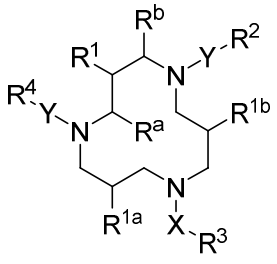
We Claim:

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



(I)

wherein:

each of R^a and R^b is independently H or $C_{1\text{-}3}$alkyl;

R^1 is H, OH, $C_{1\text{-}3}$alkyl, $OC_{1\text{-}3}$alkyl, $=CH_2$, or $=NOR^5$; or R^1 is $C_{3\text{-}6}$cycloalkyl or $C_{3\text{-}6}$heterocycloalkyl 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 $C_{1\text{-}3}$ alkyl;

R^2 is ~~$C_{1\text{-}6}$alkyl, $N(R^5)_2$, $C_{3\text{-}8}$cycloalkyl, $C_{3\text{-}7}$heterocycloalkyl, $C_{3\text{-}7}$heterocycloalkenyl, or $C_{6\text{-}10}$aryl~~ $C_{3\text{-}9}$heterocycloalkyl or $C_{3\text{-}9}$heterocycloalkenyl;

R^3 is ~~H, $C_{1\text{-}6}$alkyl,~~ $C_{3\text{-}8}$cycloalkyl, $C_{3\text{-}8}$cycloalkenyl, $C_{3\text{-}7}$heterocycloalkyl, ~~$C_{6\text{-}10}$aryl,~~ or $C_{2\text{-}6}$heteroaryl;

R^4 is $C_{3\text{-}8}$cycloalkyl, $C_{3\text{-}9}$heterocycloalkyl, $C_{6\text{-}10}$aryl, or $C_{2\text{-}6}$heteroaryl;

each R^5 independently is H, $C_{1\text{-}3}$alkyl, or $C_{0\text{-}2}$alkylene-$C_{6\text{-}10}$aryl;

X is ~~absent,~~ $C_{1\text{-}3}$alkylene~~, C=O, or (C=O)O~~;

Y is SO or SO_2;

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 SO_2.

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 $C_{1\text{-}3}$alkyl.

6. The compound of claim 5, wherein R^a is CH_3.

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 $C_{1\text{-}3}$alkyl.

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 $C_{1\text{-}3}$alkyl or $OC_{1\text{-}3}$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 $C_{3\text{-}6}$cycloalkyl or $C_{3\text{-}6}$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.

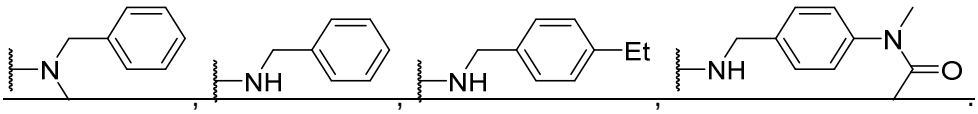
19. The compound or salt of any one of claims 1-17, wherein at least one of of R^{1a} and R^{1b} is $C_{1\text{-}3}$alkyl.

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 $C_{1\text{-}6}$alkyl or $N(R^5)_2$.

22. The compound or salt of claim 21, wherein each R^5 independently comprises H, $C_{1\text{-}3}$alkyl, or benzyl.

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



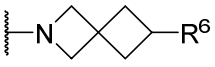
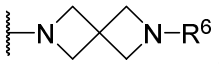
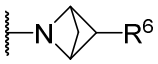
~~**24.** The compound or salt of any one claims 1-20, wherein R^2 comprises C_{3-8}cycloalkyl.~~

~~**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.~~

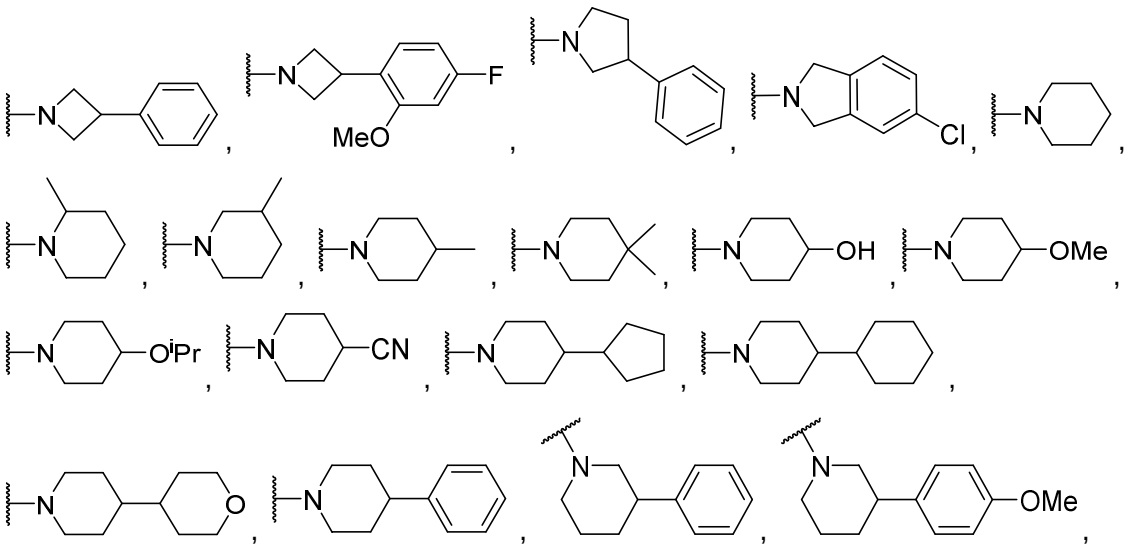
~~27.~~23. The compound or salt of any one of claims ~~26~~1-20, wherein R^2 comprises oxetanyl, azetidinyl, tetrahydrofuranyl, pyrrolidinyl, tetrahydropyranyl, pyranyl, piperidinyl, piperazinyl, azepanyl, ~~morpholinyl,~~ or tetrahydropyridinyl.

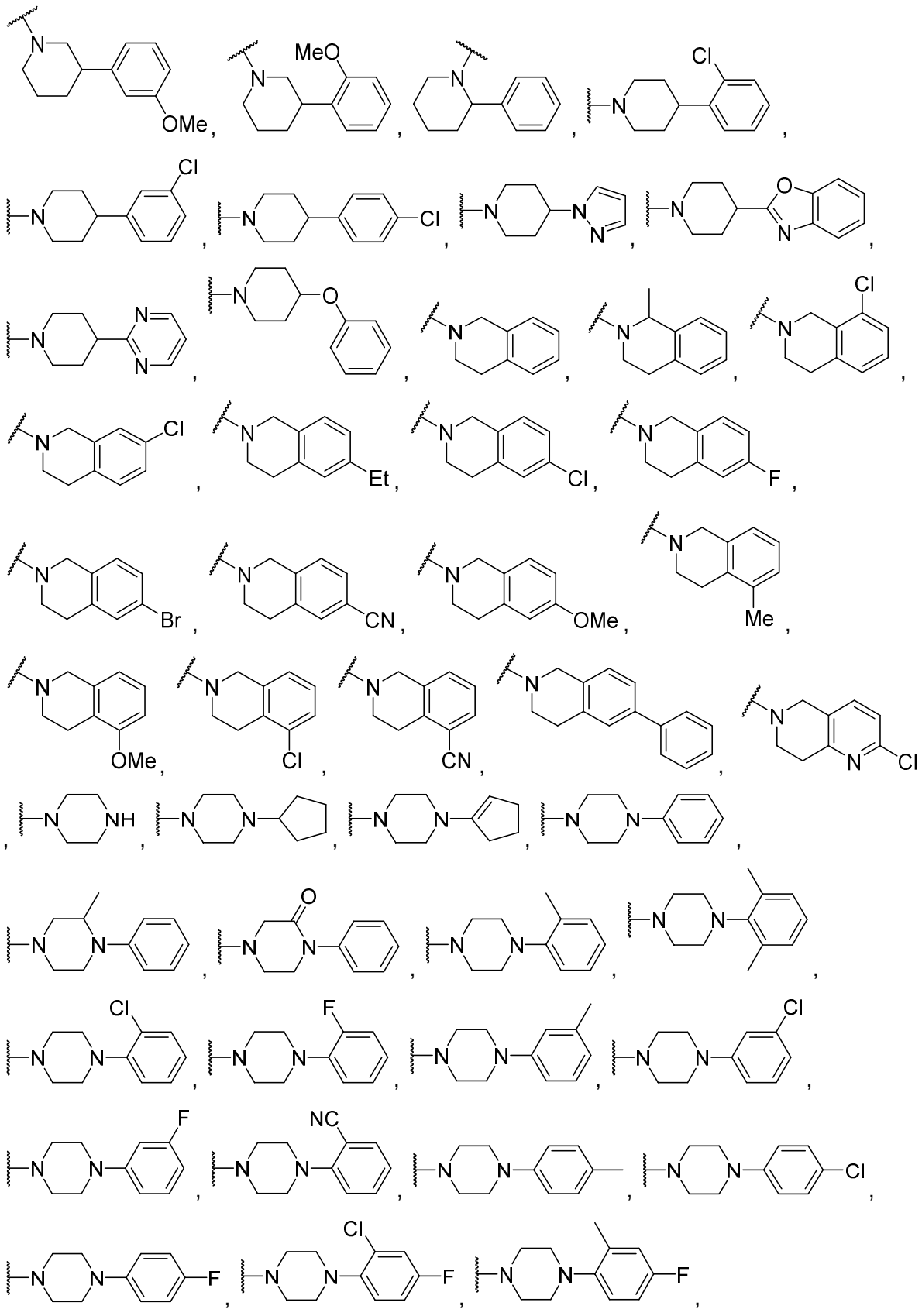
~~28.~~24. The compound or salt of any one of claims ~~26~~1-20, wherein the C_{3-7}heterocycloalkyl or C_{3-7}heterocycloalkenyl of R^2 comprises a bridge or a spiro group.

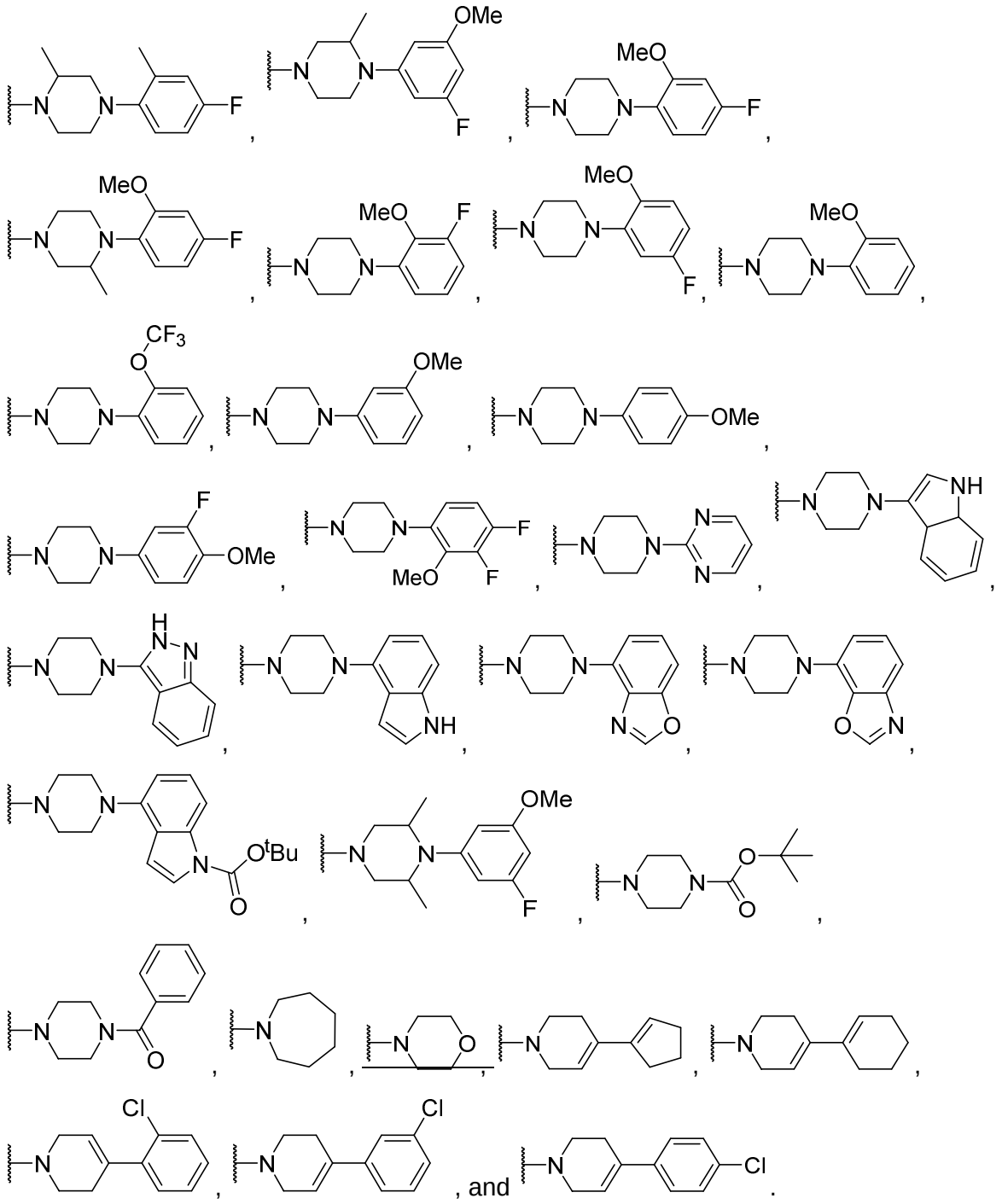
~~29.~~25. The compound of claim ~~28~~24, wherein the C_{3-9}heterocycloalkyl comprising a bridge or a spiro group is selected from the group consisting of  ,  , and  , and R^6 is C_{1-6}alkyl, C_{3-8}cycloalkyl, or C_{6-10}aryl.

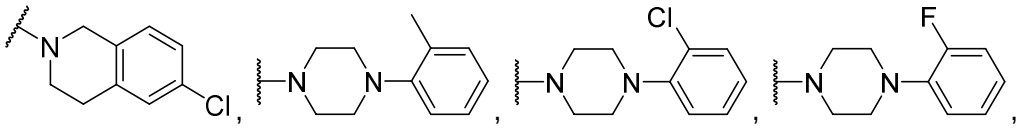
~~30.~~26. The compound of claim ~~29~~25, wherein R^6 is phenyl optionally substituted with one to three groups independently selected from halo, C_{1-3}alkyl, C_{1-3}alkoxy, and CN.

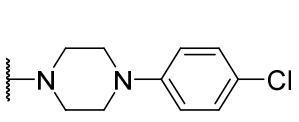
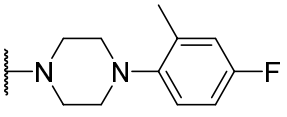
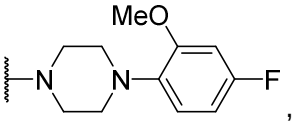
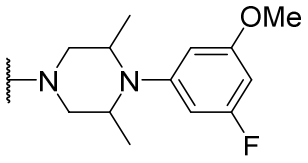
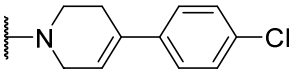
~~31.~~27. The compound or salt of claim ~~27~~23, wherein R^2 is selected from the group consisting of



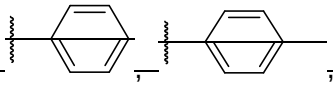
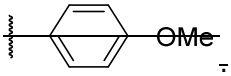




~~32.~~28. The compound or salt of claim ~~31~~27, wherein R^2 is selected from the group consisting of  .


, 
, 
, 
, and 
.

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

~~**34.** The compound or salt of claim 33, wherein R^2 is~~ 
~~, or~~ 
~~.~~

~~35.~~29. The compound or salt of any one of claims 1-~~34~~28, 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 $CH_2CH_2CF_3$.~~

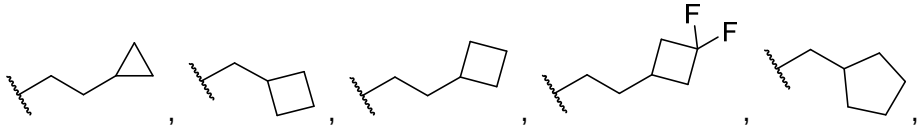
~~**38.** The compound or salt of claim 37, wherein R^3 is isobutyl.~~

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

~~40.~~30. The compound or salt of any one of claims ~~39~~1-28, 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.~~31. The compound or salt of claim ~~41~~30, 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.~~32. The compound or salt of claim ~~42~~31, wherein X-R^3 is selected from the group consisting of 
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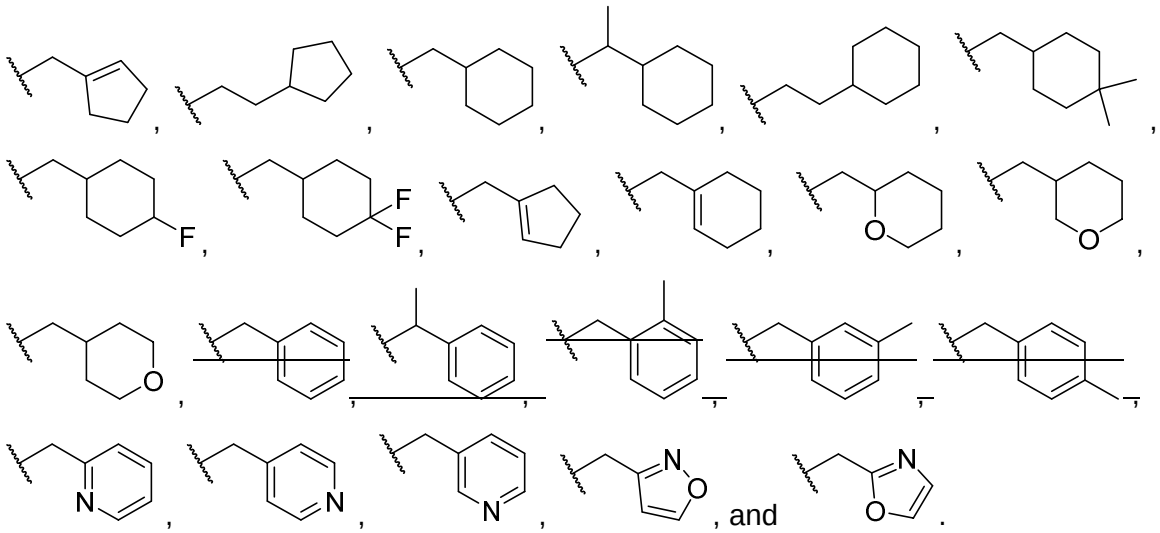
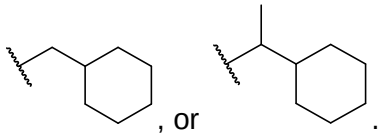
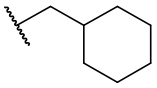
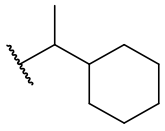


~~44.~~33. The compound or salt of claim ~~43~~32, wherein X-R^3 is 

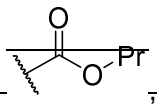


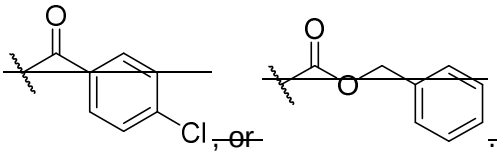
~~45.~~34. The compound or salt of claim ~~44~~33, wherein X-R^3 is  , or



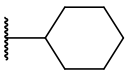
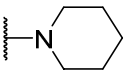
~~46. The compound or salt of any one of claims 1-34, wherein X is C=O or (C=O)O.~~

~~47. The compound or salt of claim 46, wherein R^3 comprises C_{1-6}alkyl or C_{6-10}aryl.~~

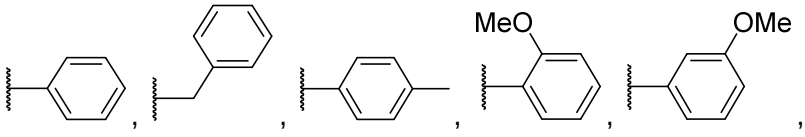
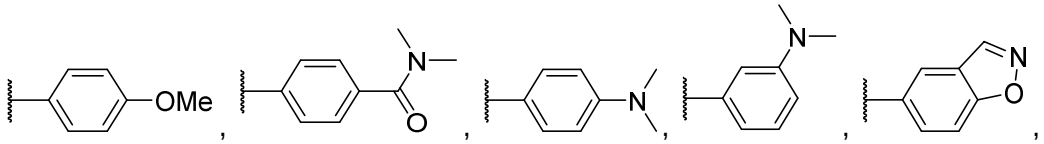
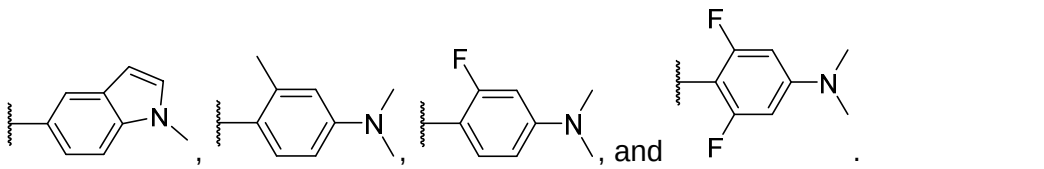
~~48. The compound or salt of claim 47, wherein X-R^3 is~~ 

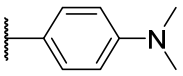


~~49.~~35. The compound or salt of any one of claims 1-~~48~~34, wherein R^4 comprises C_{3-8}cycloalkyl or C_{3-9}heterocycloalkyl.

~~50.~~36. The compound or salt of claim ~~49~~35, wherein R^4 is  or  .

~~51.~~37. The compound or salt of any one of claims 1-~~48~~34, 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.

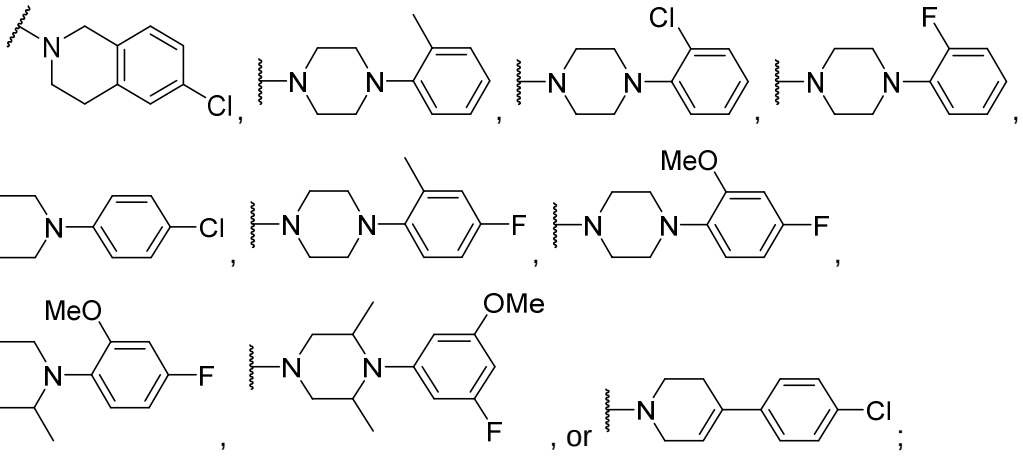
~~52.~~38. The compound or salt of claim ~~51~~37, wherein R^4 is selected from the group consisting of  ,  ,  , and .

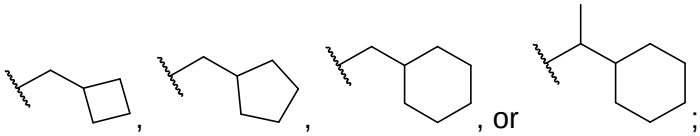
~~53.~~39. The compound or salt of claim ~~52~~38, wherein R^4 is  .

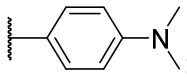
~~54.~~40. The compound or salt of claim 1, wherein:

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

R^1 is $=CH_2$ or CH_3;

R^2 is  ;

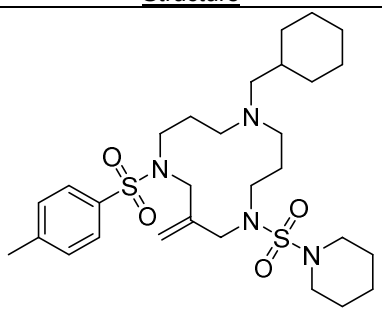
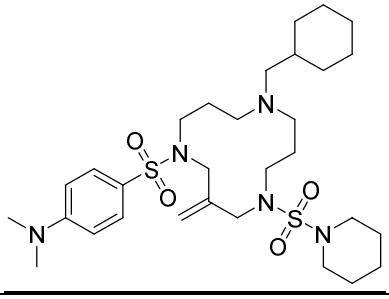
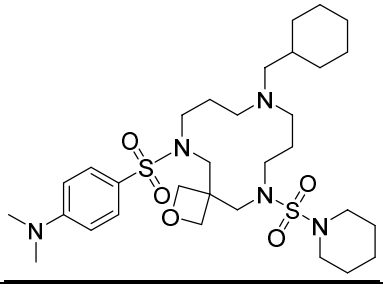
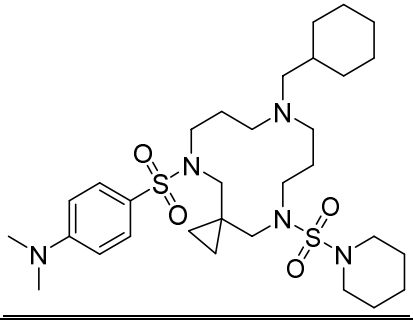
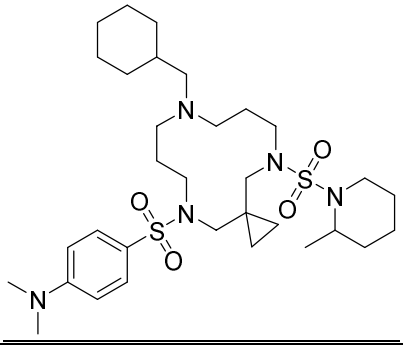
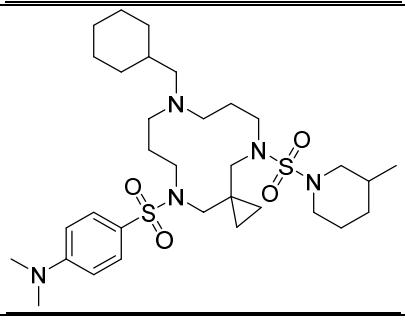
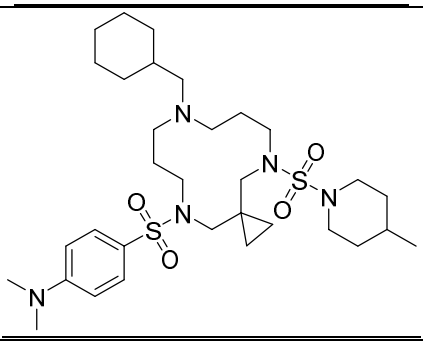
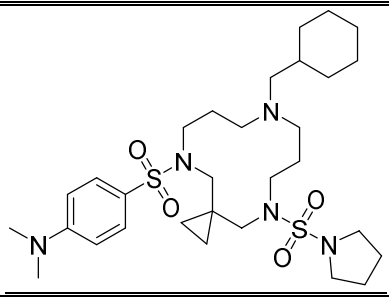
X-R^3 is ~~isobutyl,~~  ;

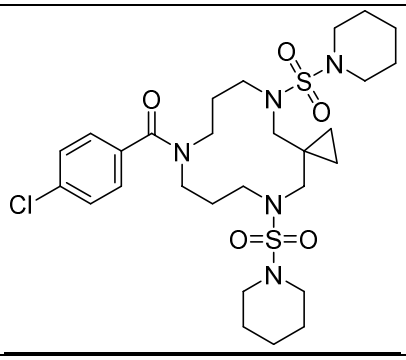
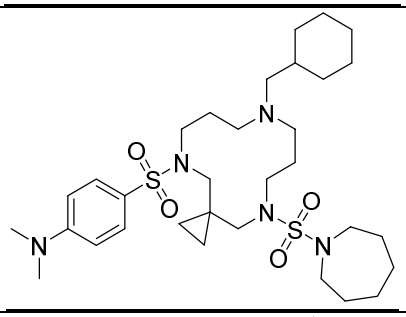
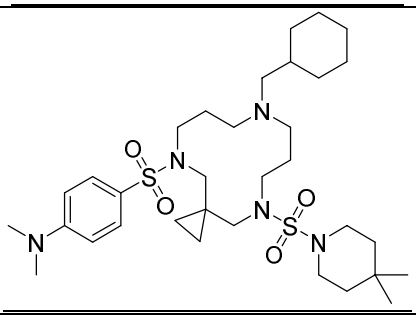
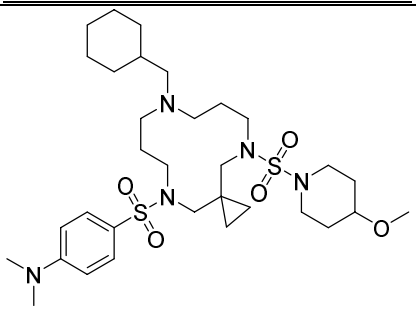
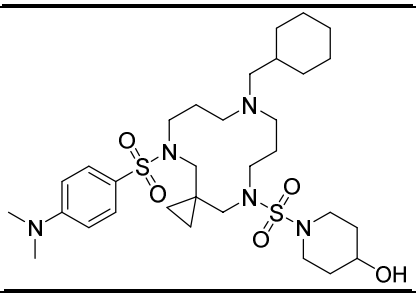
R^4 is  ; and

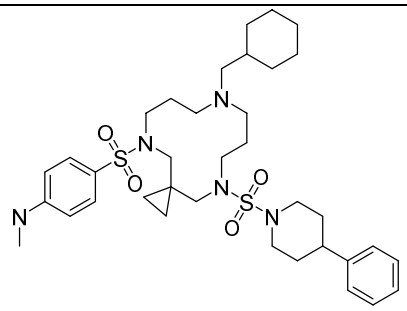
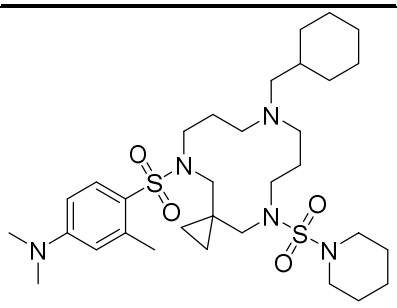
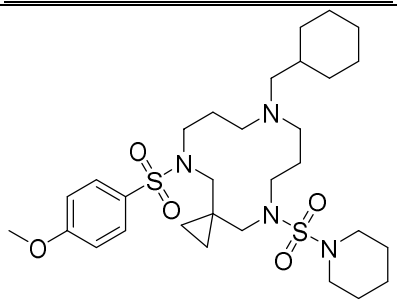
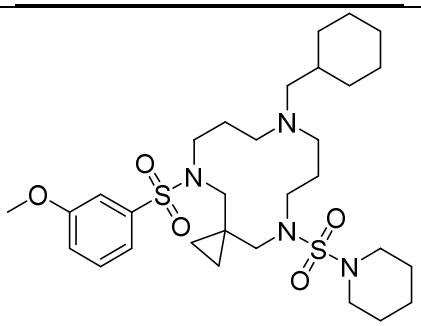
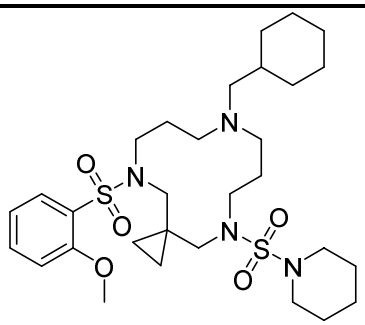
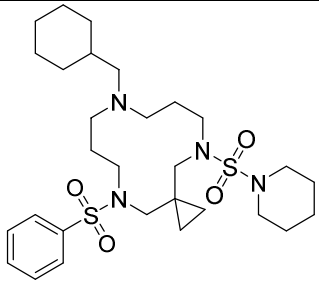
each Y is SO_2.

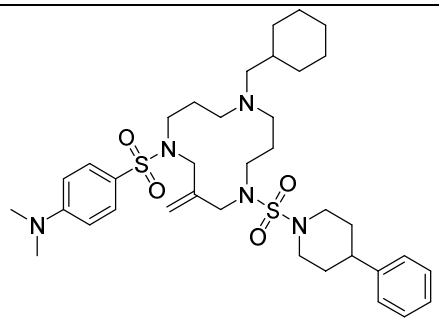
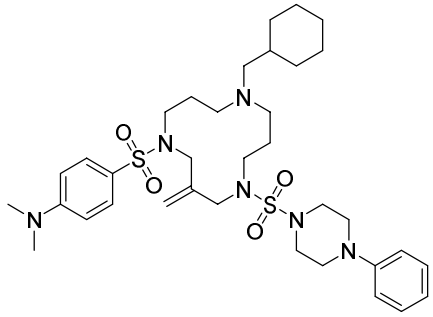
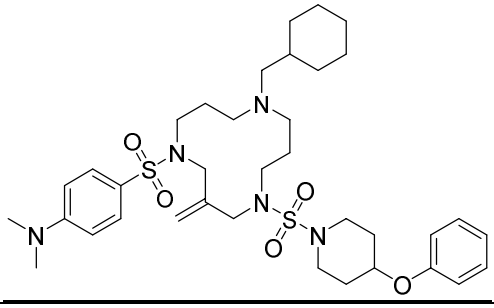
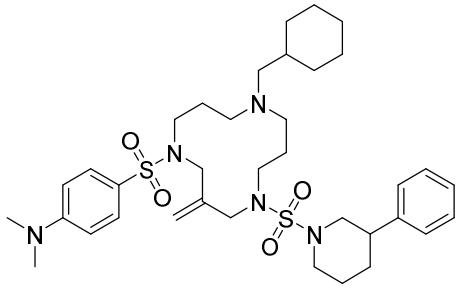
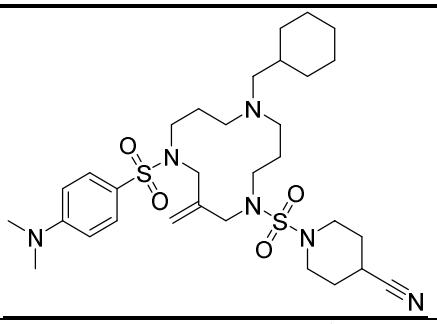
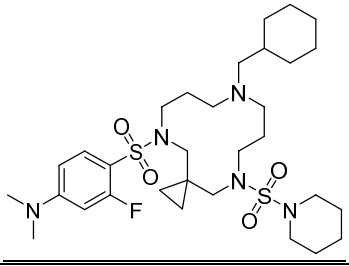
~~55.~~41. The compound or salt of any one of claims 1-~~54~~40, wherein R^1 is in a *(S)* configuration.

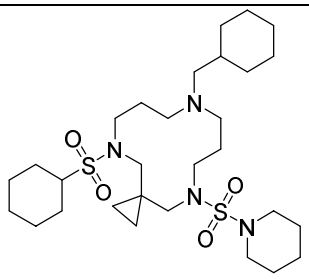
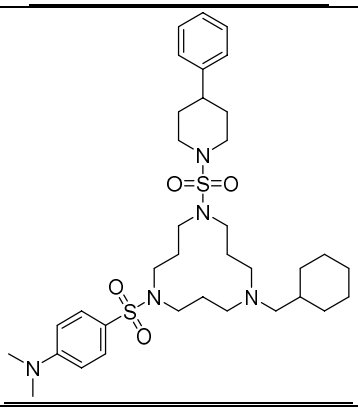
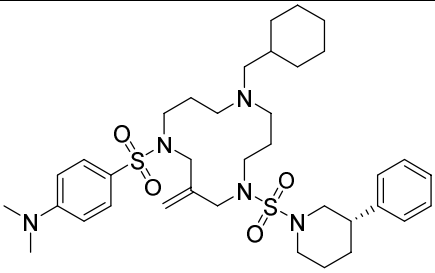
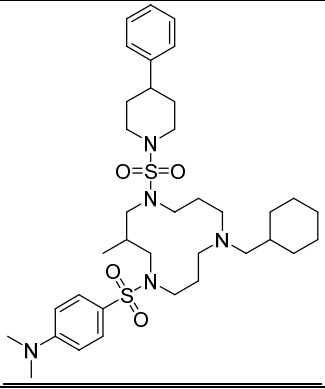
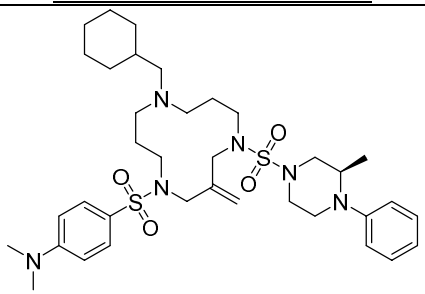
~~56.~~42. A compound listed in Table A, or a pharmaceutically acceptable salt thereof.

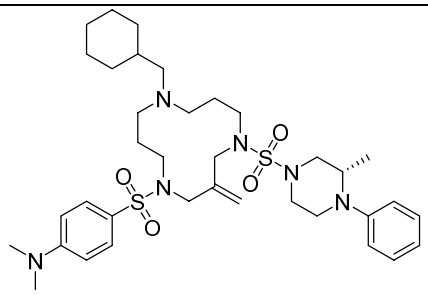
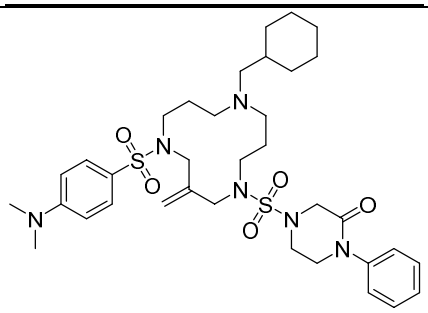
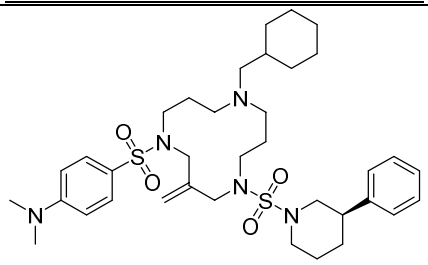
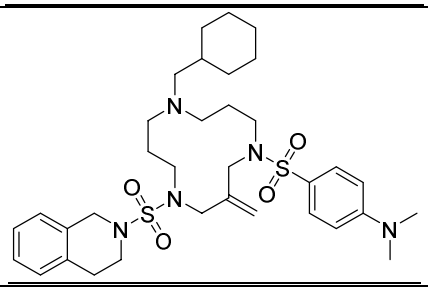
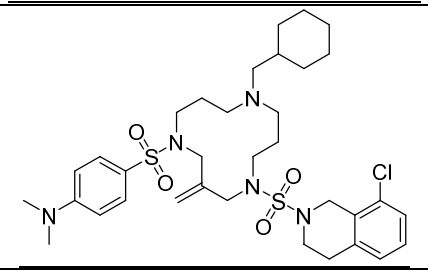
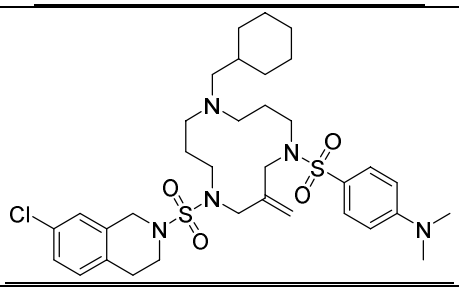
No.	Structure
A5	
A13	
A17	
A19	
A20	
A21	
A22	
A23	

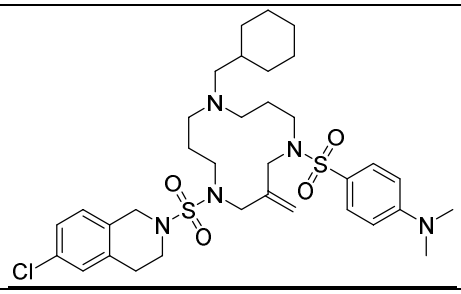
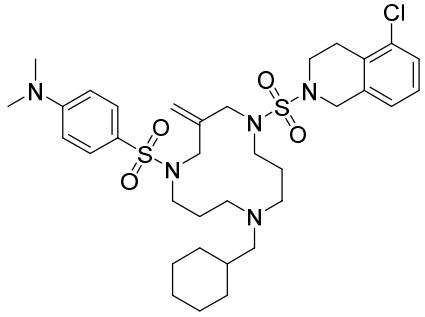
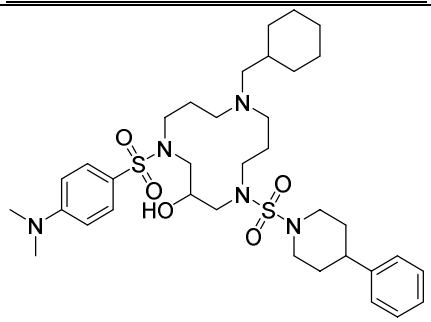
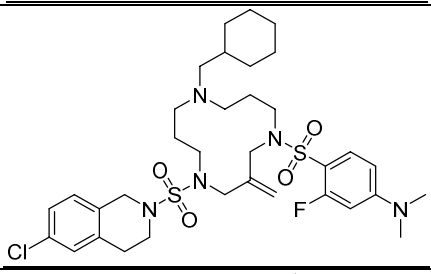
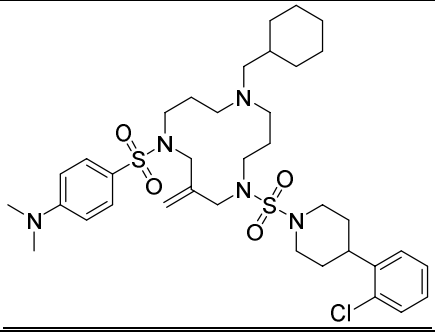
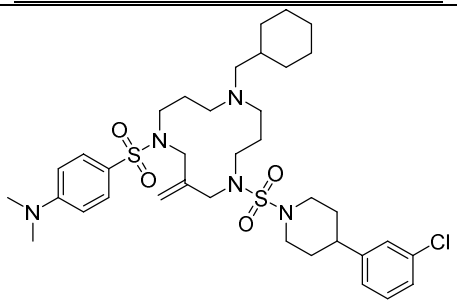
A24	
A25	
A26	
A27	
A28	

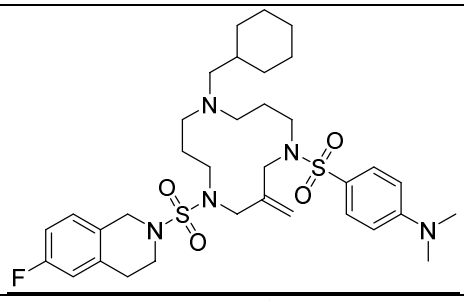
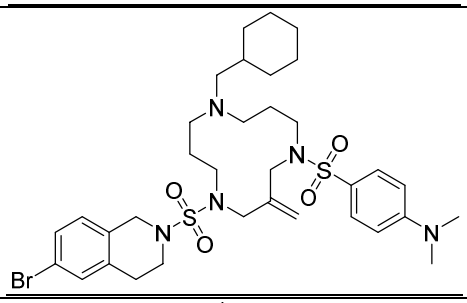
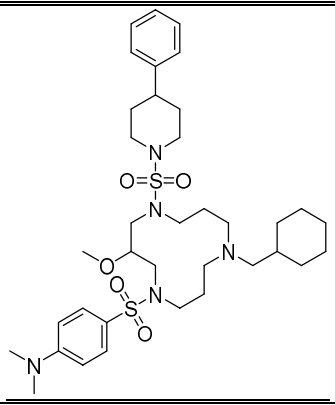
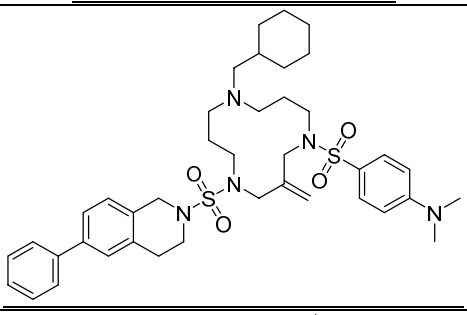
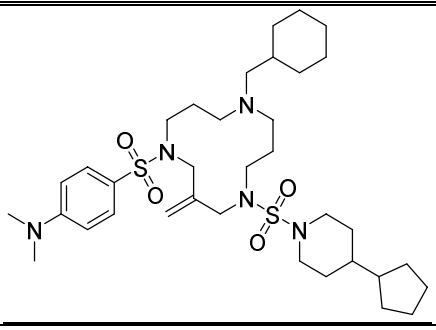
A29	
A30	
A31	
A32	
A33	
A34	

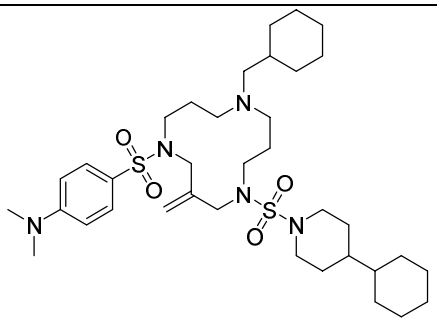
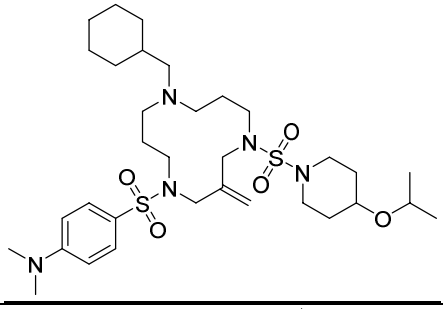
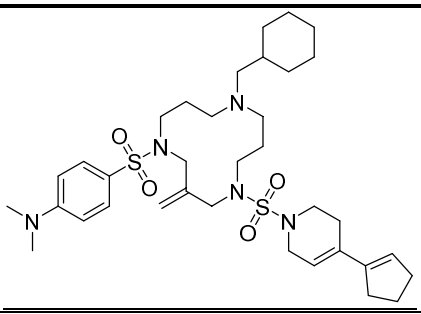
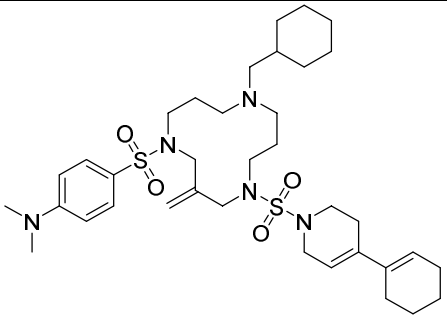
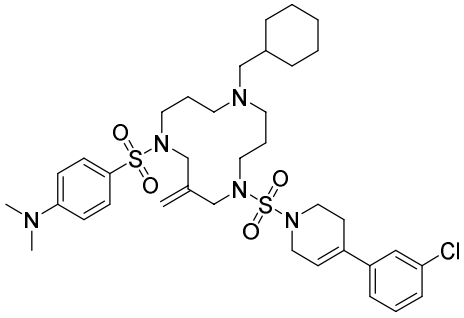
A35	
A36	
A37	
A38	
A39	
A40	

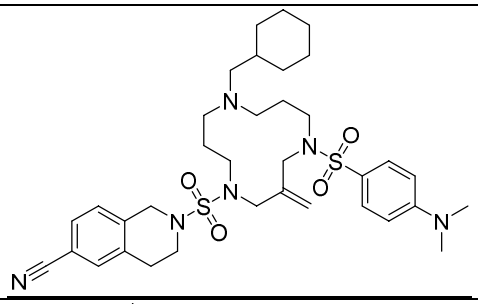
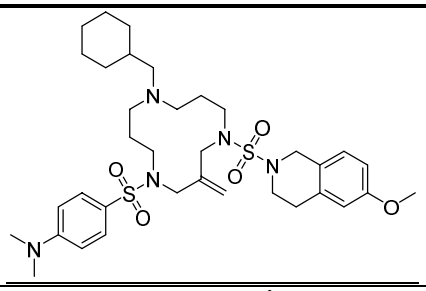
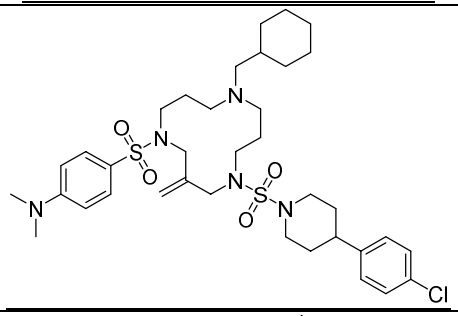
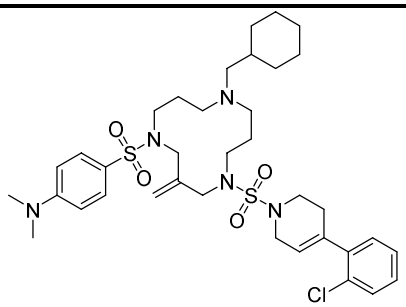
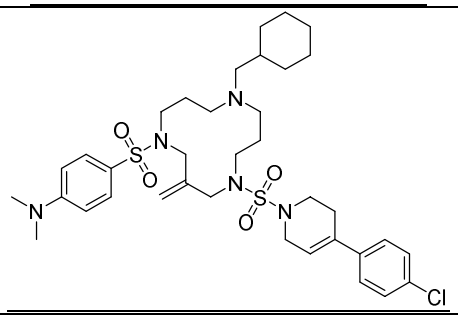
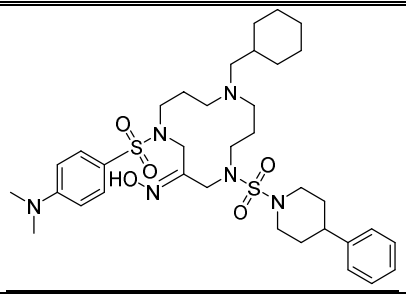
A41	
A42	
A43	
A44	
A46	

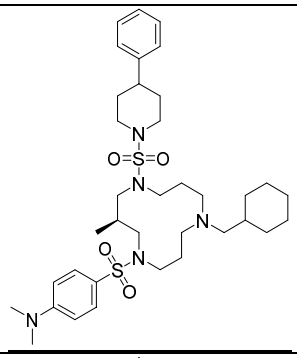
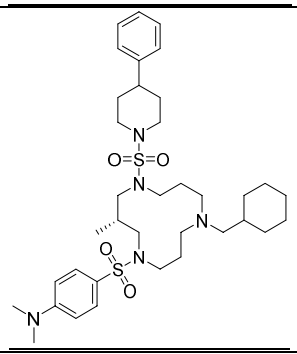
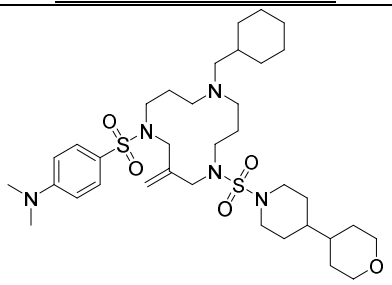
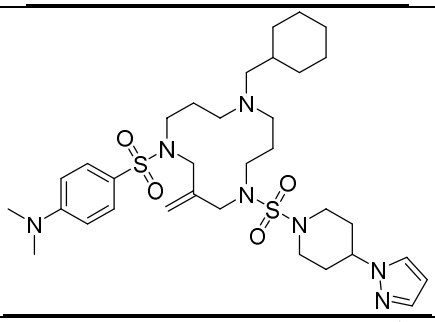
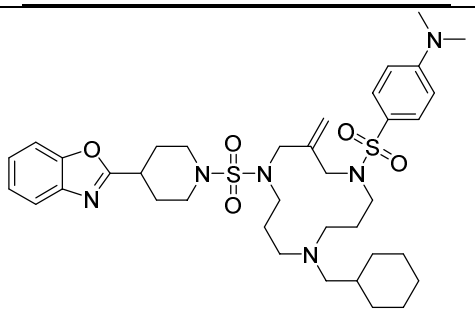
A47	
A48	
A49	
A50	
A51	
A52	

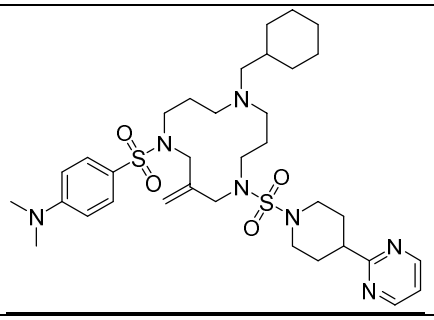
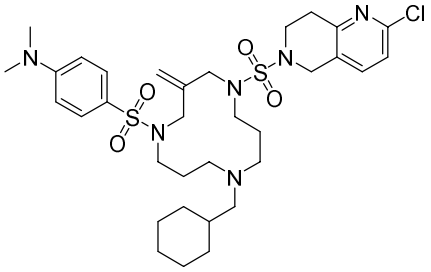
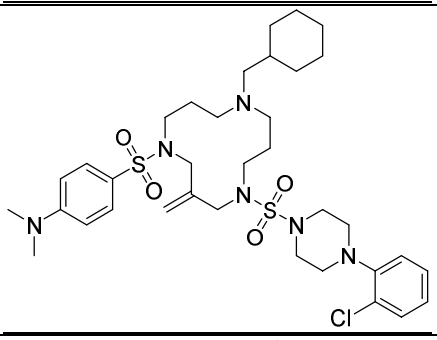
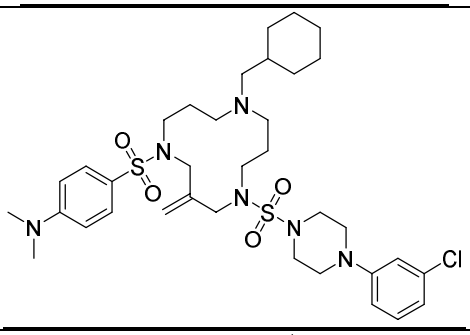
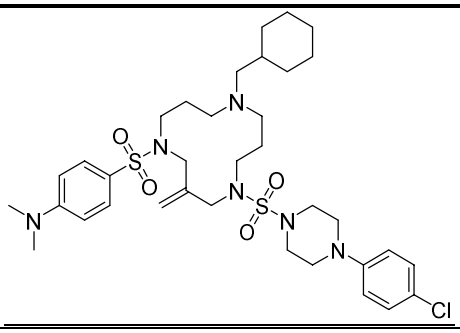
A53	
A54	
A55	
A56	
A57	
A58	

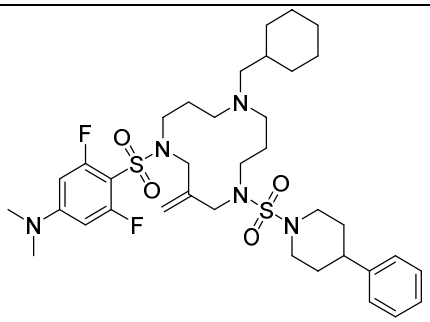
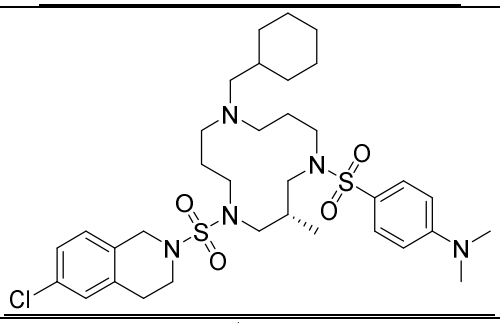
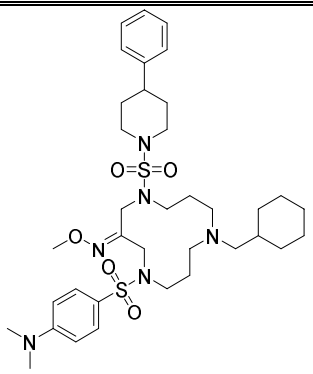
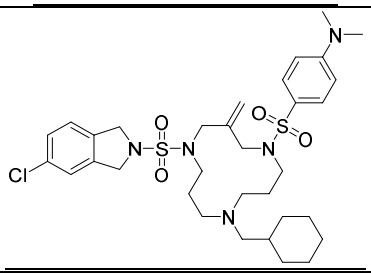
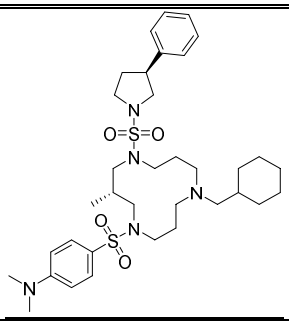
A59	
A60	
A61	
A63	
A64	

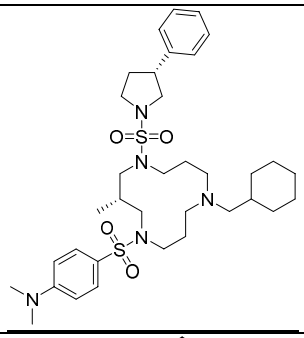
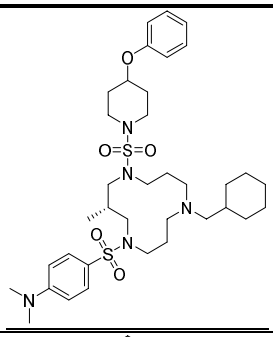
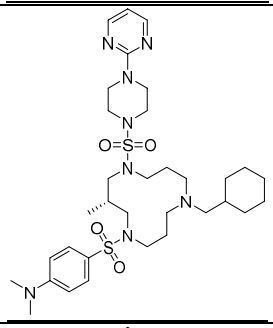
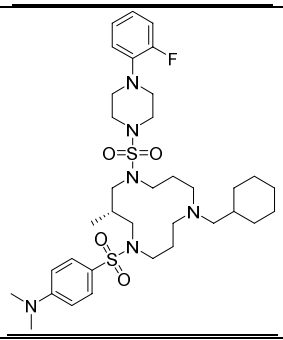
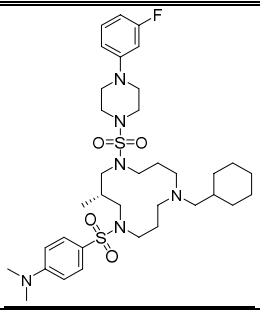
A65	
A66	
A67	
A68	
A69	

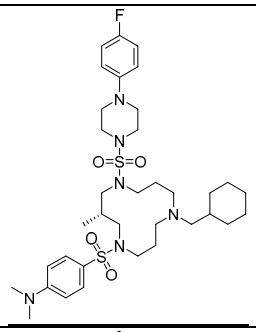
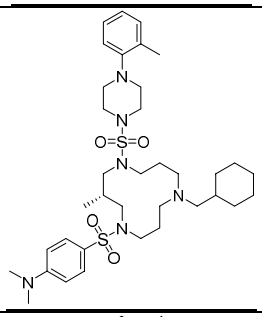
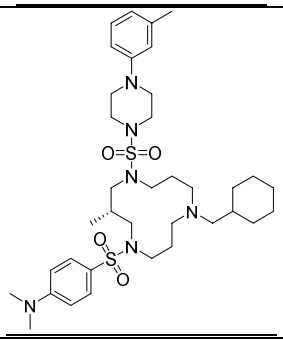
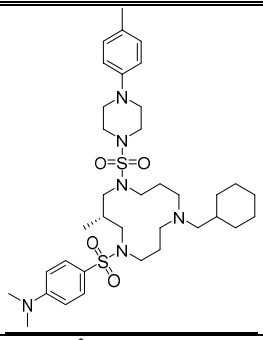
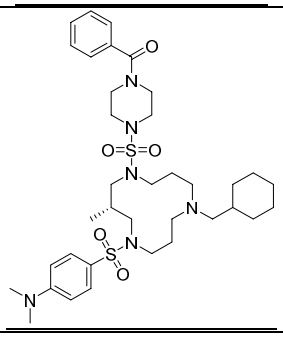
A70	
A71	
A72	
A73	
A74	
A75	

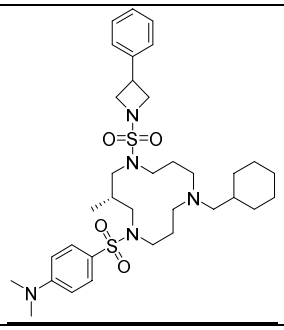
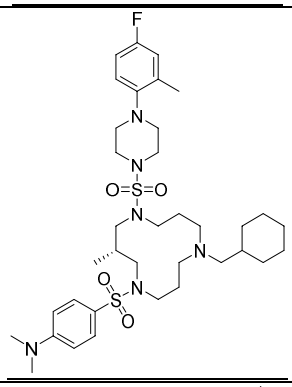
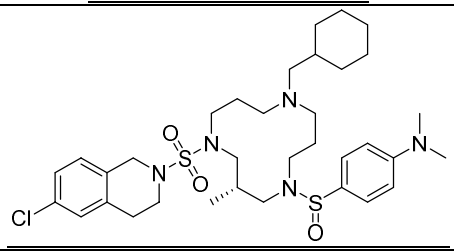
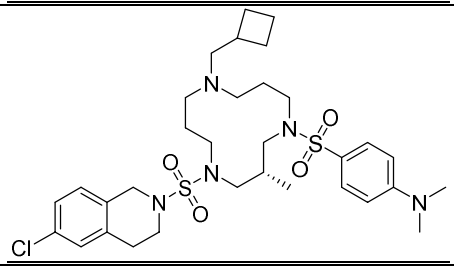
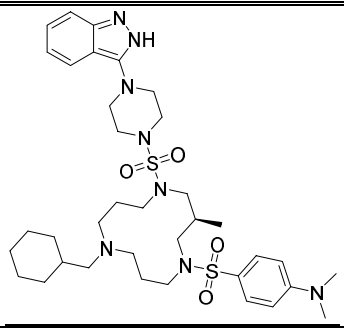
A76	
A77	
A78	
A79	
A80	

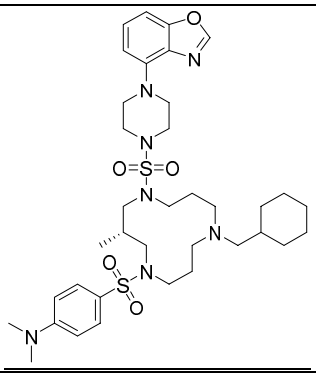
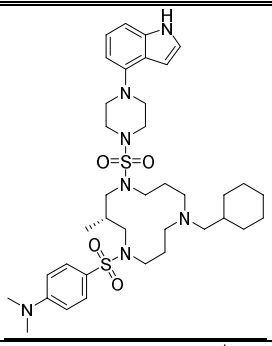
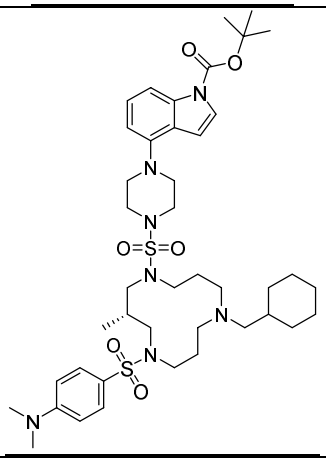
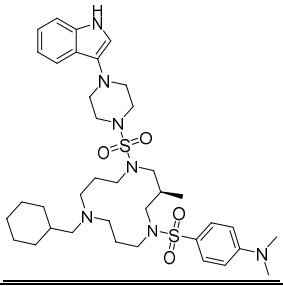
A81	
A82	
A83	
A84	
A85	

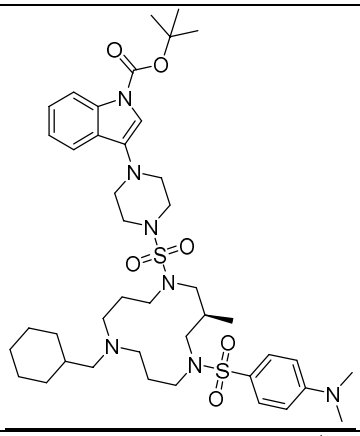
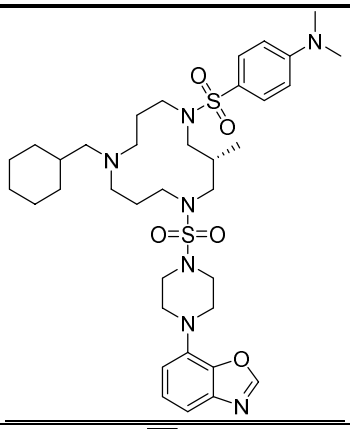
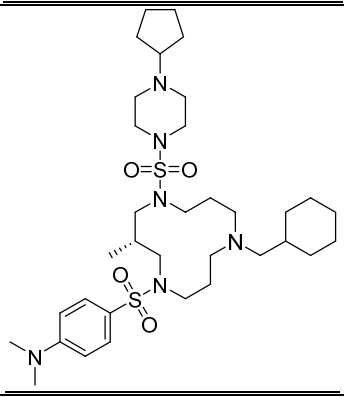
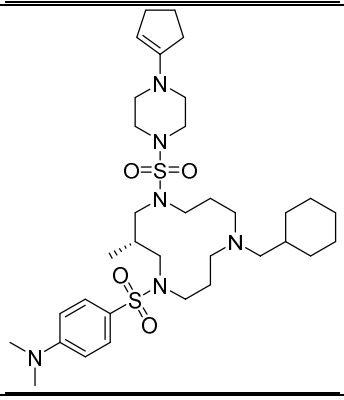
A86	
A87	
A88	
A89	
A90	

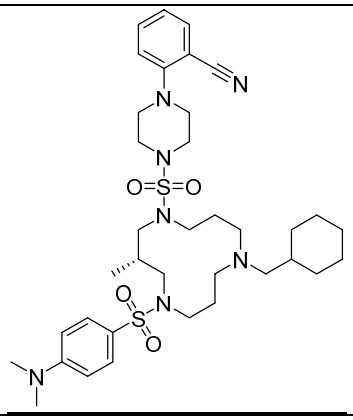
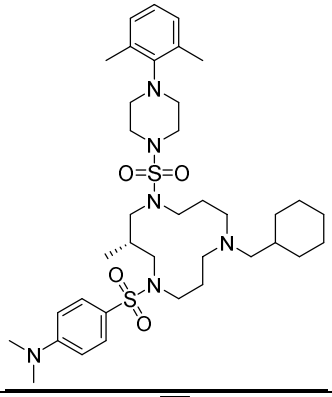
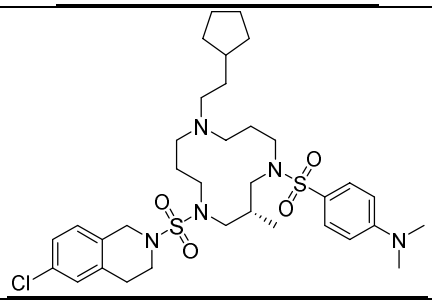
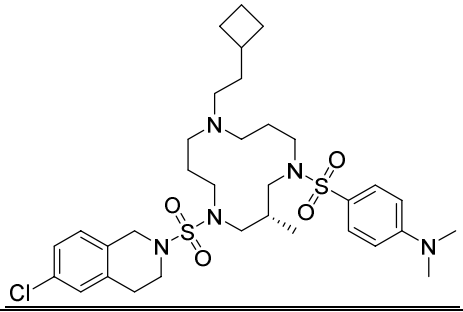
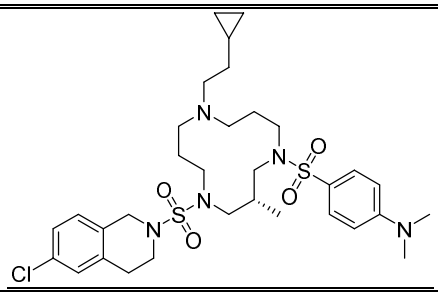
A91	
A92	
A93	
A94	
A95	

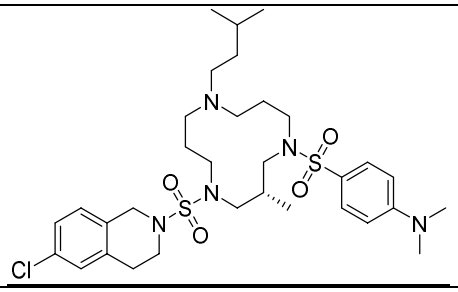
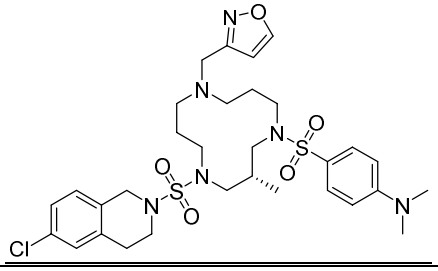
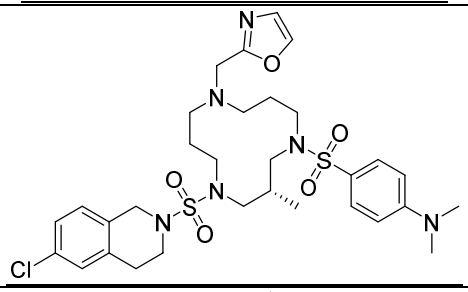
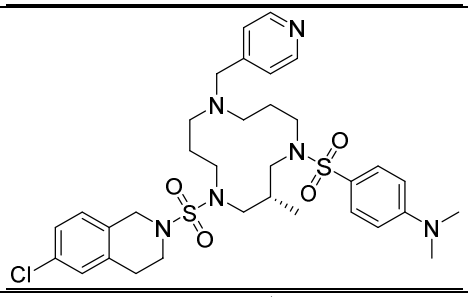
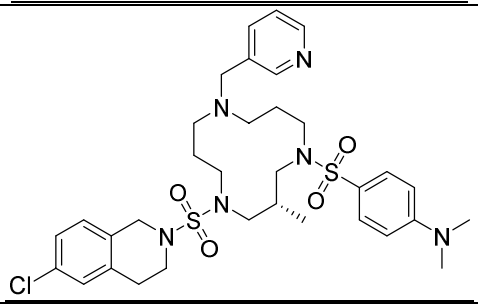
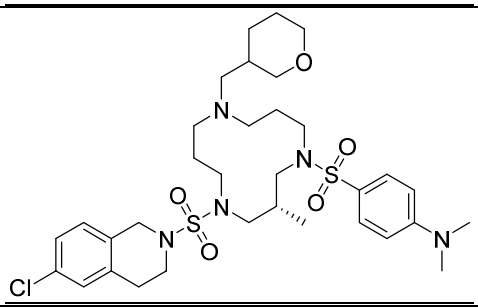
A96	
A97	
A98	
A99	
A100	

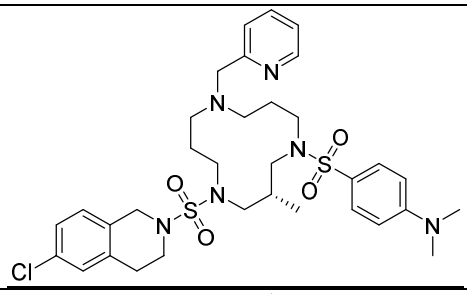
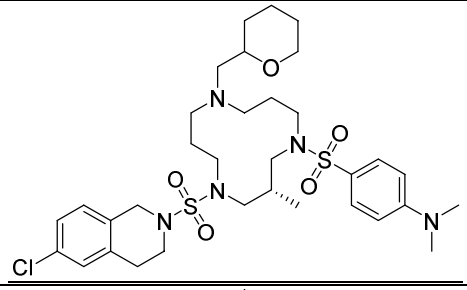
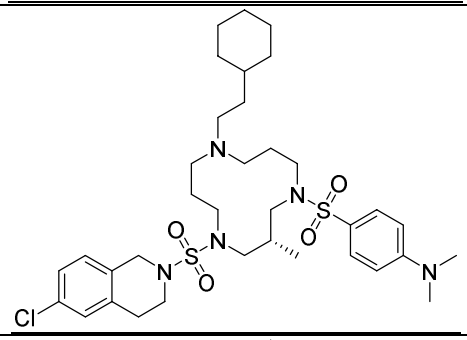
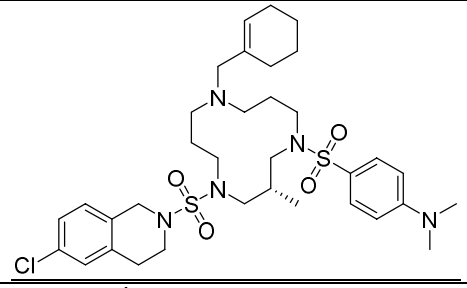
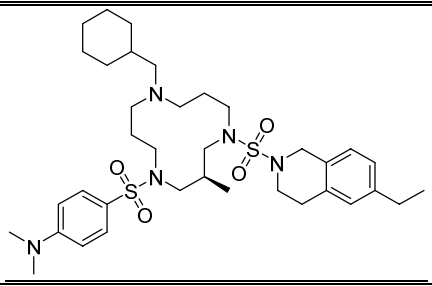
A101	
A102	
A104	
A108	
A109	

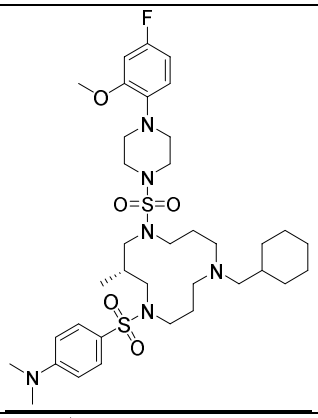
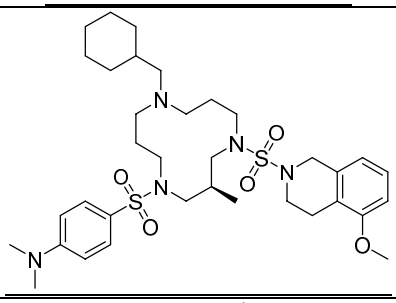
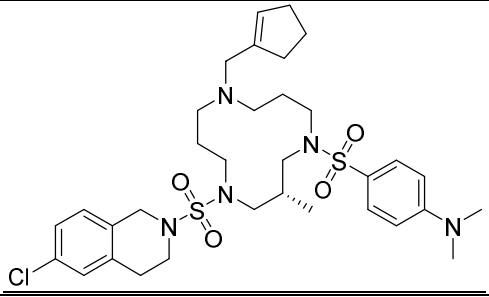
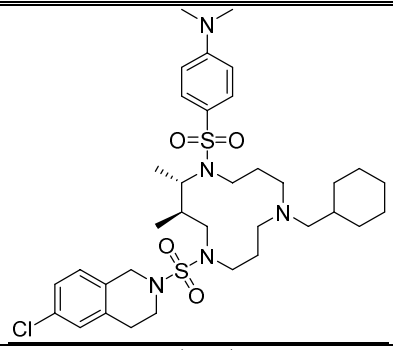
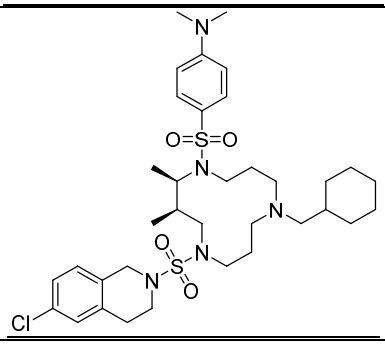
A110	
A111	
A112	
A113	

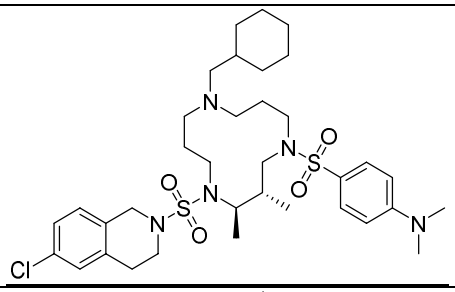
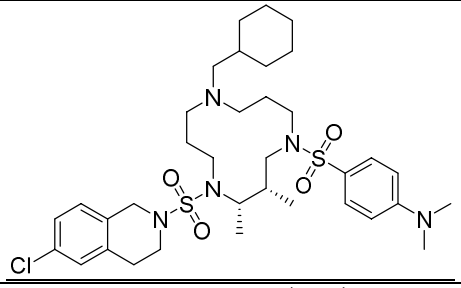
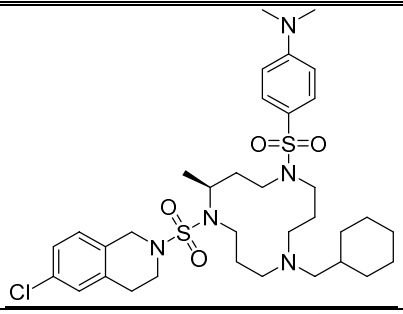
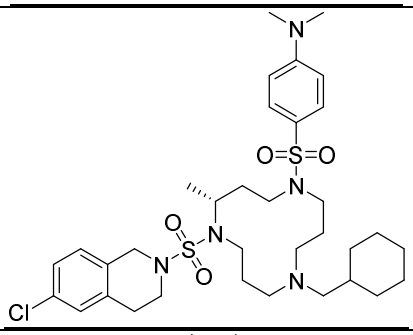
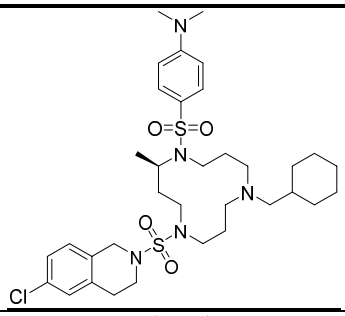
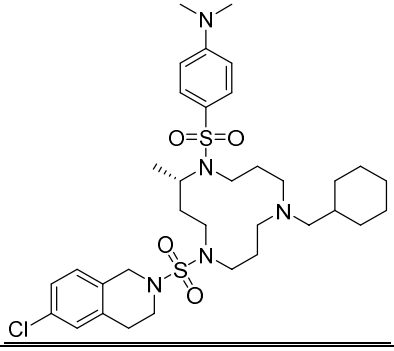
A114	
A115	
A116	
A117	

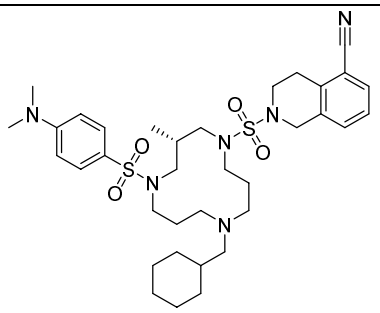
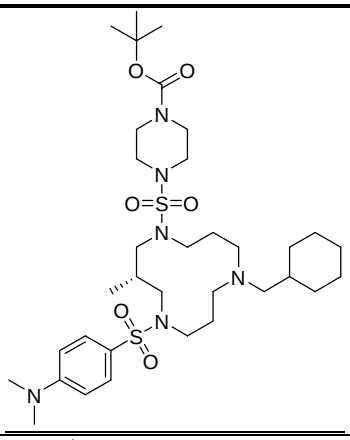
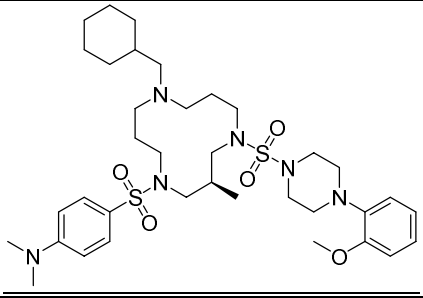
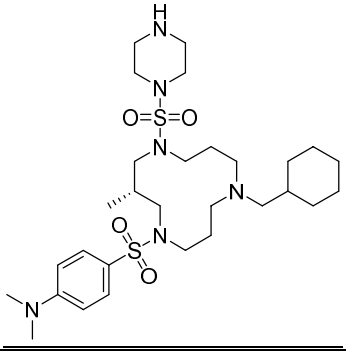
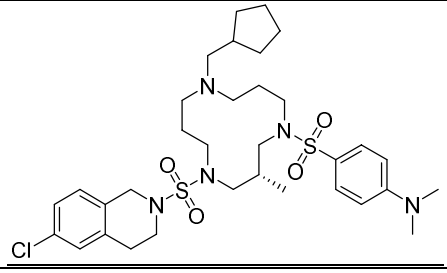
A118	
A119	
A120	
A121	
A122	

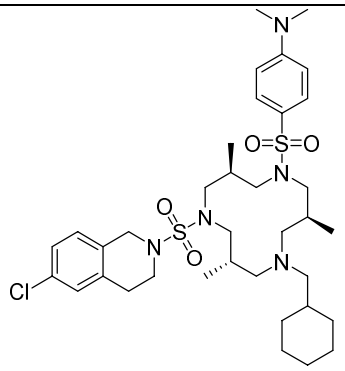
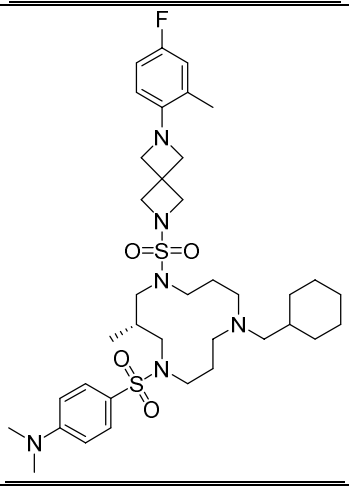
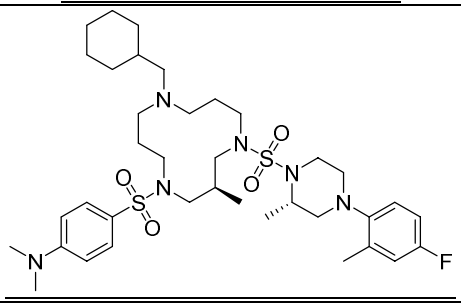
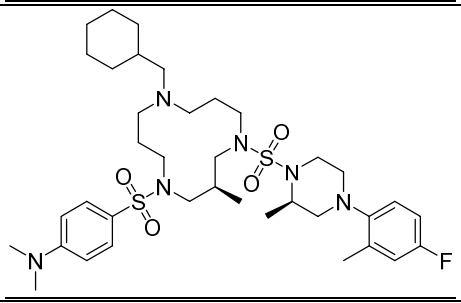
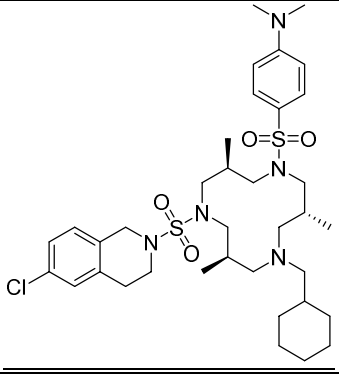
A123	
A124	
A125	
A126	
A127	
A128	

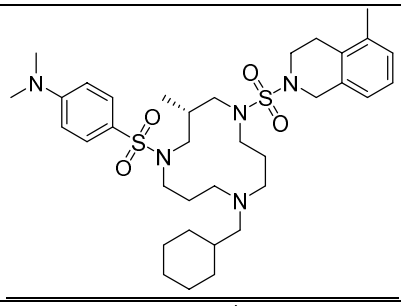
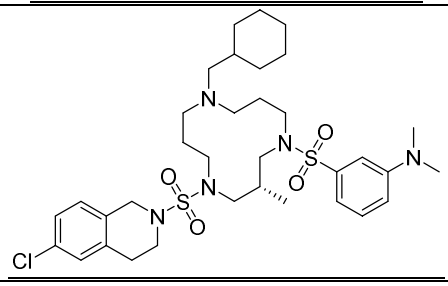
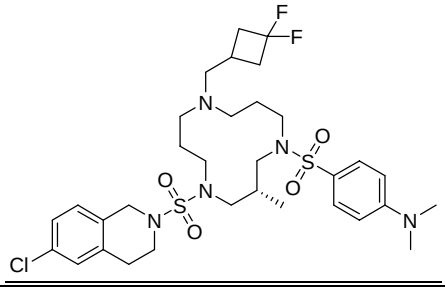
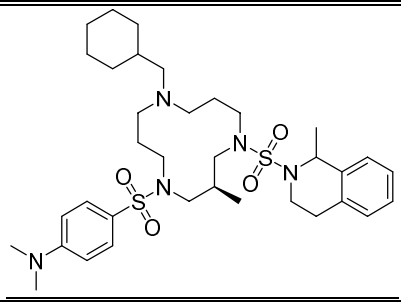
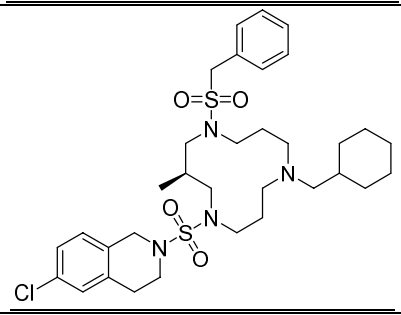
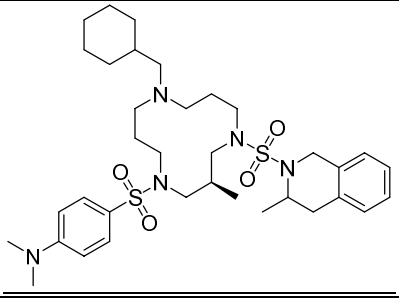
A129	
A130	
A134	
A135	
A136	

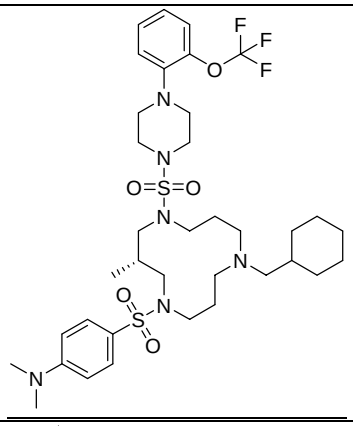
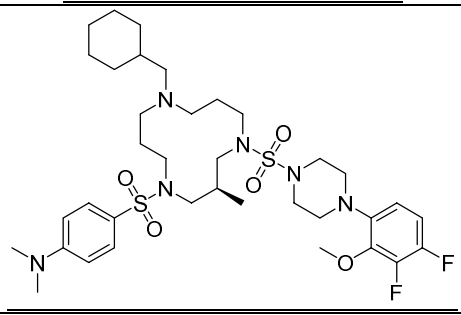
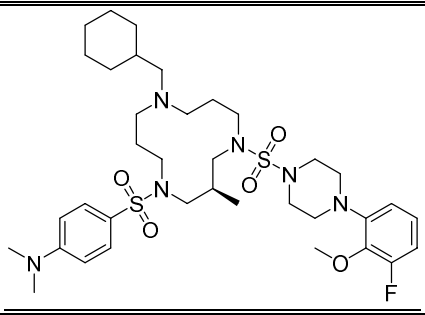
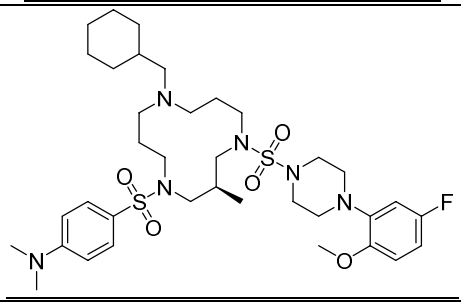
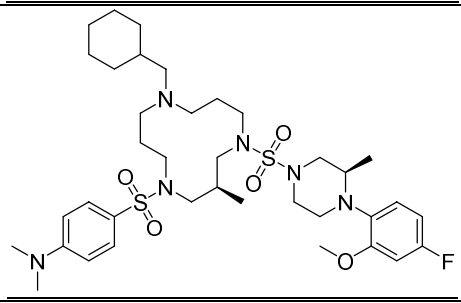
A137	
A138	
A142	
A143	
A144	

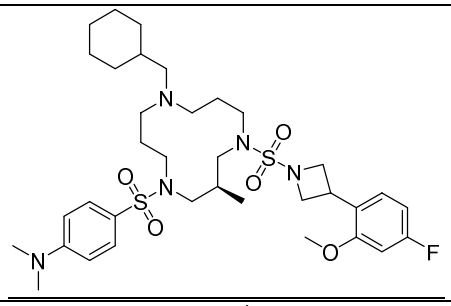
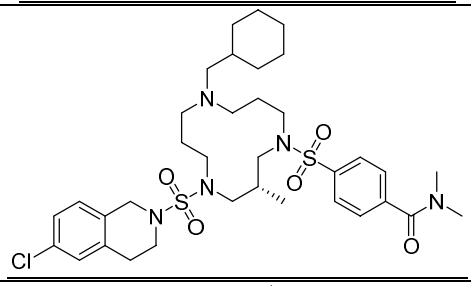
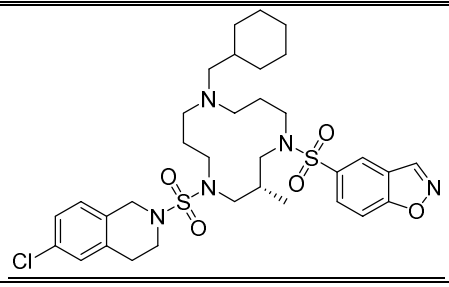
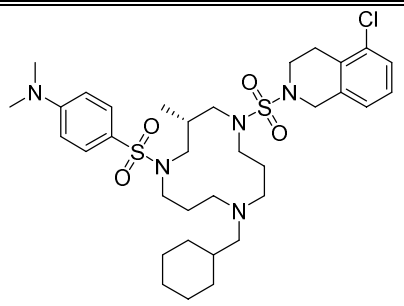
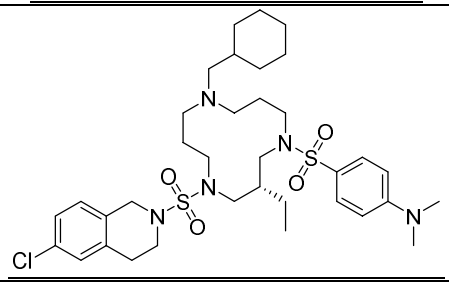
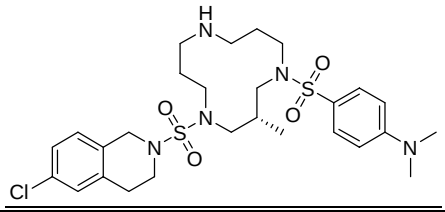
A145	
A146	
A147	
A148	
A149	
A150	

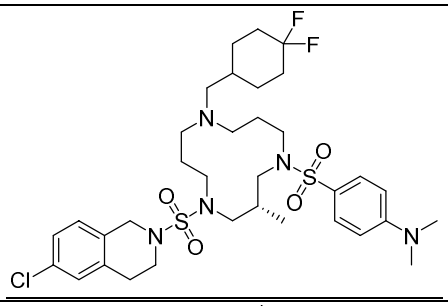
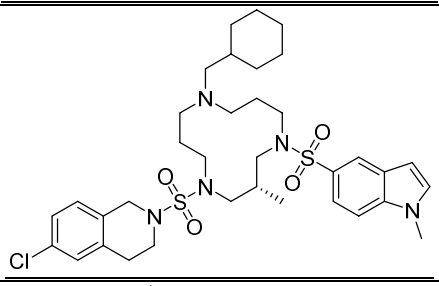
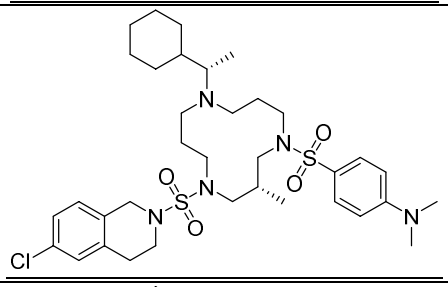
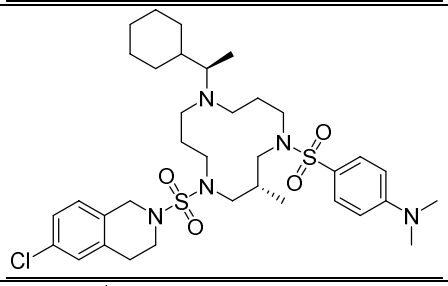
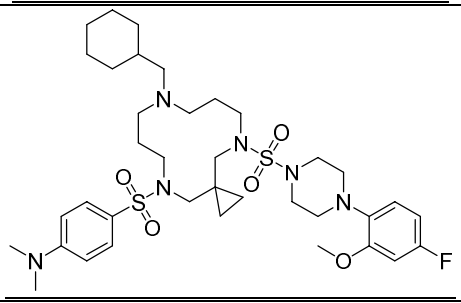
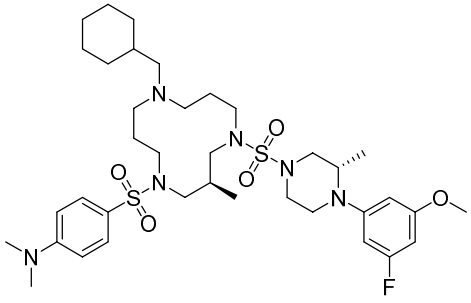
A151	
A153	
A154	
A155	
A157	

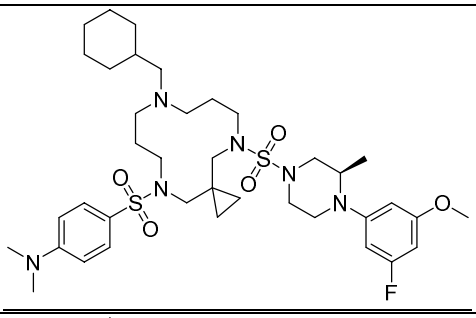
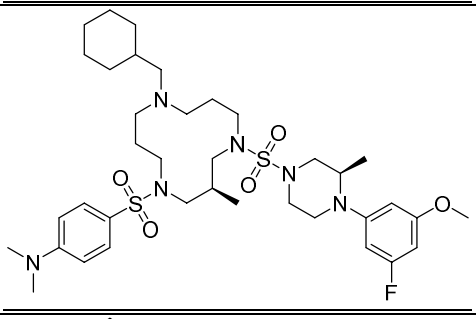
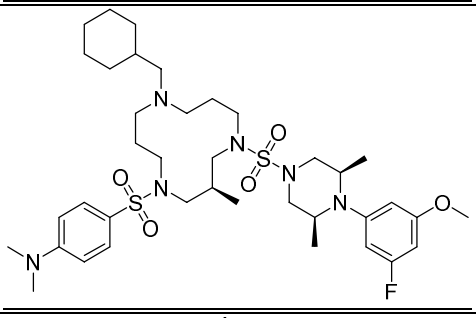
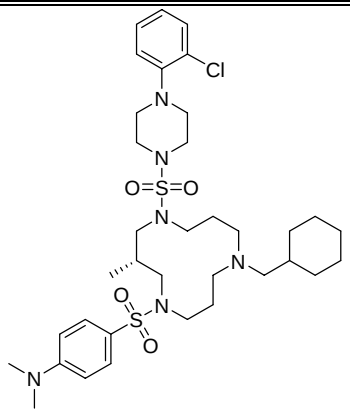
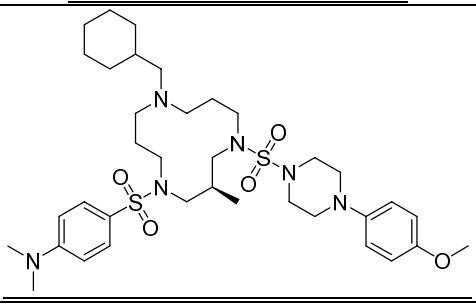
A160	
A161	
A162	
A163	
A164	

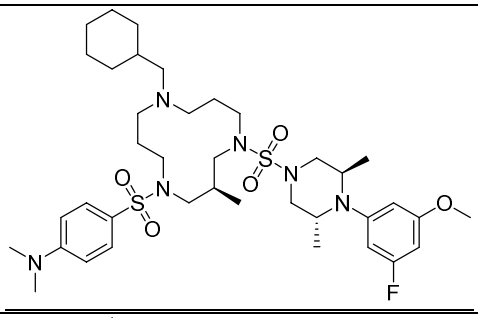
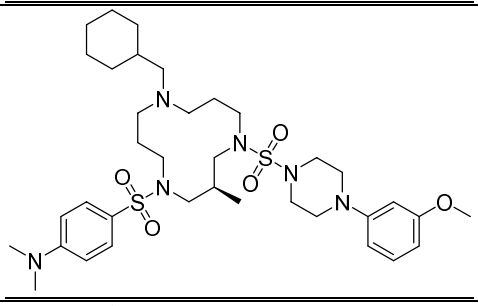
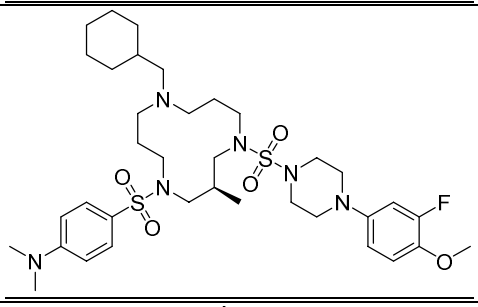
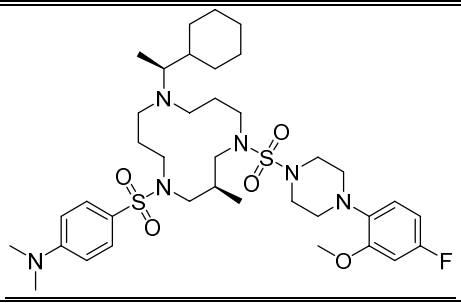
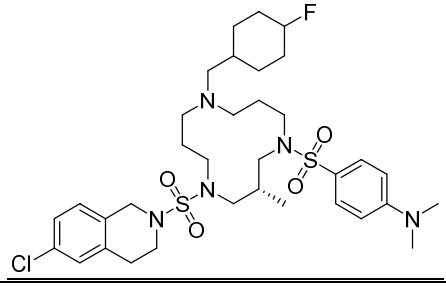
A166	
A168	
A169	
A170	
A171	
A172	

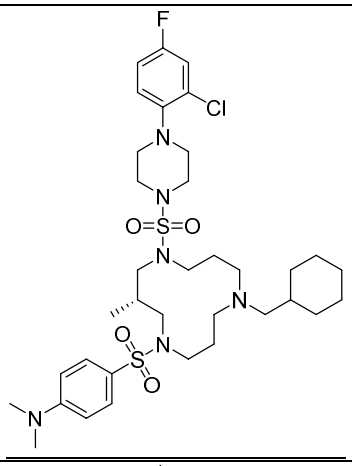
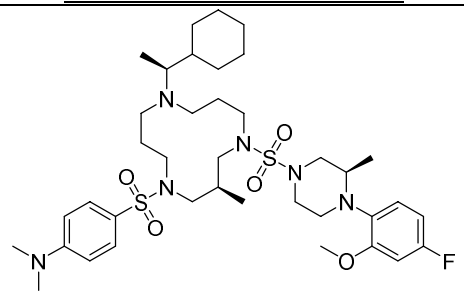
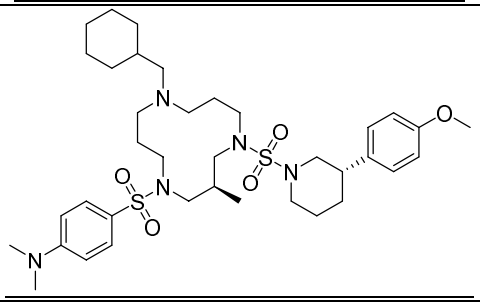
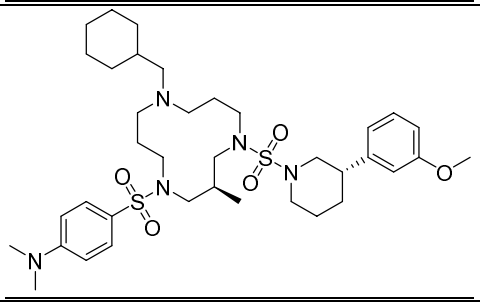
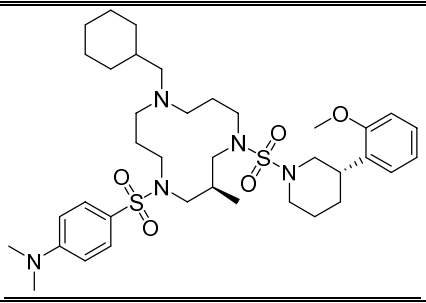
A173	
A174	
A175	
A176	
A177	

A178	
A179	
A180	
A181	
A182	
A183	

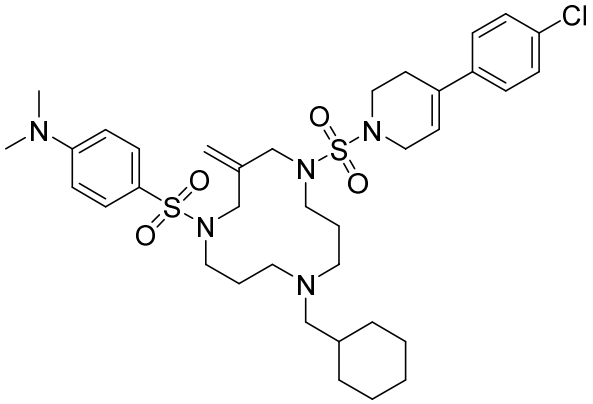
A185	
A188	
A190	
A191	
A193	
A194	

A195	
A196	
A197	
A198	
A199	

A200	
A201	
A202	
A203	
A204	

A206	
A207	
A208	
A209	
A210	

~~57.~~43. The compound or salt of claim ~~56~~42, wherein the compound is selected from the group consisting of: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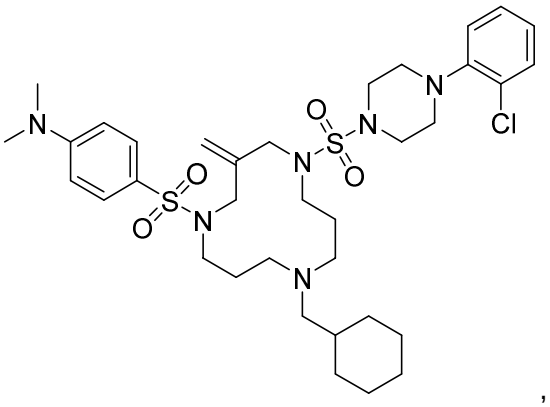
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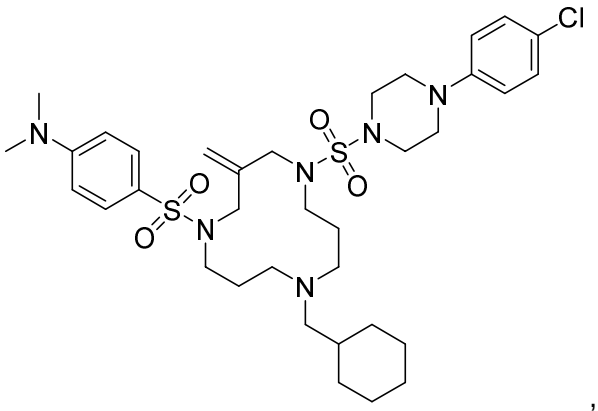
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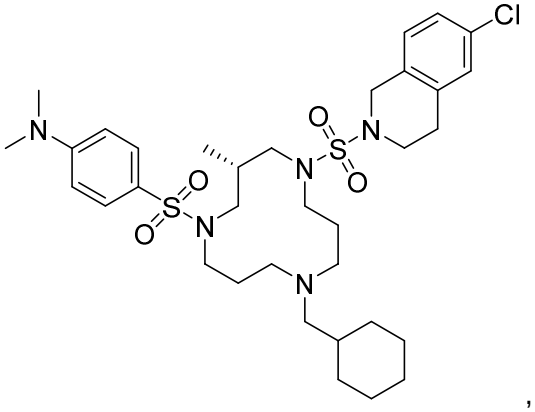
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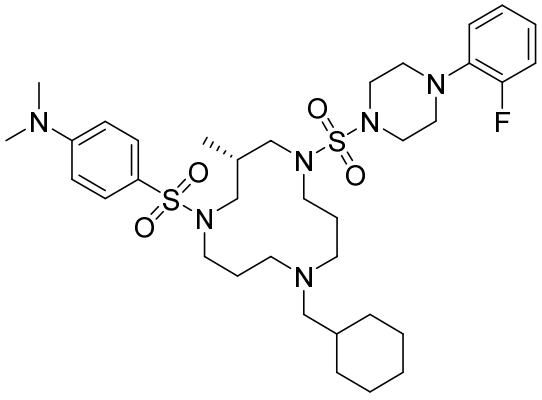
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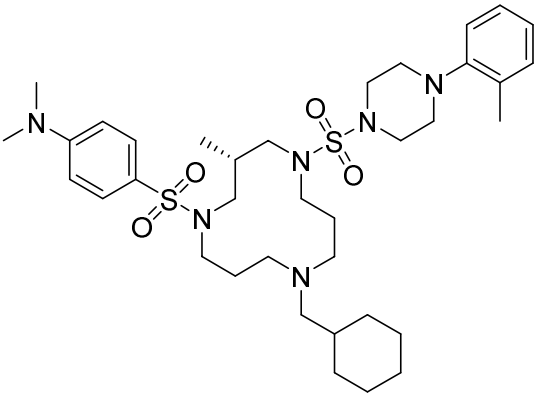
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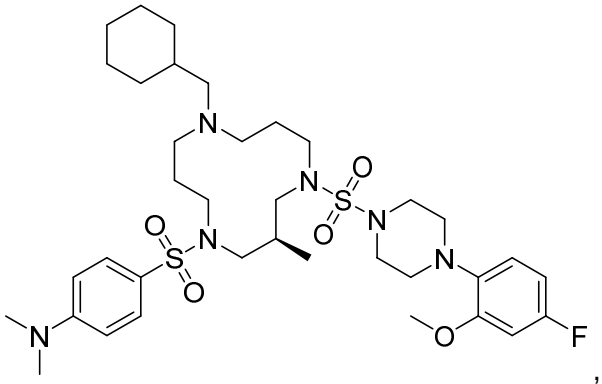
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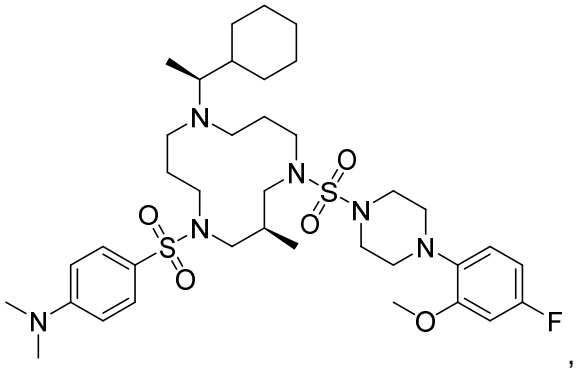
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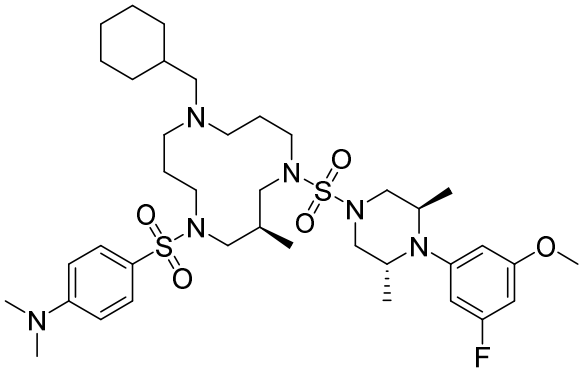
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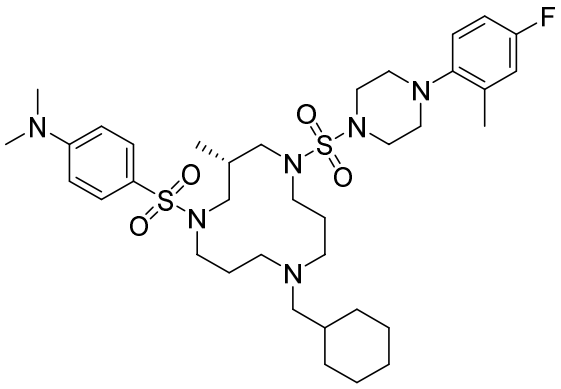
.

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

~~**59.**~~**44.** A pharmaceutical composition comprising the compound or salt of any one of claims 1-~~58~~43 and a pharmaceutically acceptable carrier.

~~**60.**~~**45.** ~~Use of the~~ The compound or salt of any one of claims 1-~~58~~43, or the pharmaceutical composition of claim ~~59~~44, ~~in the manufacture of a medicament for inhibiting protein secretion in a cell ,in an amount effective to inhibit secretion~~ for use as a treatment of cancer.

~~**61.** The use of claim 60, wherein the protein is a checkpoint protein.~~

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

~~**63.** The use 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, TGFRβ and combinations thereof.~~

~~**64.** The use of any one of claims 60-63, wherein the contacting comprises the compound or the composition is to be administed to a subject.~~

~~**65.**__**46.**__ The compound or salt of any one of claims 1-~~58~~__43__, or the pharmaceutical composition of claim ~~59~~__44__, for use as a medicament.

~~**66.**__**47.**__ Use of the compound or salt of any one of claims 1-~~58~~__43__ or the pharmaceutical composition of claim ~~59~~__44__, in the manufacture of a medicament for treating inflammation in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

~~**67.**__**48.**__ Use of the compound or salt of any one of claims 1-~~58~~__43__ or the pharmaceutical composition of claim ~~59~~__44__, in the manufacture of a medicament for treating or preventing cancer or a precancerous condition in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

~~**68.**__**49.**__ The use of claim ~~67~~__48__, 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.

~~**69.**__**50.**__ The use of claim ~~67~~__48__, 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.

~~**70.**__**51.**__ The use of claim ~~67~~__48__, wherein the cancer is a solid tumor.

~~**71.**__**52.**__ The use of claim ~~67~~__48__, wherein the cancer is head and neck cancer, squamous cell carcinoma, gastric carcinoma, or pancreatic cancer.

~~72.~~**53.** Use of the compound or salt of any one of claims 1-~~58~~43 or the pharmaceutical composition of claim ~~59~~44, in the manufacture of a medicament for treating an autoimmune disease in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

~~73.~~**54.** The use of claim ~~72~~53, 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.

~~74.~~**55.** Use of the compound or salt of any one of claims 1-~~58~~43 or the pharmaceutical composition of claim ~~59~~44, in the manufacture of a medicament for the treatment of an immune-related disease in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

~~75.~~**56.** The use of claim ~~74~~55, wherein the immune-related disease is rheumatoid arthritis, lupus, inflammatory bowel disease, multiple sclerosis, or Crohn's disease.

~~76.~~**57.** Use of the compound or salt of any one of claims 1-~~58~~43 or the pharmaceutical composition of claim ~~59~~44, in the manufacture of a medicament for treating neurodegenerative disease in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

~~77.~~**58.** The use of claim ~~76~~57, wherein the neurodegenerative disease is multiple sclerosis.

~~78.~~**59.** Use of the compound or salt of any one of claims 1-~~58~~43 or the pharmaceutical composition of claim ~~59~~44, in the manufacture of a medicament for treating

an inflammatory disease in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

~~79.~~**60.** The use of claim ~~78~~59, wherein the inflammatory disease is bronchitis, conjunctivitis, myocarditis, pancreatitis, chronic cholecstitis, bronchiectasis, aortic valve stenosis, restenosis, psoriasis or arthritis.