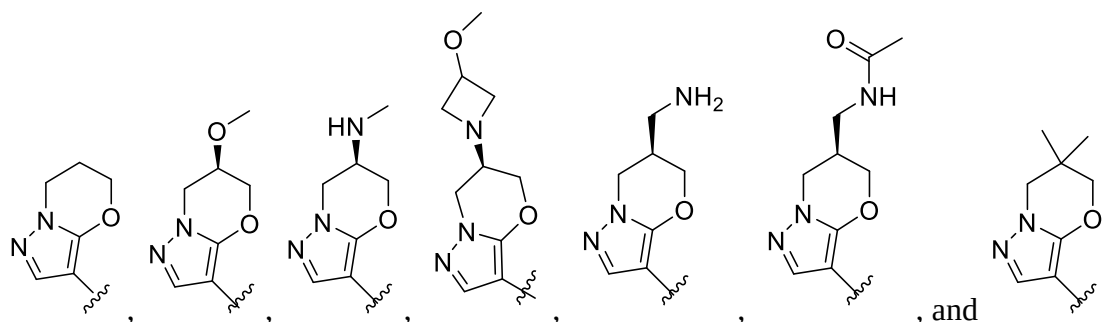
25. The compound of claim 17, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R^1 is selected from the group consisting of



26. The compound of claim 17, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R¹ is selected from the group consisting of



27. The compound of claim 17, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein R¹ is selected from the group consisting of



28. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein the compound is selected from the group consisting of Compound Nos. 1-82 in Table 1.

29. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, wherein the compound is selected from the group consisting of Compound Nos. 1-56 in Table 1.

30. A pharmaceutical composition comprising a compound of any one of claims 1 to 24, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, and a pharmaceutically acceptable carrier.

31. A compound of any one of claims 1 to 29, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, or a pharmaceutical composition of claim 30, for use as a medicament.

32. A compound of any one of claims 1 to 29, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, or a pharmaceutical composition of claim 30, for use in treating a disorder that is responsive to inhibition of inflammasome.

33. Use of a compound of any one of claims 1 to 29, or a pharmaceutically acceptable salt, solvate, isomer, or tautomer thereof, or a pharmaceutical composition of claim 30, in the manufacture of a medicament for treating a disorder that is responsive to inhibition of inflammasome.

34. The use of claim 33, wherein the disorder is one which is responsive to inhibition of activation of the NLRP3 inflammasome.

35. The use of claim 33 or 34, wherein the disorder is responsive to modulation of one or more of IL-6, IL-1 β , IL-17, IL-18, IL-1 α , IL-37, IL-22, IL-33 and Th17 cells.

36. The use of any one of claims 33 to 35, wherein the disorder is a disorder of an immune system, a disorder of a liver, a disorder of a lung, a disorder of a skin, a disorder of a cardiovascular system, a disorder of a renal system, a disorder of a gastro-intestinal tract, a disorder of a respiratory system, a disorder of an endocrine system, a disorder of a central nervous system (CNS), an inflammatory disorder, an autoimmune disorder, or a cancer, tumor, or other malignancy.

37. The use of any one of claims 33 to 35, wherein the disorder is selected from the group consisting of constitutive inflammation, the cryopyrin-associated periodic syndromes (CAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS), neonatal-onset multisystem inflammatory disease (NOMID), autoinflammatory diseases, familial Mediterranean fever (FMF), TNF receptor associated periodic syndrome (TRAPS), mevalonate kinase deficiency (MKD), hyperimmunoglobulinemia D, 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, 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, Schnitzler syndrome, respiratory diseases, idiopathic pulmonary fibrosis (IPF), chronic obstructive pulmonary disorder (COPD), steroid-resistant asthma, asbestosis, silicosis, cystic fibrosis, central nervous system diseases, Parkinson's disease, Alzheimer's disease, motor neuron disease, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis, metabolic diseases, Type 2 diabetes, atherosclerosis, obesity, gout, pseudo-gout, ocular disease, disease of the ocular epithelium, age-related macular degeneration (AMD), corneal infection, uveitis, dry eye, kidney disease, chronic kidney disease, oxalate nephropathy, diabetic nephropathy, liver disease, non-alcoholic steatohepatitis, alcoholic liver disease, inflammatory reactions in skin, contact hypersensitivity, sunburn, inflammatory reactions in the joints, osteoarthritis, systemic juvenile idiopathic arthritis, adult-onset Still's disease, relapsing polychondritis, viral infections, alpha virus infection, Chikungunya virus infection, Ross River virus infection, flavivirus infection, Dengue virus infection, Zika virus infection, flu, HIV infection, hidradenitis suppurativa (HS), cyst-causing skin diseases, cancers, lung cancer metastasis, pancreatic cancers, gastric cancers, myelodysplastic 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, Dressler's syndrome, ischaemia reperfusion injury, and any disease where an individual has been determined to carry a germ line or somatic non-silent mutation in NLRP3.

38. The use of any one of claims 33 to 35, wherein the disorder is a bacterial infection, a viral infection, a fungal infection, inflammatory bowel disease, celiac disease, colitis, intestinal hyperplasia, cancer, metabolic syndrome, obesity, rheumatoid arthritis, liver disease, hepatic steatosis, fatty liver disease, liver fibrosis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), lupus, lupus nephritis, cryopyrin-associated periodic syndromes (CAPS), myelodysplastic syndromes (MDS), gout, myeloproliferative neoplasms (MPN), atherosclerosis, Crohn's disease, or inflammatory bowel disease (IBD).