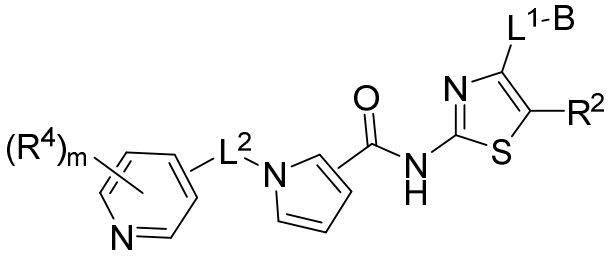
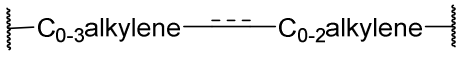
Claims

1. A compound having a structure of Formula (III):



(III)

wherein:

L^1 is a bond, C_{1-6}alkylene, or  , wherein ---indicates a double bond, a triple bond, or a fused cyclopropyl;

B is C_{0-3}alkylene-X;

X is an aromatic or nonaromatic C_{4-10}carbocycle, or an aromatic or nonaromatic 4-10 membered heterocycle having 1-3 ring heteroatoms selected from N, O, and S;

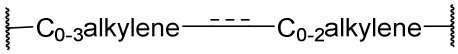
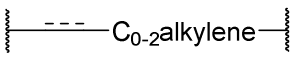
R^2 is H or C_{1-3}alkyl;

L^2 is C_{0-3}alkylene;

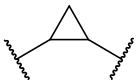
m is 0 to 2; and

each R^4 independently is C_{1-3}alkyl, C_{2-3}alkynyl, C_{1-3}haloalkyl, C_{1-3}alkoxy, halo, or NHC_{1-3}alkylene-aryl;

or a pharmaceutically acceptable salt thereof.

2. The compound or salt of claim 1, wherein L^1 is a bond.
3. The compound or salt of claim 1, wherein L^1 is C_{1-6}alkylene.
4. The compound or salt of claim 3, wherein L^1 is CH_2, CH_2CH_2, $C(CH_3)_2$, $C(CH_3)_2CH_2$, or $C(CH_3)_2CH_2CH_2$.
5. The compound or salt of claim 1, wherein L^1 is  .
6. The compound or salt of claim 5, wherein L^1 is  .
7. The compound or salt of claim 5, wherein L^1 is  .
8. The compound or salt of claim 5, wherein L^1 is  .
9. The compound or salt of any one of claims 5-8, wherein --- indicates a double bond.
10. The compound or salt of claim 9, wherein the double bond is further substituted with C_{1-3}alkyl.

11. The compound or salt of any one of claims 5-8, wherein ⋯ indicates a triple bond.

12. The compound or salt of any one of claims 5-8, wherein ⋯ indicates a fused cyclopropyl, e.g.,  .

13. The compound or salt of any one of claims 1-12, wherein B is C_{1-3}alkylene-X.

14. The compound or salt of any one of claims 1-12, wherein B is X.

15. The compound or salt of any one of claims 1-14, wherein X is pyrrolidinyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, phenyl, piperidinyl, pyridinyl, piperazinyl, tetrahydrofuranyl, furanyl, tetrahydropyranyl, quinolinyl, morpholinyl, pyrrolidonyl, pyrimidinyl, pyridazinyl, indenyl, dihydroindenyl, dihydrobenzofuranyl, chromanyl, isochromanyl, dihydroisoquinolinyl, or indolyl.

16. The compound or salt of any one of claims 1-15,
wherein

X is substituted with 1-3 G;

each G independently is selected from the group consisting of halo, OH, =O, CN, NO_2, $N(R^N)_2$, $N(R^N)C(O)C_{1-3}$alkyl, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, $C(O)C_{1-3}$alkyl, $S(O_2)$-Z, C(O)-Z, $C(O)N(R^N)_2$, silyl ether, and $[O]_{0-1}$-C_{0-3}alkylene-Z;

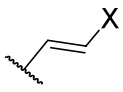
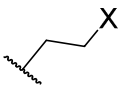
each R^N independently is H or C_{1-4}alkyl;

Z is aromatic or nonaromatic C_{3-10}carbocycle, or aromatic or nonaromatic 4-10 membered heterocycle having 1-3 heteroatoms selected from the group consisting of N, O, and S;

Z is optionally substituted with 1-3 E; and,

each E independently is selected from C_{1-3}alkyl, C_{1-3}alkoxy, =O, C_{1-3}haloalkoxy, CN, and halo.

17. The compound or salt of claim 1,
wherein

L^1-B is selected from the group consisting of  ,  , and  ;

X is aromatic or nonaromatic C_{4-7} carbocycle, or an aromatic or nonaromatic 4-9 membered heterocycle having 1 ring heteroatom;

X is optionally substituted with 1-3 G;

each G independently is selected from the group consisting of halo, OH, =O, CN, NO_2, $N(R^N)_2$, $N(R^N)C(O)C_{1-3}$alkyl, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, $C(O)C_{1-3}$alkyl, $S(O_2)$-Z, C(O)-Z, $C(O)N(R^N)_2$, silyl ether, and $[O]_{0-1}$-C_{0-3}alkylene-Z;

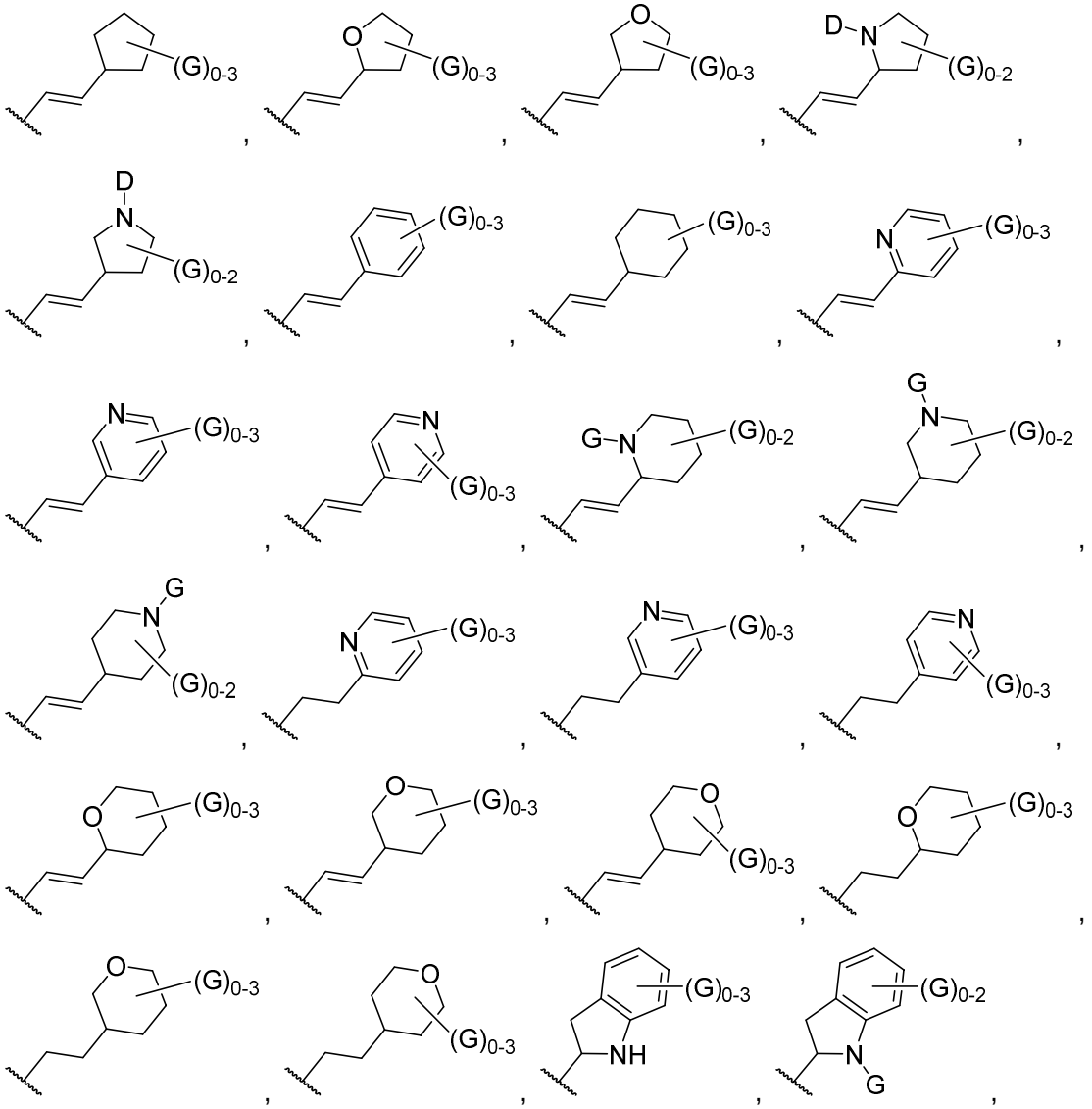
each R^N independently is H or C_{1-4}alkyl;

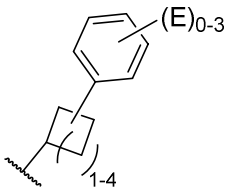
Z is aromatic or nonaromatic C_{3-10}carbocycle, or aromatic or nonaromatic 4-10 membered heterocycle having 1-3 heteroatoms selected from the group consisting of N, O, and S;

Z is optionally substituted with 1-3 E; and,

each E independently is selected from C_{1-3}alkyl, C_{1-3}alkoxy, =O, C_{1-3}haloalkoxy, CN, and halo.

18. The compound or salt of claim 17, wherein L^1-B is selected from the group consisting of:

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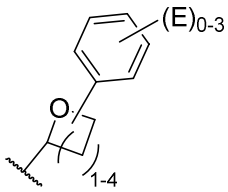
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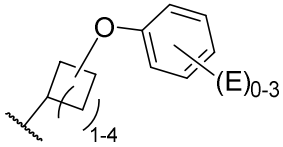
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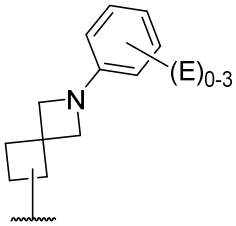
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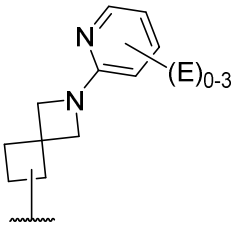
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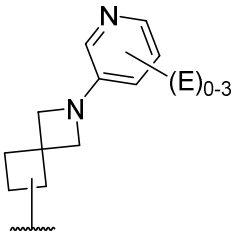
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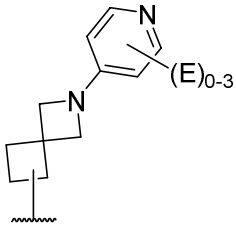
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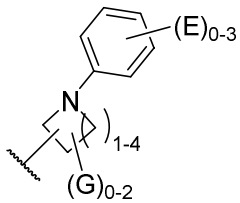
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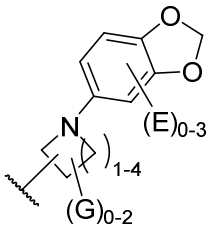
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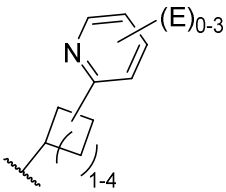
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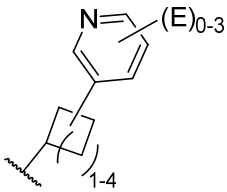
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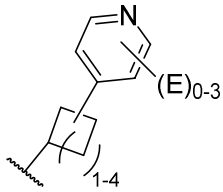
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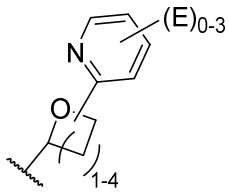
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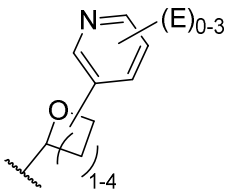
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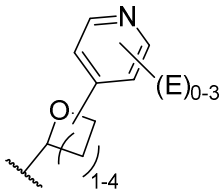
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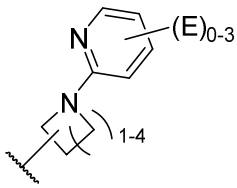
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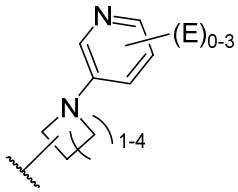
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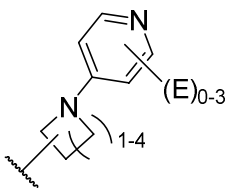
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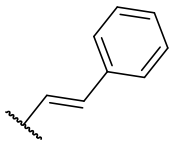
19. The compound or salt of claim 17 or 18, wherein L^1-B is selected from the group consisting of:

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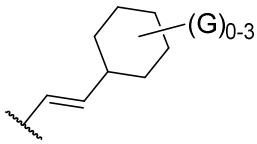
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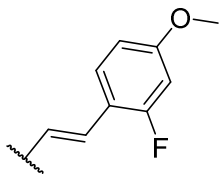
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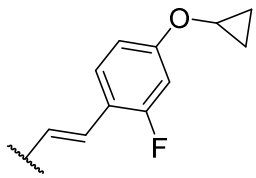
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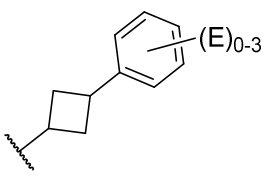
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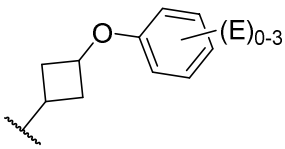
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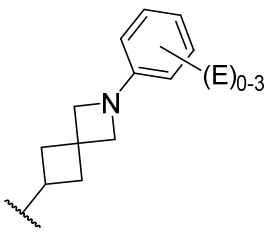
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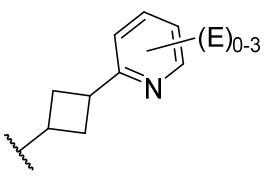
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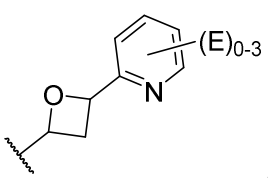

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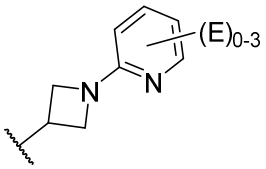

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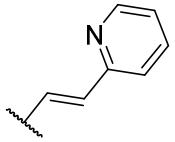

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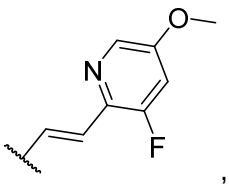

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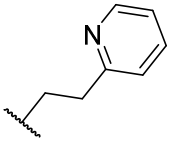

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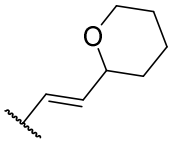

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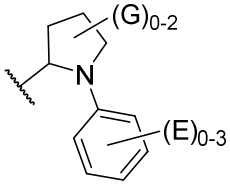

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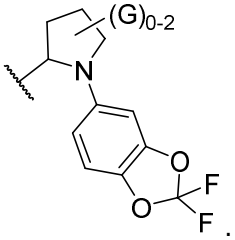

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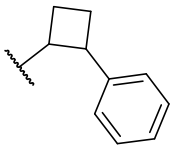
20. The compound or salt of claim 1, wherein L^1-B is selected from the group consisting of:.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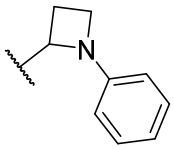

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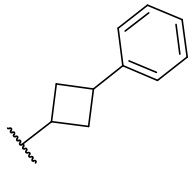
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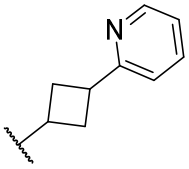

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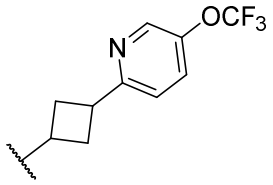

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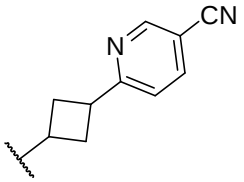

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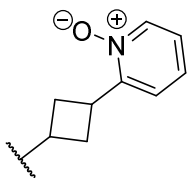

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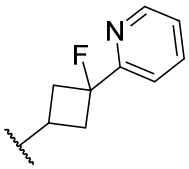

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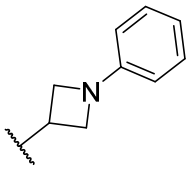

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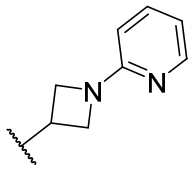

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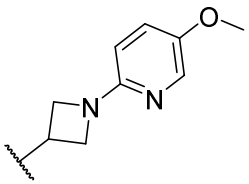

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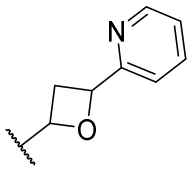

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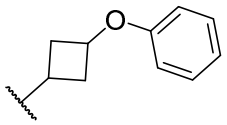

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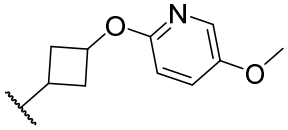

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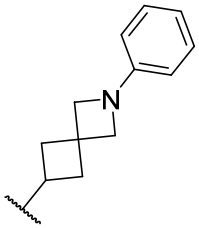

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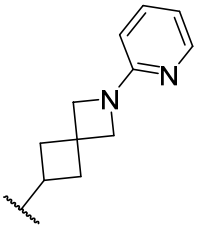

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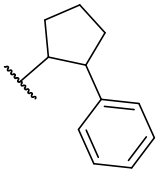
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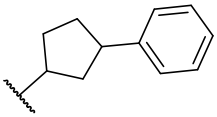
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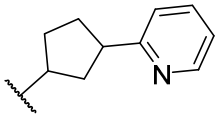

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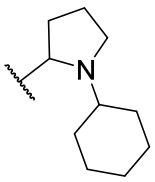

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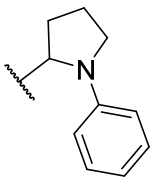

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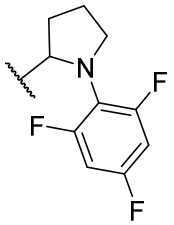

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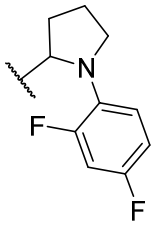

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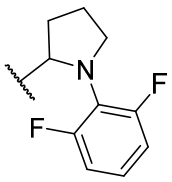

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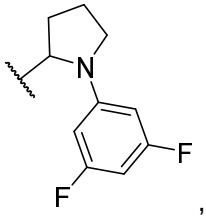

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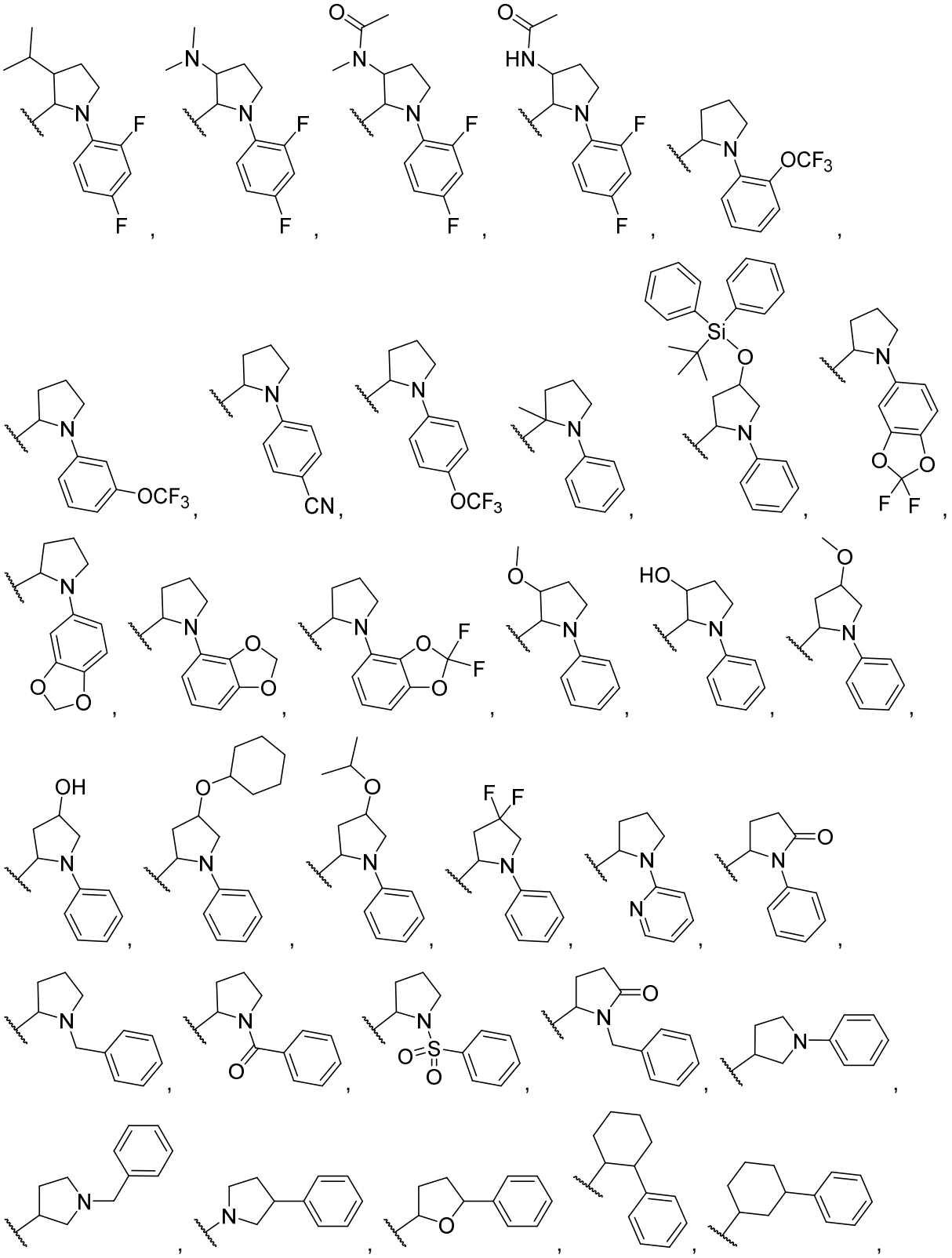
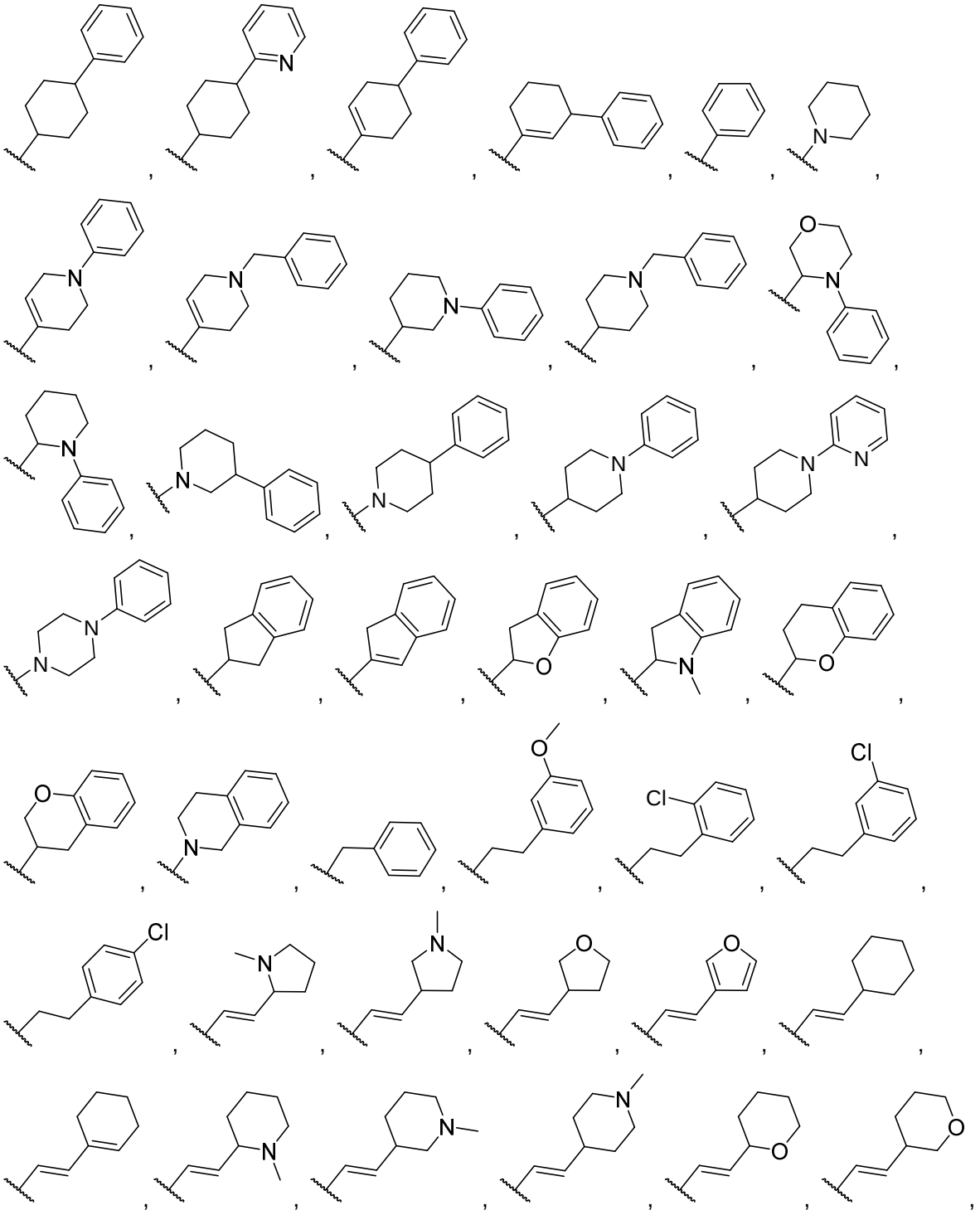
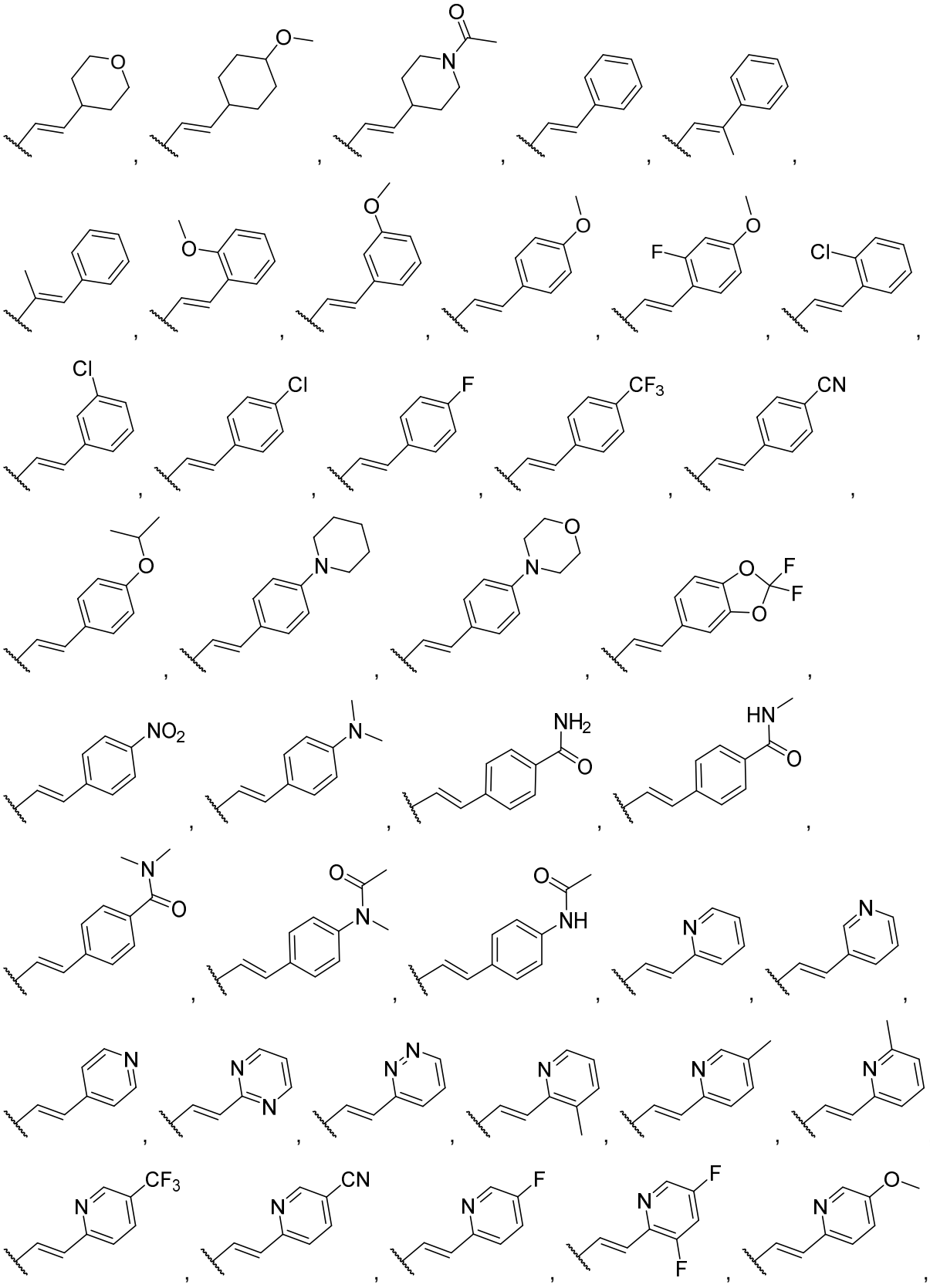
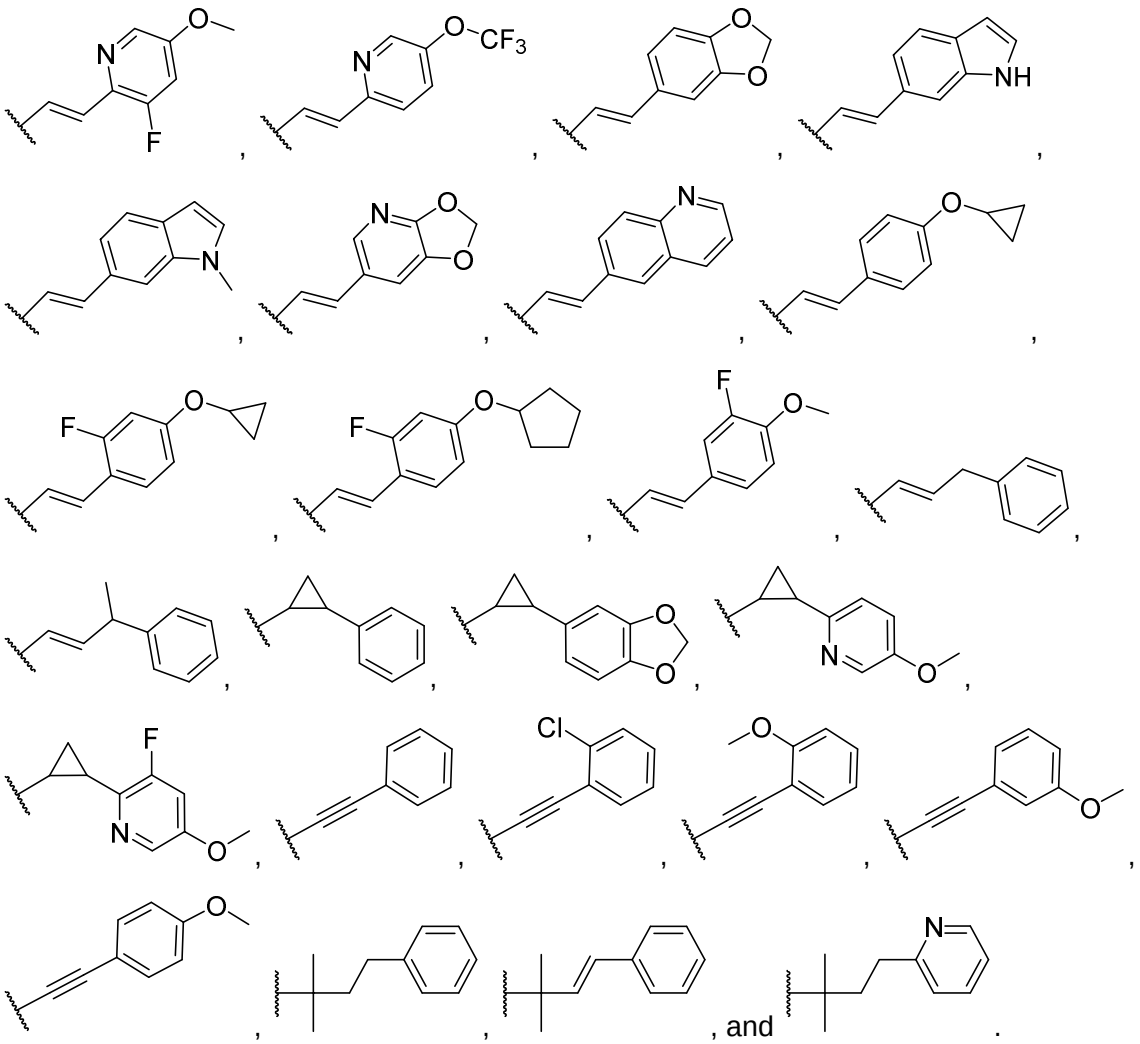








21. The compound or salt of any one of claims 1-20, wherein R^2 is H.
22. The compound or salt of any one of claims 1-20, wherein R^2 is $C_{1\text{-}3}$alkyl.
23. The compound or salt of claim 22, wherein R^2 is methyl.
24. The compound or salt of any one of claims 1-23, wherein L^2 is C_0alkylene.
25. The compound or salt of any one of claims 1-23, wherein L^2 is C_1alkylene.
26. The compound or salt of any one of claims 1-23, wherein L^2 is C_2alkylene.
27. The compound or salt of any one of claims 1-23, wherein L^2 is C_3alkylene.
28. The compound or salt of any one of claims 1-27, wherein m is 0.
29. The compound or salt of any one of claims 1-27, wherein m is 1 or 2.
30. The compound or salt of claim 29, wherein R^4 is $C_{1\text{-}3}$alkyl.
31. The compound or salt of claim 30, wherein R^4 is methyl or ethyl.
32. The compound or salt of claim 29, wherein R^4 is halo.
33. The compound or salt of claim 32, wherein R^4 is F.

34. The compound or salt of claim 32, wherein R^4 is Cl.

35. The compound or salt of claim 29, wherein R^4 is $C_{2\text{-}3}$alkynyl.

36. The compound or salt of claim 35, wherein R^4 is C_2alkynyl.

37. The compound or salt of claim 29, wherein R^4 is $C_{1\text{-}3}$haloalkyl.

38. The compound or salt of claim 37, wherein R^4 is CF_3.

39. The compound or salt of claim 29, wherein R^4 is $C_{1\text{-}3}$alkoxy.

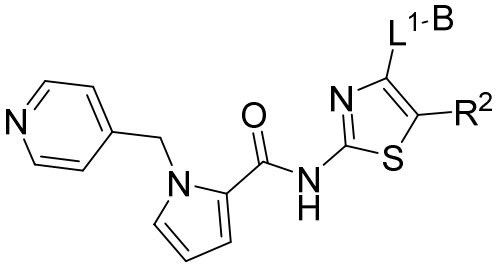
40. The compound or salt of claim 39, wherein R^4 is methoxy.

41. The compound or salt of claim 29, wherein R^4 is $NHC_{1\text{-}3}$alkylene-aryl.

42. The compound or salt of claim 41, wherein R^4 is NH-CH_2-phenyl.

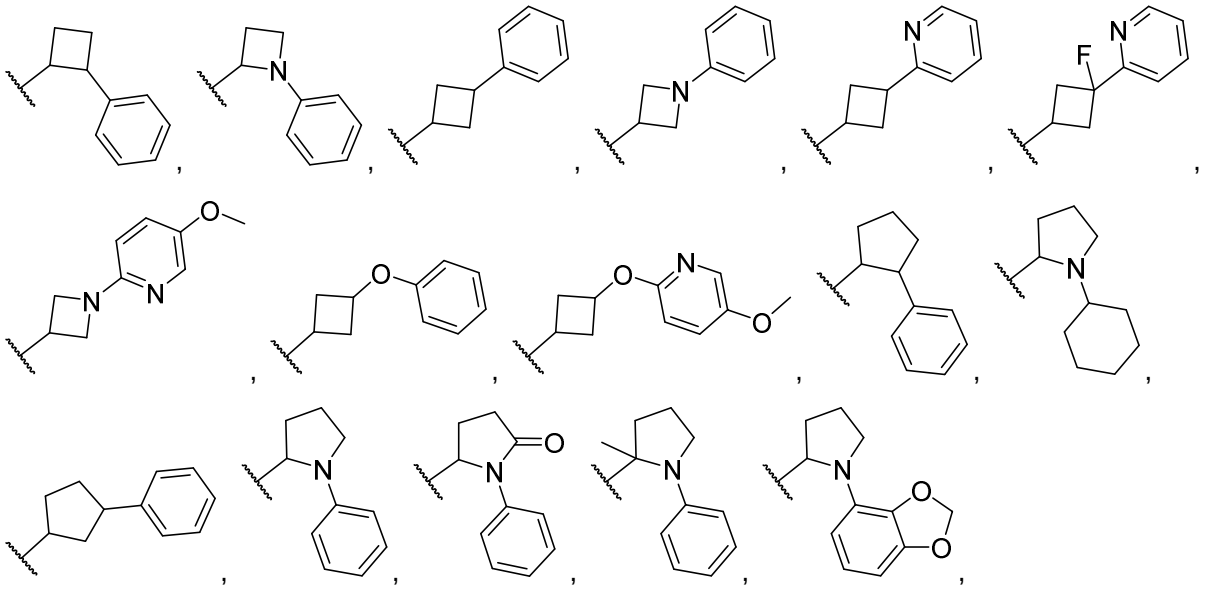
43. The compound or salt of claim 29, wherein m is 2, and one R^4 is halo, and the other R^4 is halo or methyl.

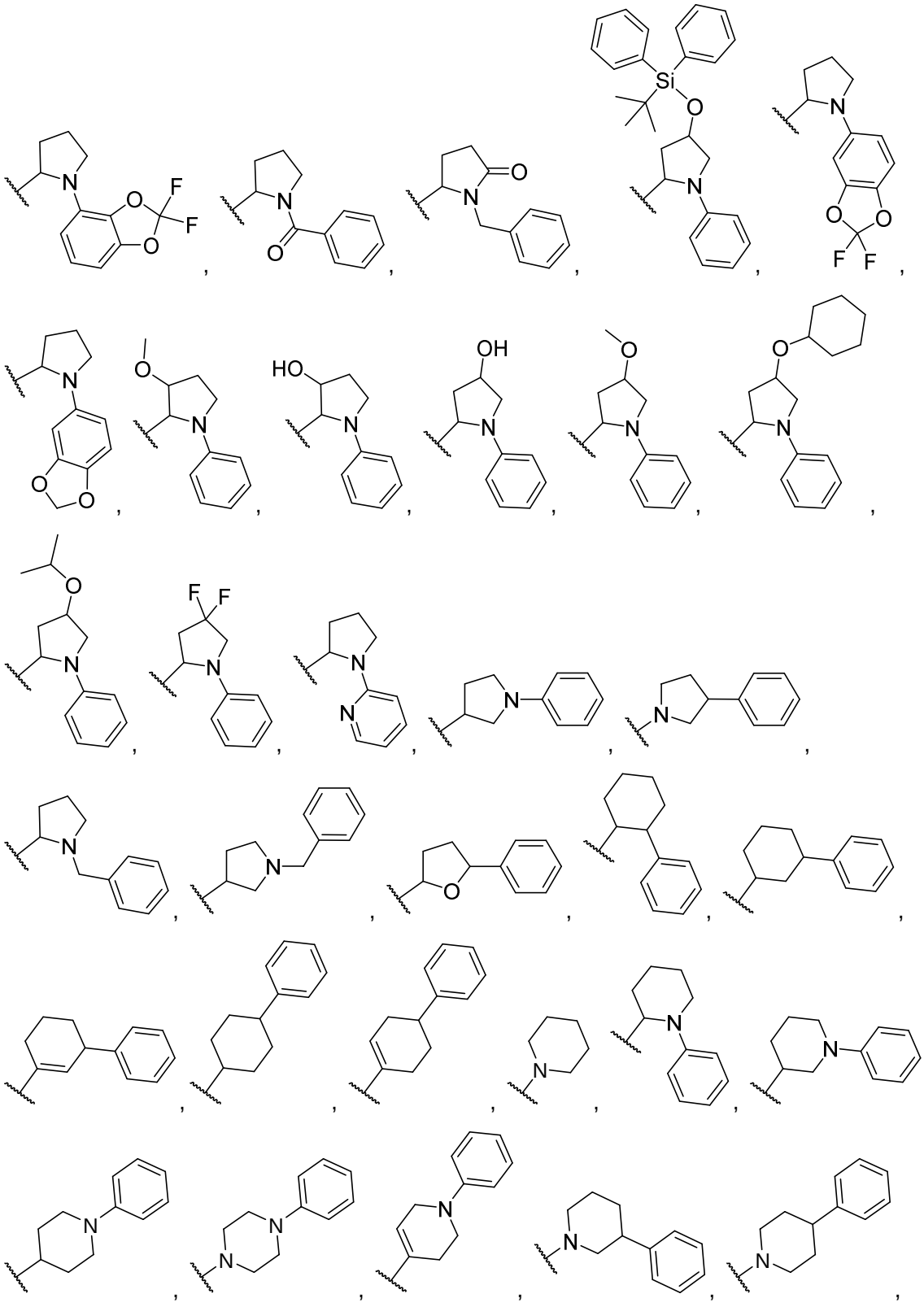
44. The compound or salt of any one of claims 1 to 23, having the structure of Formula (IIIA):

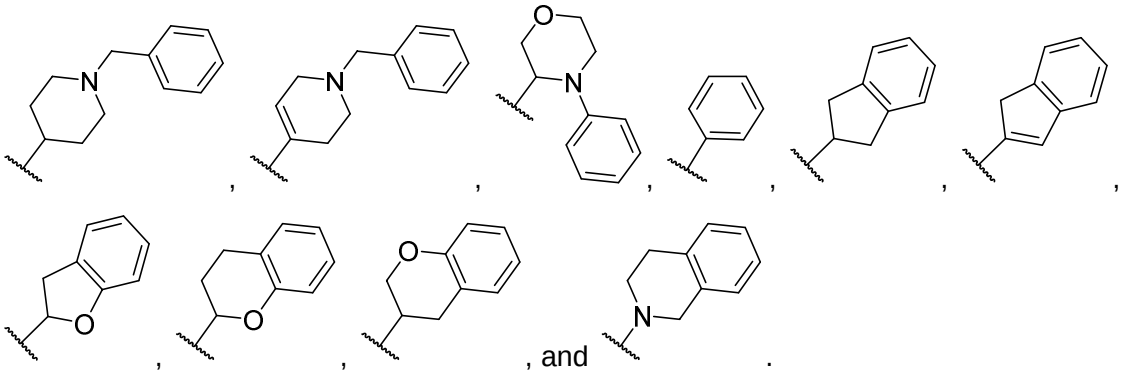


(IIIA).

45. The compound or salt of claim 44, wherein L^1-B is selected from the group consisting of:

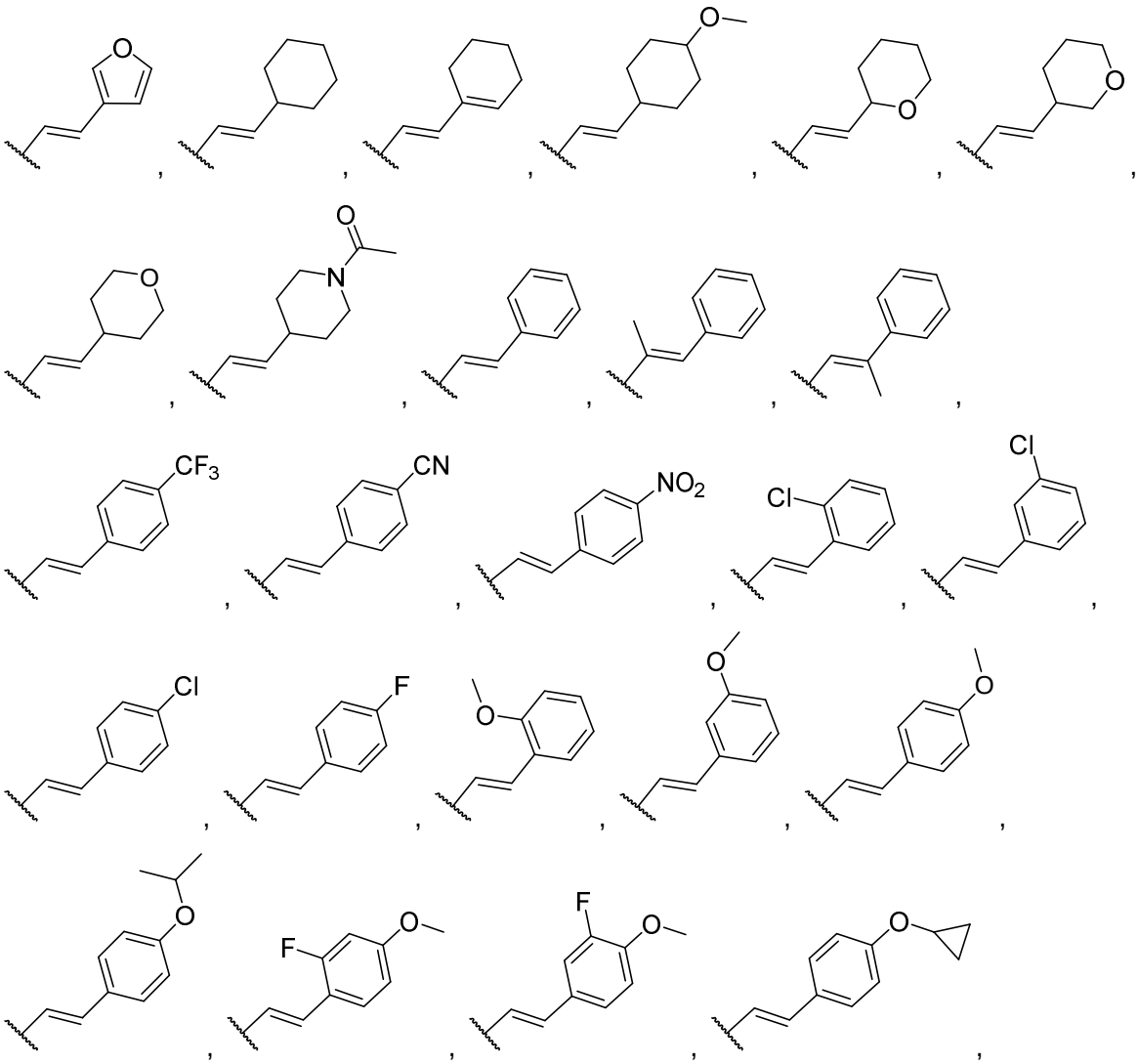


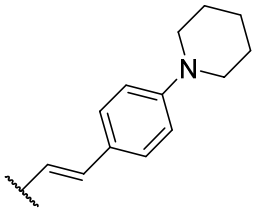
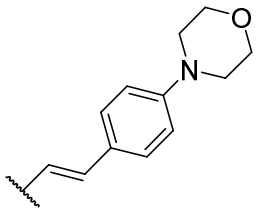
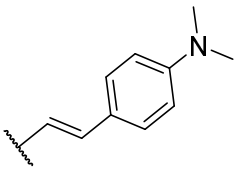
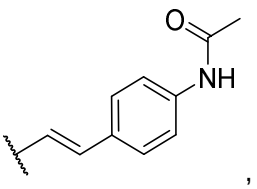


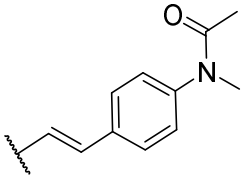
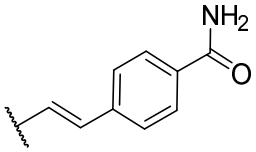
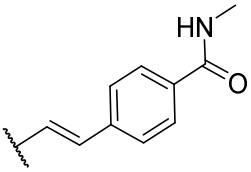
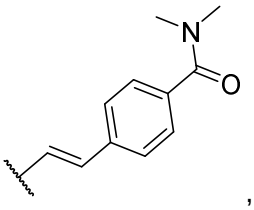


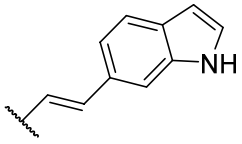
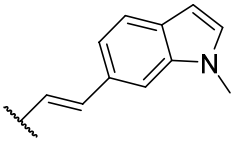
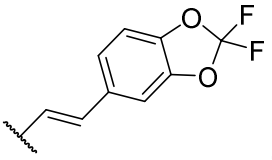
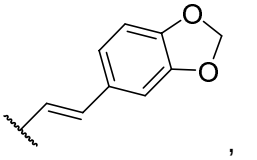
, and .

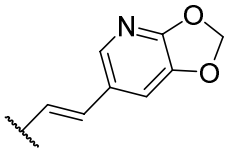
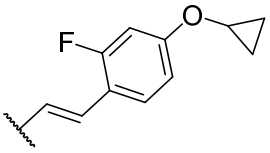
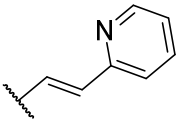
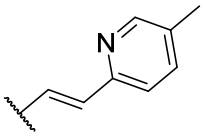
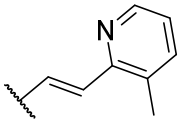
46. The compound or salt of claim 44, wherein L^1-B is selected from the group consisting of:

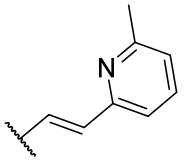
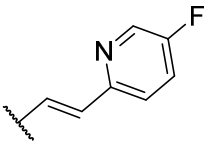
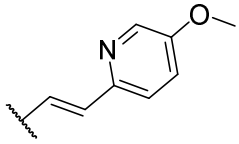
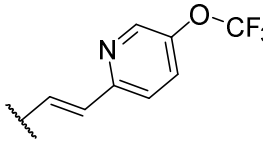
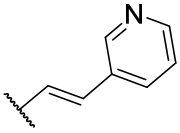


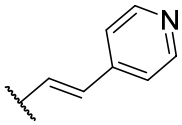
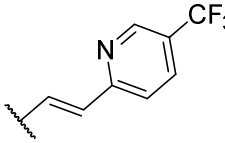
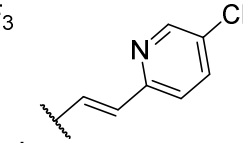
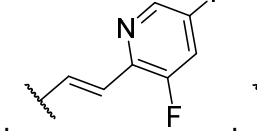
 ,  ,  ,  ,

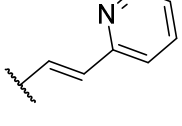
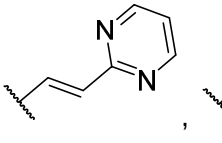
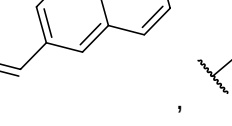
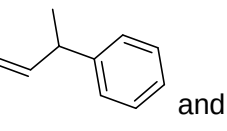
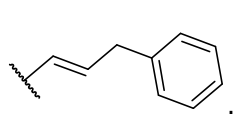
 ,  ,  ,  ,

 ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

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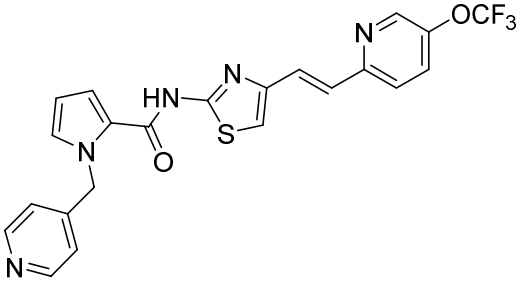
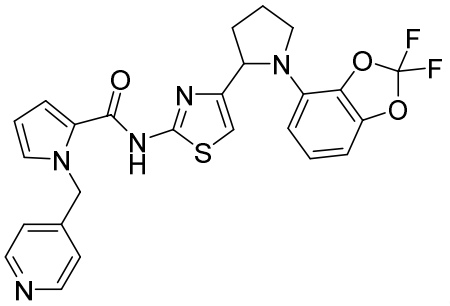
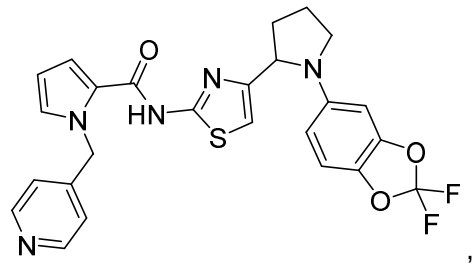
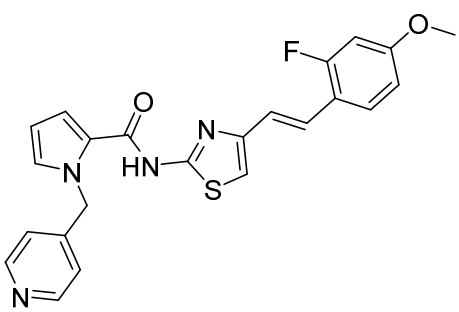
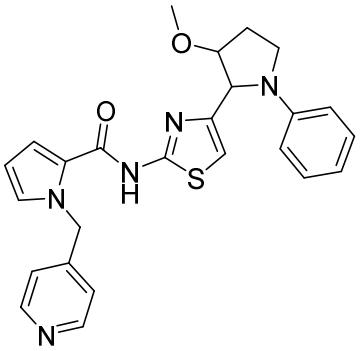
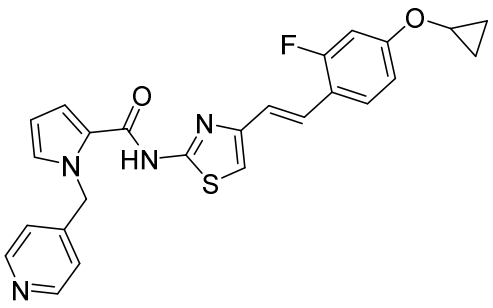
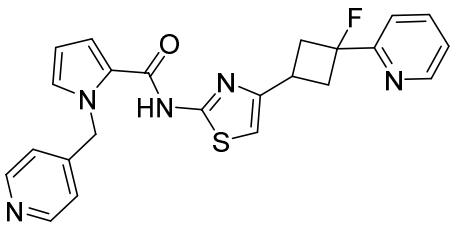
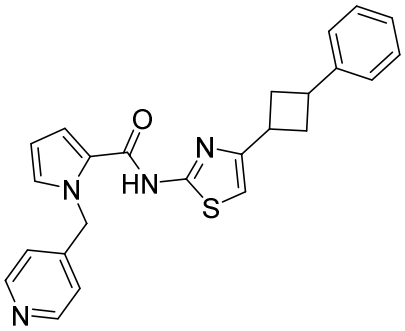
47. The compound or salt of claim 1, wherein the compound or salt is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  .



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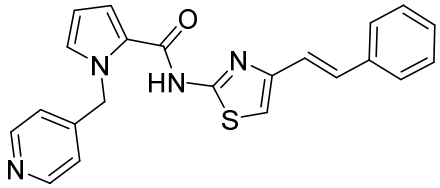

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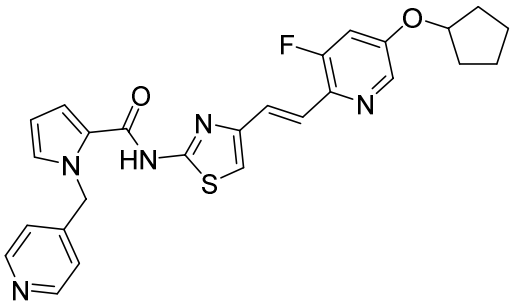

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48. A compound listed in Table A, or a pharmaceutically salt thereof.

49. The compound or salt of any one of claims 1-48 for use in inhibiting protein secretion.

50. The compound or salt for use of claim 49, 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.

51. Use of the compound or salt of any one of claims 1-48 in the manufacture of a medicament for the treatment of inflammation, or a disease selected from a group comprising cancer, autoimmune disease, immune-related disease, neurodegenerative disease and inflammatory disease.