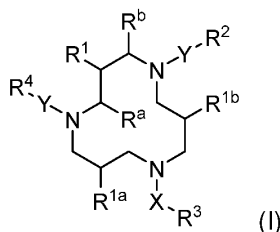


We Claim:

1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof:



wherein:

each of R^a and R^b is independently H or C₁₋₃alkyl;

R¹ is H, OH, C₁₋₃alkyl, OC₁₋₃alkyl, =CH₂, or =NOR⁵; or R¹ is C₃₋₆cycloalkyl or C₃₋₆heterocycloalkyl and forms a spiro group with the ring carbon to which it is attached;

each of R^{1a} and R^{1b} is independently H or C₁₋₃alkyl;

R² is C₁₋₆alkyl, N(R⁵)₂, C₃₋₈cycloalkyl, C₃₋₇heterocycloalkyl, C₃₋₇heterocycloalkenyl, or C₆₋₁₀aryl;

R³ is H, C₁₋₆alkyl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, C₃₋₇heterocycloalkyl, C₆₋₁₀aryl, or C₂₋₆heteroaryl;

R⁴ is C₃₋₈cycloalkyl, C₃₋₉heterocycloalkyl, C₆₋₁₀aryl, or C₂₋₆heteroaryl;

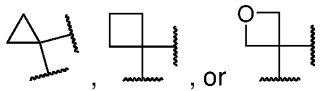
each R⁵ independently is H, C₁₋₃alkyl, or C₀₋₂alkylene-C₆₋₁₀aryl;

X is absent, C₁₋₃alkylene, C=O, or (C=O)O;

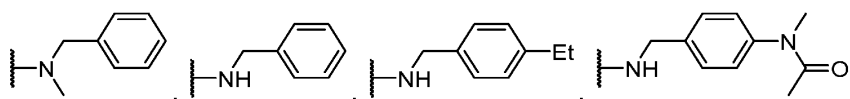
Y is SO or SO₂;

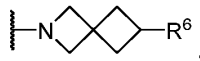
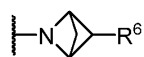
each heterocycloalkyl, heterocycloalkenyl, and heteroaryl group independently has 1, 2, or 3 ring heteroatoms selected from N, O, and S.

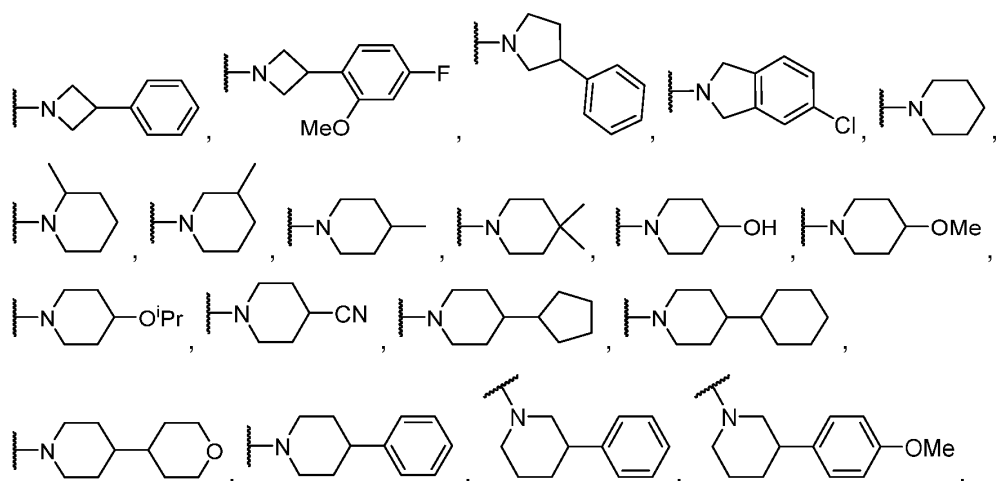
2. The compound or salt of claim 1, wherein each Y is SO.
3. The compound or salt of claim 1, wherein each Y is SO₂.
4. The compound of any one of claims 1-3, wherein R^a is H.
5. The compound of any one of claims 1-3, wherein R^a is C₁₋₃alkyl.
6. The compound of claim 5, wherein R^a is CH₃.
7. The compound of any one of claims 1-6, wherein R^b is H.
8. The compound of any one of claims 1-6, wherein R^b is C₁₋₃alkyl.

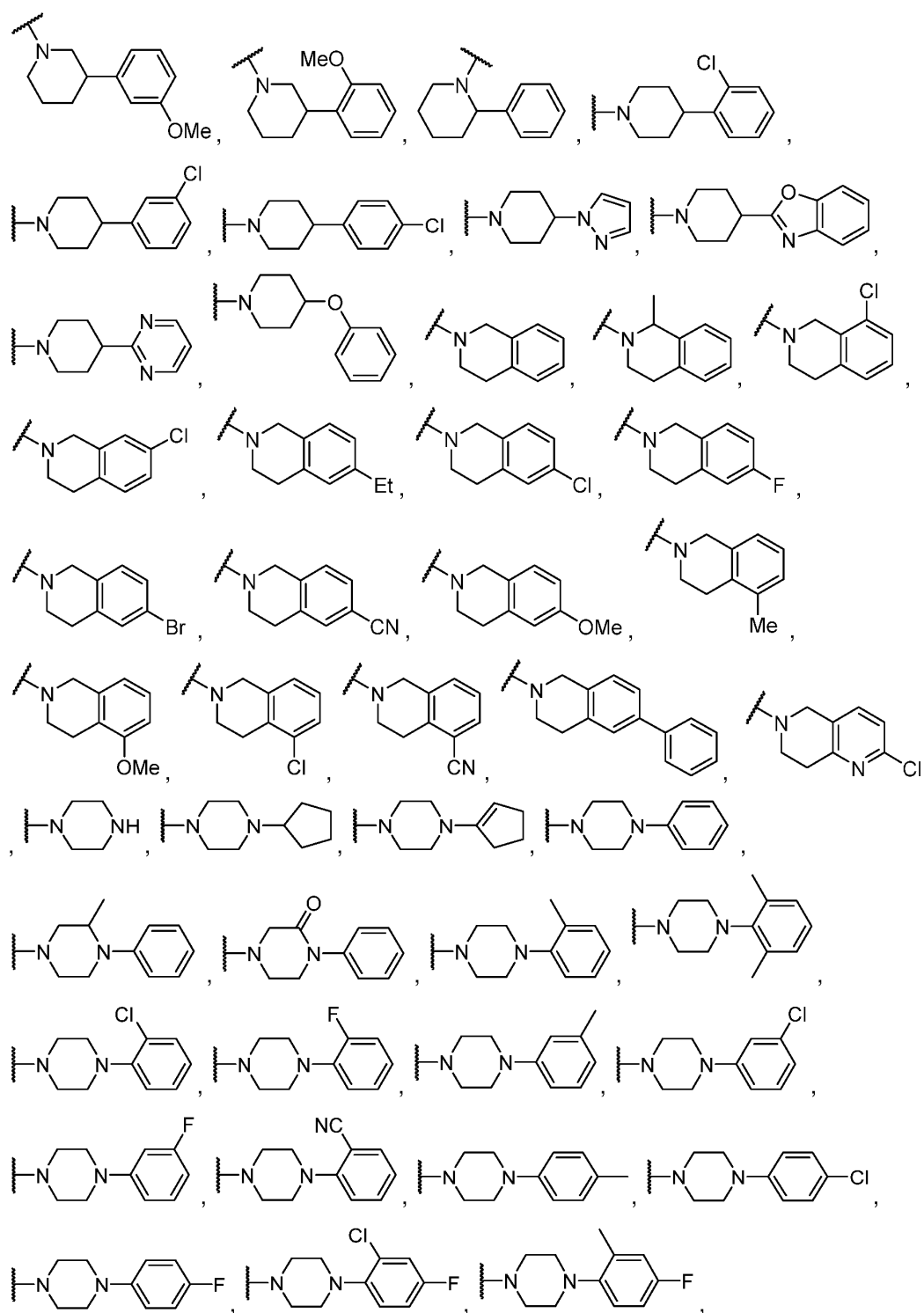
9. The compound of claim 8, wherein R^a is CH_3 .
10. The compound or salt of any one of claims 1-9, wherein R^1 is H, OH, or $=NOR^5$.
11. The compound or salt of claim 10, wherein R^5 is H or CH_3 .
12. The compound or salt of any one of claims 1-9, wherein R^1 is C_{1-3} alkyl or OC_{1-3} alkyl.
13. The compound or salt of claim 12, wherein R^1 is CH_3 or OCH_3 .
14. The compound or salt of claim 13, wherein R^1 is CH_3 and exhibits *S* stereochemistry.
15. The compound or salt of any one of claims 1-9, wherein R^1 is C_{3-6} cycloalkyl or C_{3-6} heterocycloalkyl and forms a spiro group with the ring carbon to which it is attached.
16. The compound or salt of claim 15, wherein R^1 together with the ring atom to which it is attached forms  , or .
17. The compound or salt of any one of claims 1-9, wherein R^1 is $=CH_2$.
18. The compound or salt of any one of claims 1-17, wherein each of R^{1a} and R^{1b} is H.
19. The compound or salt of any one of claims 1-17, wherein at least one of R^{1a} and R^{1b} is C_{1-3} alkyl.
20. The compound or salt of claim 19, wherein each of R^{1a} and R^{1b} is CH_3 .
21. The compound or salt of any one of claims 1-20, wherein R^2 is C_{1-6} alkyl or $N(R^5)_2$.
22. The compound or salt of claim 21, wherein each R^5 independently comprises H, C_{1-3} alkyl, or benzyl.

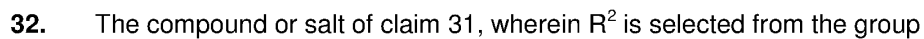
23. The compound or salt of claim 21, wherein R^2 is Et, iPr, $N(CH_3)_2$,

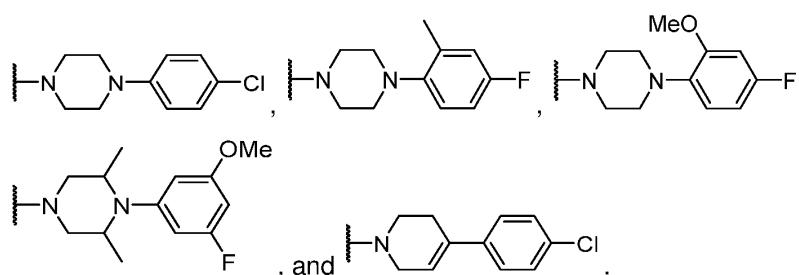


- 24.** The compound or salt of any one claims 1-20, wherein R^2 comprises C_{3-8} cycloalkyl.
- 25.** The compound or salt of claim 24, wherein R^2 comprises cyclopentyl or cyclohexyl.
- 26.** The compound or salt of any one of claims 1-20, wherein R^2 is C_{3-9} heterocycloalkyl or C_{3-9} heterocycloalkenyl.
- 27.** The compound or salt of claim 26, wherein R^2 comprises oxetanyl, azetidiny, tetrahydrofuranyl, pyrrolidinyl, tetrahydropyranyl, pyranly, piperidinyl, piperazinyl, azepanyl, morpholinyl, or tetrahydropyridinyl.
- 28.** The compound or salt of claim 26, wherein the C_{3-7} heterocycloalkyl or C_{3-7} heterocycloalkenyl comprises a bridge or a spiro group.
- 29.** The compound of claim 28, wherein the C_{3-9} heterocycloalkyl comprising a bridge or a spiro group is selected from the group consisting of , , and , and R^6 is C_{1-6} alkyl, C_{3-8} cycloalkyl, or C_{6-10} aryl.
- 30.** The compound of claim 29, wherein R^6 is phenyl optionally substituted with one to three groups independently selected from halo, C_{1-3} alkyl, C_{1-3} alkoxy, and CN.
- 31.** The compound or salt of claim 27, wherein R^2 is selected from the group consisting of

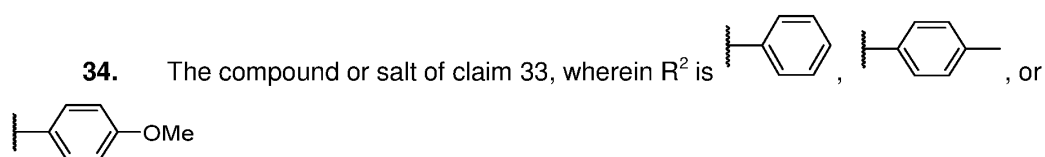








33. The compound or salt of any one of claims 1-20, wherein R^2 is C_{6-10} aryl.



35. The compound or salt of any one of claims 1-34, wherein X is absent.

36. The compound or salt of claim 35, wherein R^3 comprises C_{1-6} alkyl or H.

37. The compound or salt of claim 36, wherein R^3 is 2-methylbutyl, isopropyl, isopentyl, $CH_2CH_2OCH_3$, $CH_2C(CH_3)_2CN$, CH_2CF_3 , or $CH_2CH_2CF_3$.

38. The compound or salt of claim 37, wherein R^3 is isobutyl.

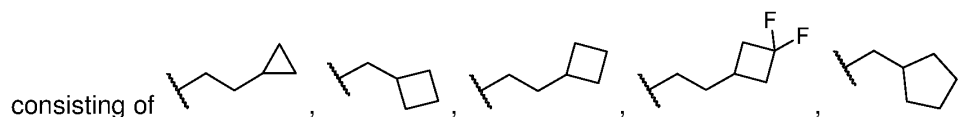
39. The compound or salt of any one of claims 1-34, wherein X is C_{1-3} alkylene.

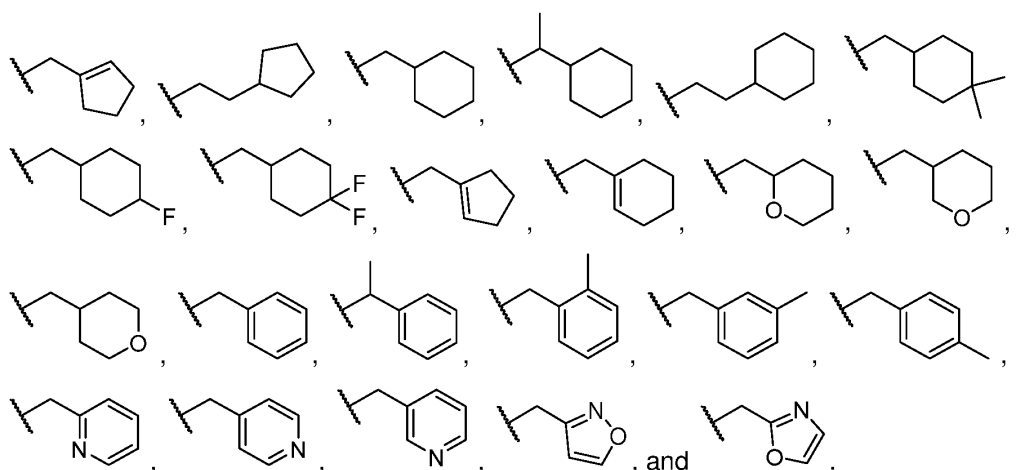
40. The compound or salt of claim 39, wherein X is CH_2 , CH_2CH_2 , or $CH(CH_3)$.

41. The compound or salt of claim 39 or 40, wherein R^3 comprises C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, C_{3-7} heterocycloalkyl, C_{6-10} aryl, or C_{2-6} heteroaryl.

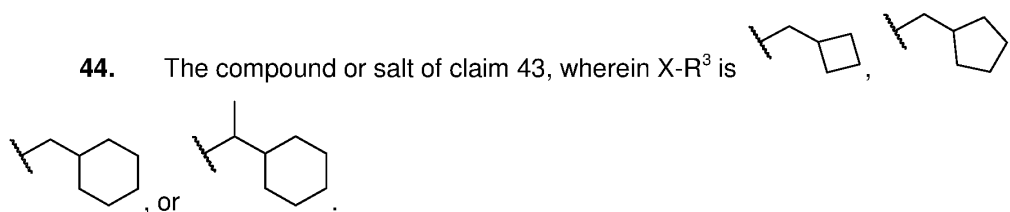
42. The compound or salt of claim 41, wherein R^3 comprises cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopentenyl, cyclohexenyl, tetrahydropyranyl, phenyl, pyrrolyl, pyrazolyl, imidazolyl, tetrazolyl, furanyl, thiophenyl, thiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, pyridinyl, pyrazinyl, or pyrimidinyl.

43. The compound or salt of claim 42, wherein $X-R^3$ is selected from the group

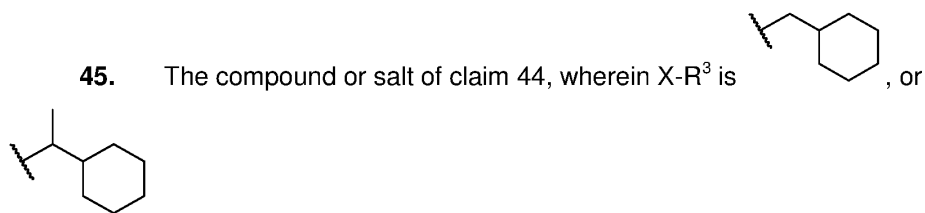




44. The compound or salt of claim 43, wherein X-R³ is



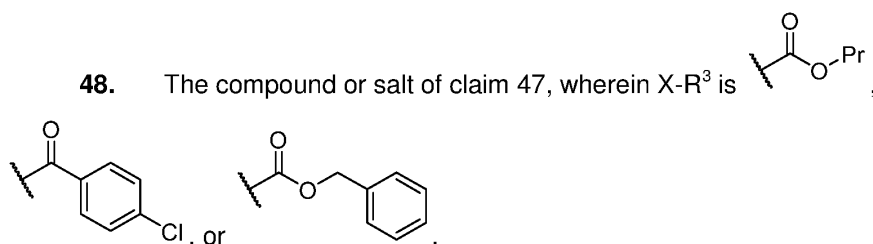
45. The compound or salt of claim 44, wherein X-R³ is



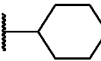
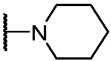
46. The compound or salt of any one of claims 1-34, wherein X is C=O or (C=O)O.

47. The compound or salt of claim 46, wherein R³ comprises C₁₋₆alkyl or C₆₋₁₀aryl.

48. The compound or salt of claim 47, wherein X-R³ is

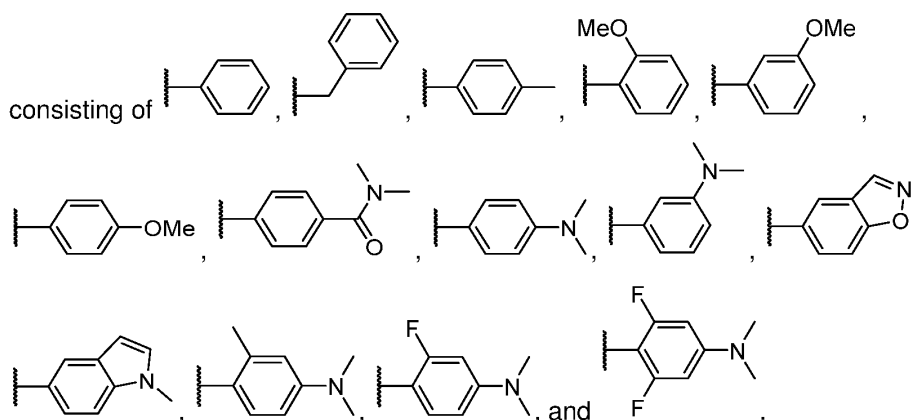


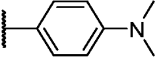
49. The compound or salt of any one of claims 1-48, wherein R⁴ comprises C₃₋₈cycloalkyl or C₃₋₉heterocycloalkyl.

50. The compound or salt of claim 49, wherein R^4 is  or .

51. The compound or salt of any one of claims 1-48, wherein R^4 comprises C_{6-10} aryl or C_{2-9} heteroaryl, and R^4 is optionally substituted with one to three groups independently selected from halo, C_{1-3} alkyl, C_{1-3} alkoxy, $C(O)N(R^N)_2$, and $N(R^N)_2$, and each R^N is independently H or C_{1-3} alkyl.

52. The compound or salt of claim 51, wherein R^4 is selected from the group

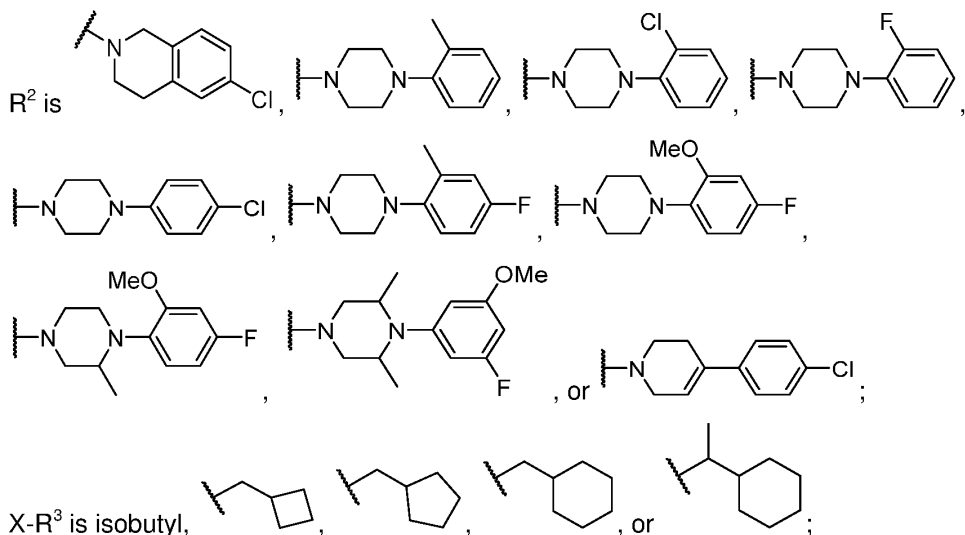


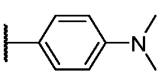
53. The compound or salt of claim 52, wherein R^4 is .

54. The compound or salt of claim 1, wherein:

R^a , R^b , R^{1a} , and R^{1b} are each H;

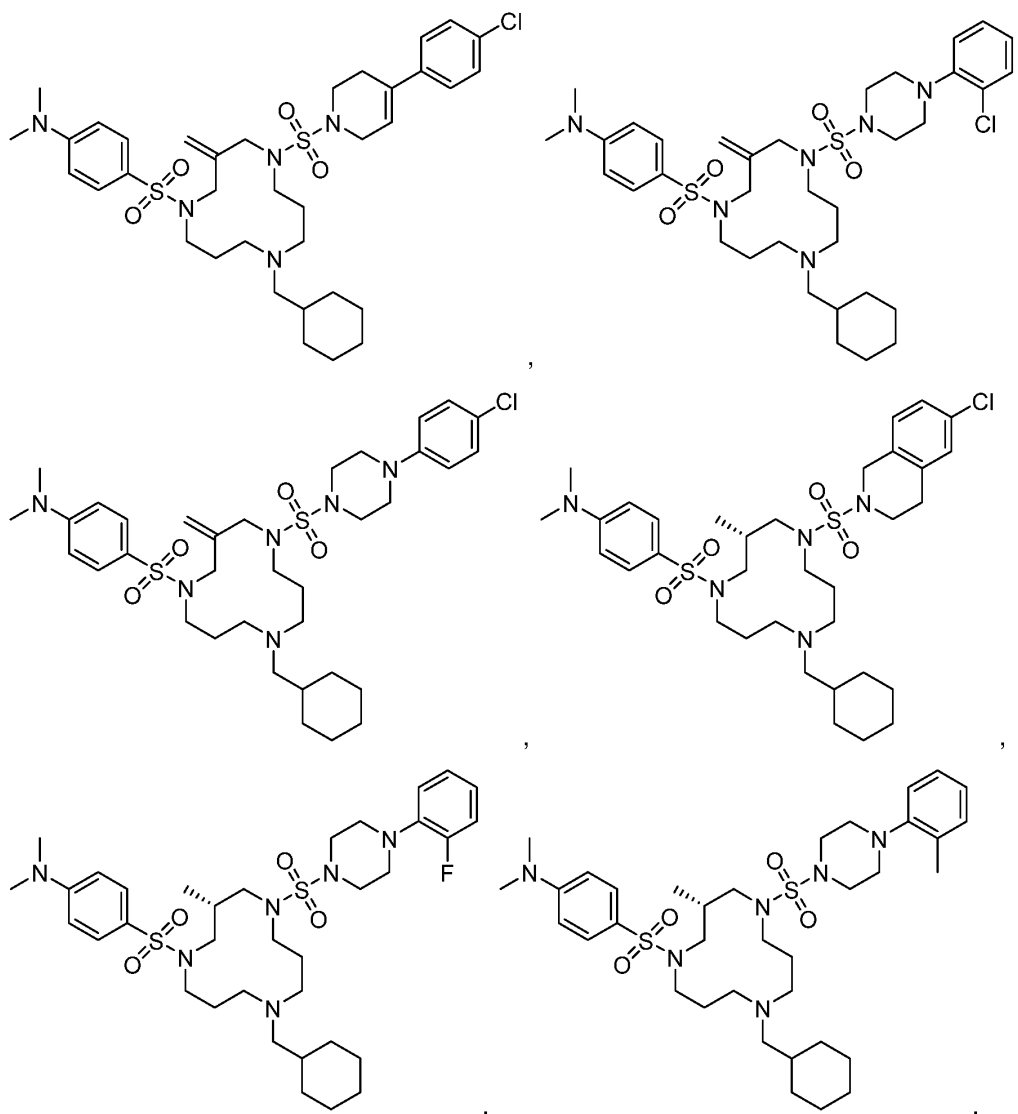
R^1 is $=CH_2$ or CH_3 ;

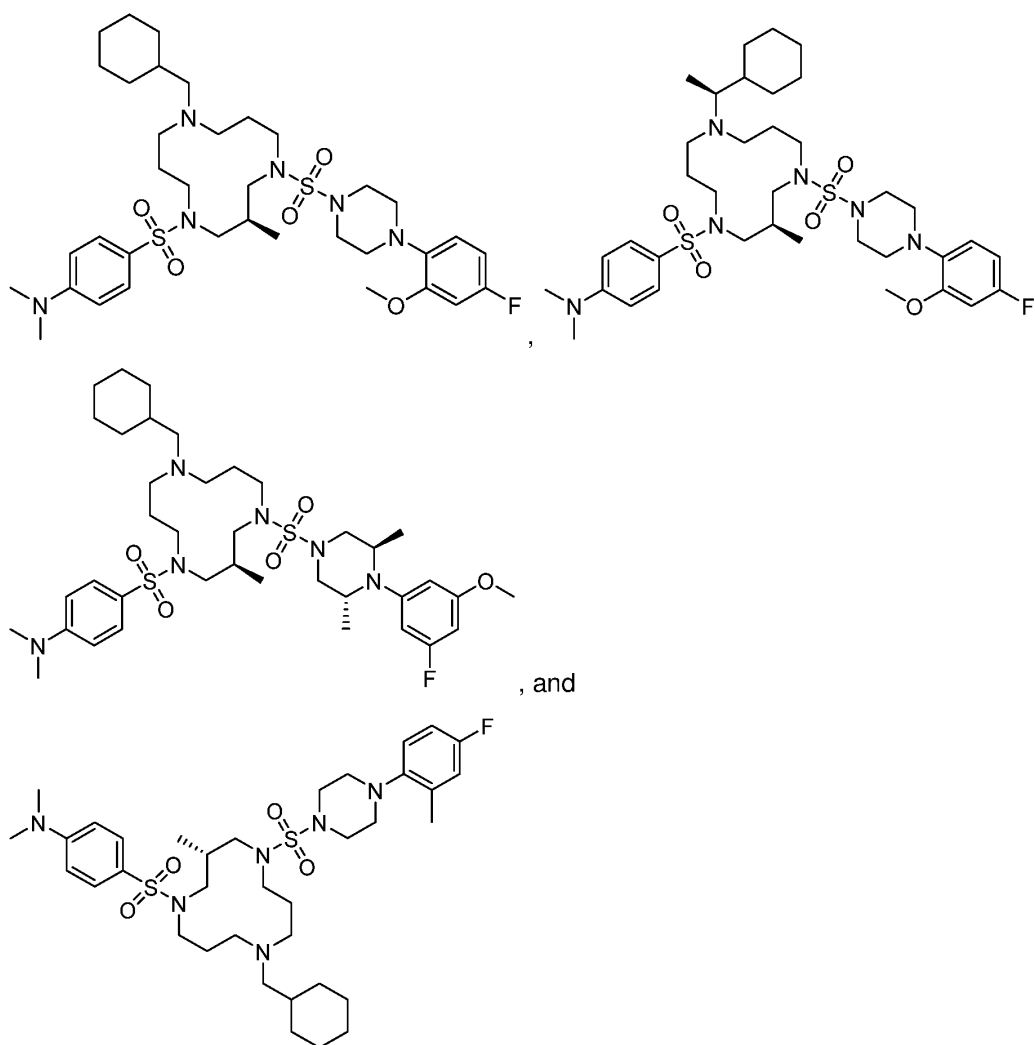


R⁴ is ; and

each Y is SO₂.

- 55.** The compound or salt of any one of claims 1-54, wherein R¹ is in a (*S*) configuration.
- 56.** A compound listed in Table A, or a pharmaceutically acceptable salt thereof.
- 57.** The compound or salt of claim 56, wherein the compound is selected from the group consisting of:





58. A compound selected from a compound listed in Table B, or a pharmaceutically acceptable salt thereof.

59. A pharmaceutical composition comprising the compound or salt of any one of claims 1-58 and a pharmaceutically acceptable carrier.

60. A method of inhibiting protein secretion in a cell comprising contacting the cell with the compound or salt of any one of claims 1-58, or the pharmaceutical composition of claim 59 in an amount effective to inhibit secretion.

61. The method of claim 60, wherein the protein is a checkpoint protein.

62. The method of claim 60, wherein the protein is a cell-surface protein, endoplasmic reticulum associated protein, or secreted protein involved in regulation of anti-tumor immune response.

63. The method of claim 60, wherein the protein is at least one of PD-1, PD-L1, TIM-1, LAG-3, CTLA4, BTLA, OX-40, B7H1, B7H4, CD137, CD47, CD96, CD73, CD40, VISTA, TIGIT, LAIR1, CD160, 2B4, TIGIT, and combinations thereof.

64. The method of any one of claims 60-63, wherein the contacting comprises administering the compound or the composition to a subject.

65. A method for treating inflammation in a subject comprising administering to the subject a therapeutically effective amount of the compound or salt of any one of claims 1-58 or the pharmaceutical composition of claim 59.

66. A method for treating or preventing cancer or a precancerous condition in a subject comprising administering to the subject a therapeutically effective amount of the compound or salt of any one of claims 1-58 or the pharmaceutical composition of claim 59.

67. The method of claim 66, wherein the cancer is melanoma, multiple myeloma, prostate cancer, lung cancer, pancreatic cancer, squamous cell carcinoma, leukemia, lymphoma, a neuroendocrine tumor, bladder cancer, or colorectal cancer.

68. The method of claim 66, wherein the cancer is non small cell lung carcinoma, squamous cell carcinoma, leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, lymphoma, NPM/ALK-transformed anaplastic large cell lymphoma, diffuse large B cell lymphoma, neuroendocrine tumors, breast cancer, mantle cell lymphoma, renal cell carcinoma, rhabdomyosarcoma, ovarian cancer, endometrial cancer, small cell carcinoma, adenocarcinoma, gastric carcinoma, hepatocellular carcinoma, pancreatic cancer, thyroid carcinoma, anaplastic large cell lymphoma, hemangioma, or head and neck cancer.

69. The method of claim 66, wherein the cancer is a solid tumor.

70. The method of claim 66, wherein the cancer is head and neck cancer, squamous cell carcinoma, gastric carcinoma, or pancreatic cancer.

71. A method for treating an autoimmune disease in a subject comprising administering to the subject a therapeutically effective amount of the compound or salt of any one of claims 1-58 or the pharmaceutical composition of claim 59.

72. The method of claim 71, wherein the autoimmune disease is psoriasis, dermatitis, systemic scleroderma, sclerosis, Crohn's disease, ulcerative colitis; respiratory distress syndrome, meningitis; encephalitis; uveitis; colitis; glomerulonephritis; eczema, asthma, chronic inflammation; atherosclerosis; leukocyte adhesion deficiency; rheumatoid arthritis; systemic lupus erythematosus (SLE); diabetes mellitus; multiple sclerosis; Reynaud's syndrome; autoimmune thyroiditis; allergic encephalomyelitis; Sjorgen's syndrome; juvenile onset diabetes; tuberculosis, sarcoidosis, polymyositis, granulomatosis and vasculitis; pernicious anemia (Addison's disease); diseases involving leukocyte diapedesis; central nervous system (CNS) inflammatory disorder; multiple organ injury syndrome; hemolytic anemia; myasthenia gravis; antigen-antibody complex mediated diseases; anti-glomerular basement membrane disease; antiphospholipid syndrome; allergic neuritis; Graves' disease; Lambert-Eaton myasthenic syndrome; pemphigoid bullous; pemphigus; autoimmune polyendocrinopathies; Reiter's disease; stiff-man syndrome; Behcet disease; giant cell arteritis; immune complex nephritis; IgA nephropathy; IgM polyneuropathies; immune thrombocytopenic purpura (ITP) or autoimmune thrombocytopenia.

73. A method for the treatment of an immune-related disease in a subject comprising administering to the subject a therapeutically effective amount of the compound or salt of any one of claims 1-58 or the pharmaceutical composition of claim 59.

74. The method of claim 73, wherein the immune-related disease is rheumatoid arthritis, lupus, inflammatory bowel disease, multiple sclerosis, or Crohn's disease.

75. A method for treating neurodegenerative disease in a subject comprising administering to the subject a therapeutically effective amount of the compound or salt of any one of claims 1-58 or the pharmaceutical composition of claim 59.

76. The method of claim 75, wherein the neurodegenerative disease is multiple sclerosis.

77. A method for treating an inflammatory disease in a subject comprising administering to the subject a therapeutically effective amount of the compound or salt of any one of claims 1-58 or the pharmaceutical composition of claim 59.

78. The method of claim 77, wherein the inflammatory disease is bronchitis, conjunctivitis, myocarditis, pancreatitis, chronic cholecystitis, bronchiectasis, aortic valve stenosis, restenosis, psoriasis or arthritis.