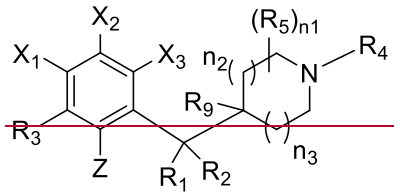
## CLAIMS:

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



I ;

wherein

Z is $OR_a$, $NR_aR_b$, or $NR_b(C=O)R_a$;

$X_1$ is H, halogen, CN, alkyl, halogenated alkyl, cycloalkyl, cycloalkenyl, or halogenated cycloalkyl;

$X_2$ is H, halogen, CN, alkyl, halogenated alkyl, cycloalkyl, or halogenated cycloalkyl;

$X_3$ is H, halogen, fluorinated alkyl, or alkyl;

or alternatively $X_1$ and $X_2$ and the carbon atoms they are connected to taken together form an optionally substituted 6-membered aryl;

or alternatively $X_2$ and $X_3$ and the carbon atoms they are connected to taken together form an optionally substituted 6-membered aryl;

$R_3$ is H, halogen, or alkyl;

or alternatively $X_1$ and $R_3$ and the carbon atoms they are connected to taken together form an optionally substituted 6-membered aryl;

$R_1$ and $R_2$ are each independently H, alkyl, $(CR_6R_7)_{n4}OR_a$, $(CR_6R_7)_{n4}NR_aR_b$, $(CR_6R_7)_{n4}NR_a(C=O)R_b$, $(CR_6R_7)_{n4}NR_aSO_2R_b$, or $(CR_6R_7)_{n4}CONR_aR_b$; or alternatively $R_1$, $R_2$ and the carbon atom they are connected to taken together form a 3-5 membered carboncycle;

$R_4$ is H, alkyl, halogenated alkyl, optionally substituted cycloalkyl, $(CR_6R_7)_{n4}OR_c$, $(CR_6R_7)_{n4}(C=O)R_c$, $(C=O)(CR_6R_7)_{n4}R_c$, $(CR_6R_7)_{n4}COOR_c$, $(CR_6R_7)_{n4}NR_c(C=O)R_d$, $(CR_6R_7)_{n4}(C=O)NR_cR_d$, $(C=O)(CR_6R_7)_{n4}NR_cR_d$, $(CR_6R_7)_{n4}(C=O)(C=O)NR_cR_d$, $(C=O)(CR_6R_7)_{n4}OR_c$, $(CR_6R_7)_{n4}SO_2R_c$, $(CR_6R_7)_{n4}SO_2NR_cR_d$, optionally substituted saturated

heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted -alkyl-cycloalkyl, or optionally substituted -cycloalkyl-alkyl;

each occurrence of $R_5$ is independently H, alkyl, cycloalkyl, or oxo;

or two $R_5$ groups taken together with the carbon atom(s) that they are connected to form a 3-7 membered optionally substituted saturated carbocycle;

or two $R_5$ groups are connected to different carbon atoms on the ring and taken together form a bond or an alkyl chain containing 1-3 carbons;

each occurrence of $R_6$ and $R_7$ are independently H, alkyl, or cycloalkyl;

each occurrence of $R_a$ and $R_b$ are independently H, alkyl, cycycloalkyl, saturated heterocycle, aryl, or heteroaryl; or alternatively $R_a$ and $R_b$ together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

each occurrence of $R_c$ and $R_d$ are independently H, alkyl, alkyl substituted by 1-4 substituents each of which is independently halogen, $OR_8$ or $N(R_8)_2$, alkenyl, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted spiroalkyl, optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted -alkyl-cycloalkyl, or optionally substituted -cycloalkyl-alkyl; or alternatively $R_c$ and $R_d$ together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

each occurrence of $R_8$ is independently H, alkyl, or an optionally substituted heterocycle; or alternatively the two $R_8$ groups together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

$R_9$ is H, alkyl, halogen, or $(CR_6R_7)_{n4}OR_b$;

the alkyl, cycloalkyl, spiroalkyl, bicycloalkyl, heterocycle, aryl, and heteroaryl in $X_1$, $X_2$, $X_3$, $R_1$, $R_2$, $R_3$, $R_4$, $R_5$, $R_6$, $R_7$, $R_9$, $R_a$, $R_b$, $R_c$, and $R_d$, where applicable, are optionally substituted

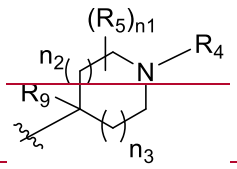
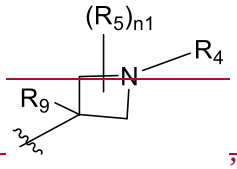
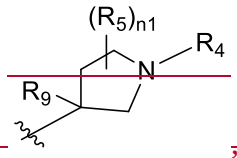
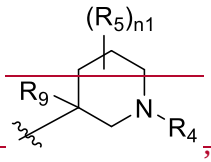
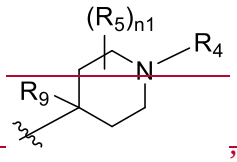
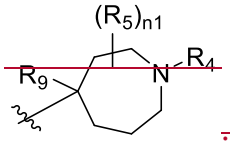
by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)C_{1-4}$alkyl, $(C=O)N(R_8)_2$, and oxo where valence permits;

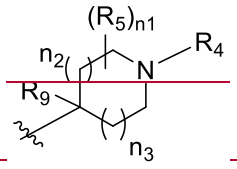
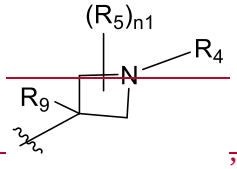
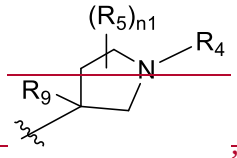
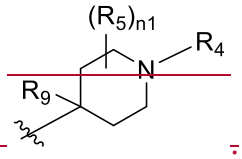
each occurrence of $n_1$ is independently an integer from 0-3 where valence permits;

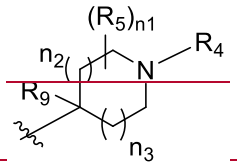
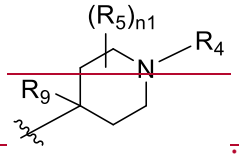
each occurrence of $n_2$ and $n_3$ is independently an integer from 0-2; and

each occurrence of $n_4$ is independently an integer from 0-3.

2. The compound of claim 1, wherein each occurrence of $n_2$ and $n_3$ is independently an integer from 0-1.

3. The compound of claim 1, wherein the structural motif  has the structure of , , , , or .

4. The compound of claim 1, wherein the structural motif  has the structure of , , or .

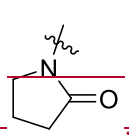
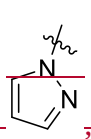
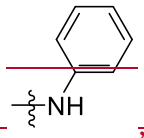
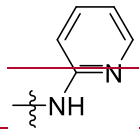
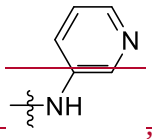
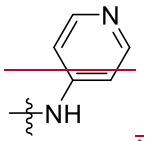
5. The compound of claim 1, wherein the structural motif  has the structure of .

6. The compound of any one of the preceding claims, wherein at least one occurrence of $R_1$ and $R_2$ is H or alkyl.

7. The compound of any one of claims 1-5, wherein at least one occurrence of $R_1$ and $R_2$ is $(CR_6R_7)_{n4}OR_a$, $(CR_6R_7)_{n4}NR_aR_b$, $(CR_6R_7)_{n4}NR_a(C=O)R_b$, $(CR_6R_7)_{n4}NR_aSO_2R_b$, or $(CR_6R_7)_{n4}CONR_aR_b$.

8. The compound of claim 7, wherein at least one occurrence of $R_1$ and $R_2$ is $OR_a$ or $NR_aR_b$.

9. The compound of any one of claims 1-5, wherein $R_1$, $R_2$, and the carbon atom they are connected to taken together form a 3-5 membered carboncycle.

10. The compound of any one of claims 1-5, wherein $R_1$ and $R_2$ are each independently H, Me, OH, $CH_2OH$, $NH_2$, NHMe, $NMe_2$, $CH_2NH_2$, $CONH_2$, $CONHMe_2$, $CONMe_2$, NH(C=O)Me, NMe(C=O)Me, , , , , , or .

11. The compound of any one of the preceding claims, wherein $R_4$ is H, alkyl, halogenated alkyl, or cycloalkyl.

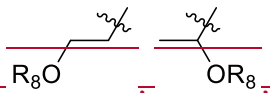
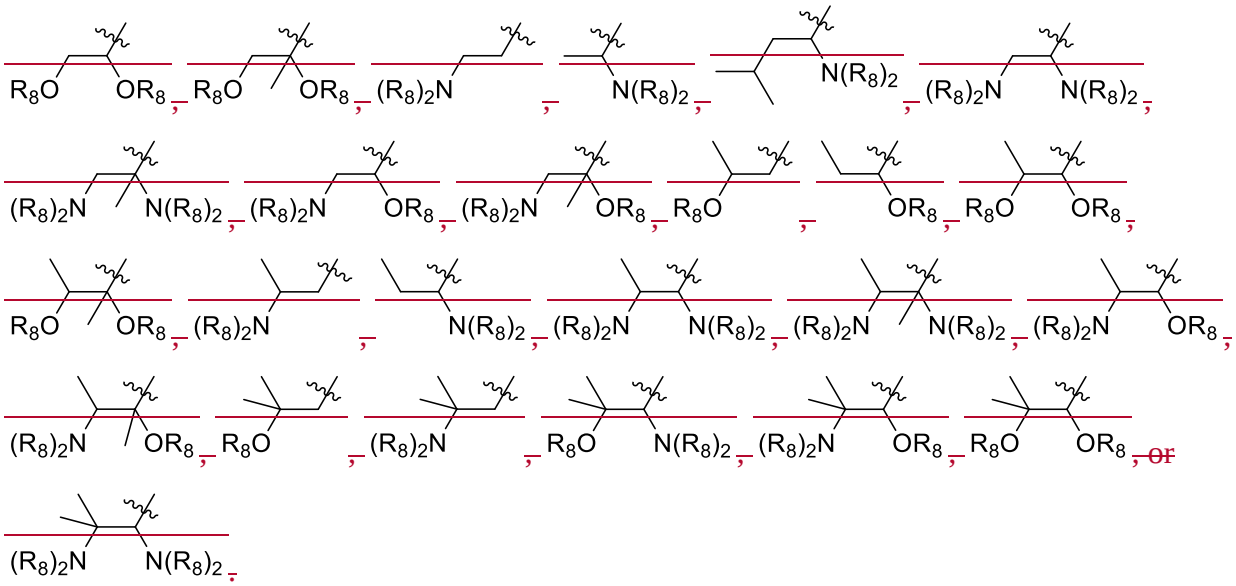
12. The compound of claim 11, wherein $R_4$ is H, Me, or fluorinated ethyl.

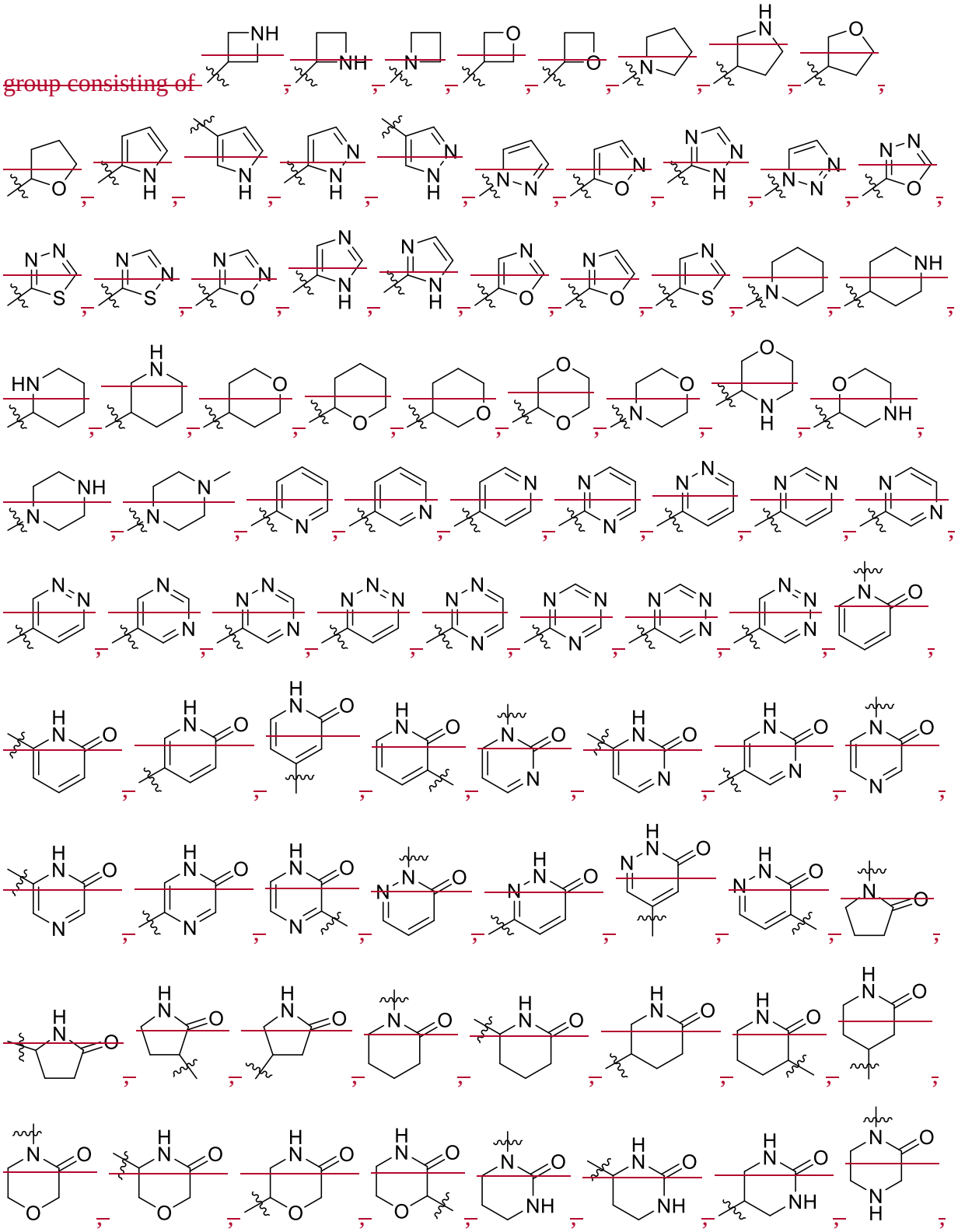
13. The compound of any one of claims 1-10, wherein $R_4$ is $(CR_6R_7)_{n4}OR_c$, $(CR_6R_7)_{n4}COR_c$, $(C=O)(CR_6R_7)_{n4}R_c$, $(CR_6R_7)_{n4}COOR_c$, $(CR_6R_7)_{n4}NR_c(C=O)R_d$, $(CR_6R_7)_{n4}(C=O)NR_cR_d$, $(CR_6R_7)_{n4}(C=O)(C=O)NR_cR_d$, $(C=O)(CR_6R_7)_{n4}OR_c$, $(CR_6R_7)_{n4}SO_2R_c$, or $(CR_6R_7)_{n4}SO_2NR_cR_d$.

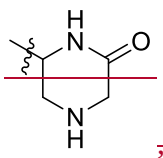
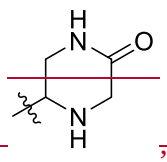
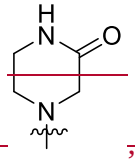
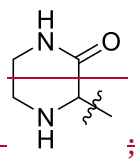
14. The compound of claim 13, wherein $R_4$ is $(CR_6R_7)_2OR_e$, $(C=O)R_e$, $(C=O)(CR_6R_7)_{1-2}R_e$, $COOR_e$, $(CR_6R_7)_{1-2}NR_eR_d$, $(C=O)NR_eR_d$, $(CR_6R_7)_{n4}(C=O)(C=O)NR_eR_d$, $(C=O)(CR_6R_7)_{1-2}OR_e$, $SO_2R_e$, or $SO_2NR_eR_d$.

15. The compound of claim 14, wherein $R_4$ is $(CH_2)_2OH$, $(CH_2)_2OMe$, $(C=O)H$, $(C=O)Me$, $(C=O)CH_2OH$, $(C=O)CH_2OMe$, $(C=O)Et$, $(C=O)Ph$, $(C=O)$isopropyl, $(C=O)NH_2$, $(C=O)NHMe$, $(C=O)NMe_2$, $(C=O)CH_2NH_2$, $(C=O)CH_2NHMe$, $(C=O)CH(OH)CH_2OH$, $(C=O)CH(OMe)CH_2OH$, $(C=O)CH(OH)CH_2OMe$, $(C=O)(C=O)NMe_2$, $(C=O)OMe$, $SO_2Me$, $SO_2Et$, $SO_2CH_2OH$, $SO_2CH_2OMe$, $SO_2NH_2$, $SO_2NHMe$, or $SO_2NMe_2$.

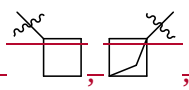
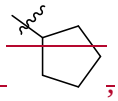
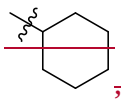
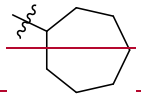
16. The compound of claim 14, wherein $R_4$ is $(C=O)R_e$, $(C=O)(CR_6R_7)_{1-2}R_e$, $(C=O)(CR_6R_7)_{1-2}OR_e$, or $SO_2R_e$; and wherein $R_e$ is selected from the group consisting of H, alkyl, alkyl substituted by 1-4 substituents each independently selected from the group consisting of halogen, $OR_8$ and $N(R_8)_2$, alkenyl, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted spiroalkyl, optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted -alkyl-cycloalkyl, and optionally substituted -cycloalkyl-alkyl.

17. The compound of claim 14, wherein $R_e$ or $R_d$ is H, Me, Et, 


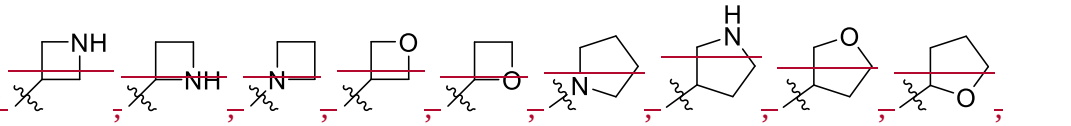
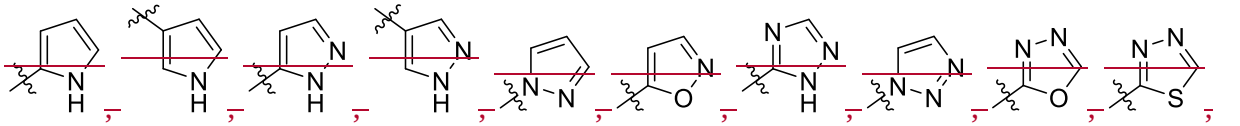
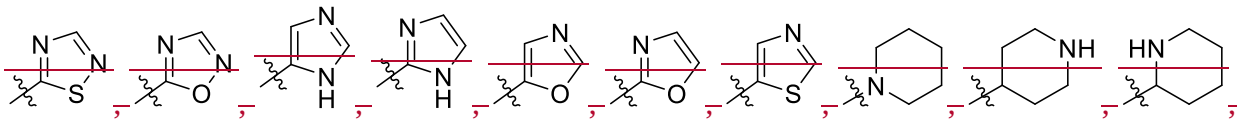
~~18. The compound of claim 14, wherein $R_e$ or $R_d$ is a heterocycle selected from the group consisting of~~ 

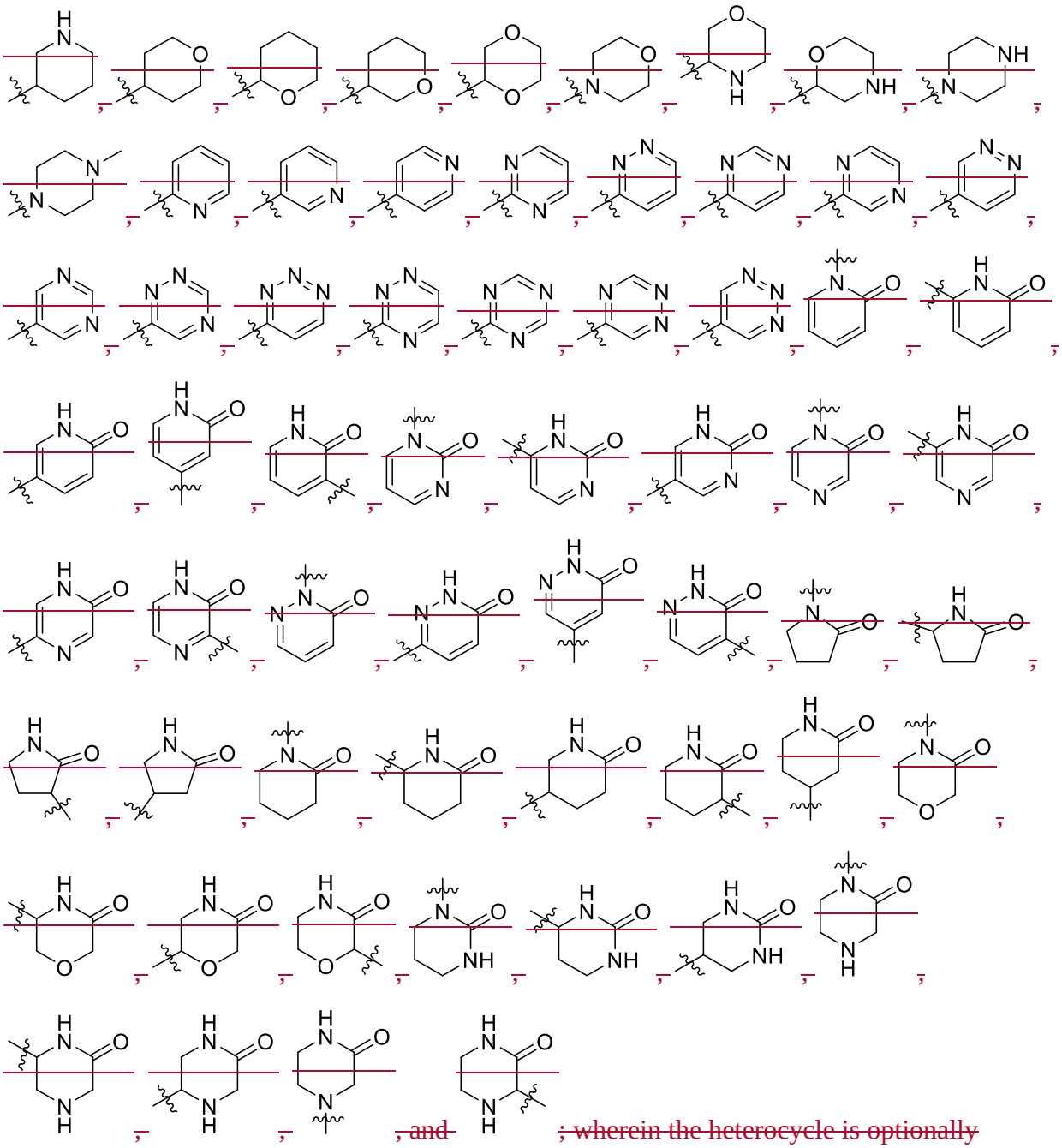
~~ ,  ,  , and  ; wherein the heterocycle is optionally substituted by one or more cyano, cycloalkyl, fluorinated alkyl, fluorinated cycloalkyl, halogen, OH, $NH_2$, oxo, or $(C=O)C_{1-4}$alkyl where valence permits.~~

~~19. The compound of claim 14, wherein $R_6$ is cycloalkyl, spiroalkyl, or bicycloalkyl each optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits.~~

~~20. The compound of claim 19, wherein $R_6$ is~~  ,  ,  ,  ,  ,  , or  ~~each optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits.~~

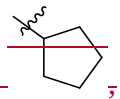
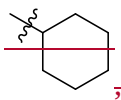
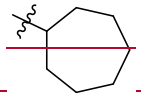
~~21. The compound of any one of claims 1-10, wherein $R_4$ is optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted cycloalkyl, optionally substituted -alkyl-cycloalkyl, or optionally substituted -cycloalkyl-alkyl.~~

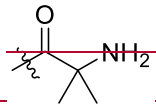
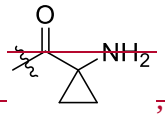
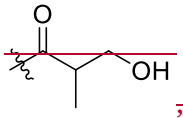
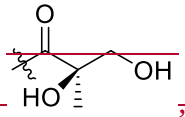
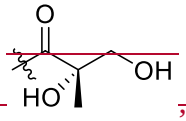
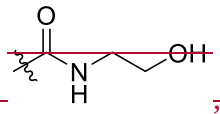
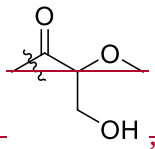
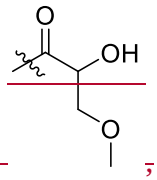
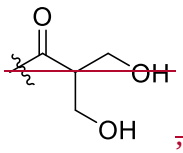
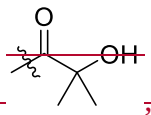
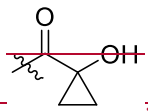
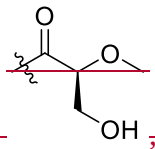
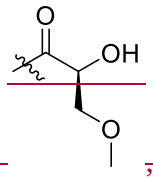
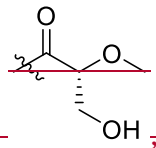
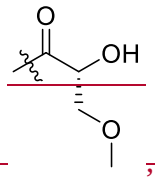
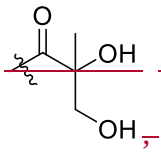
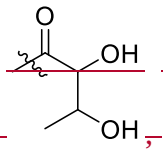
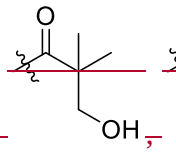
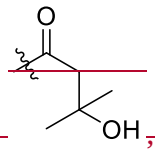
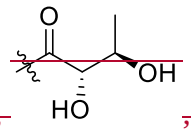
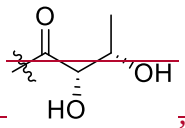
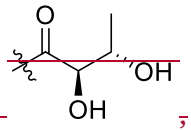
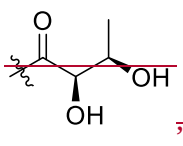
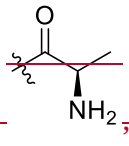
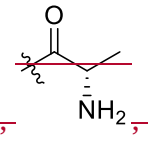
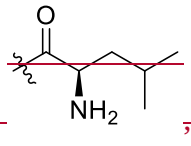
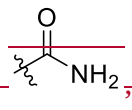
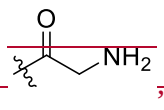
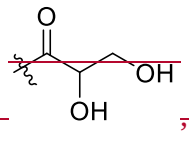
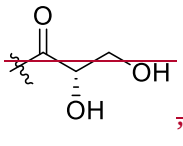
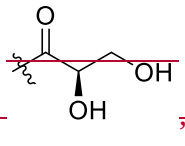
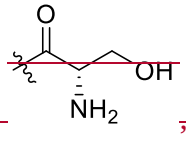
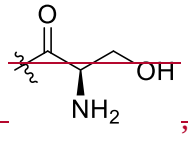
~~22. The compound of claim 21, wherein $R_4$ is a heterocycle selected from the group consisting of~~    .

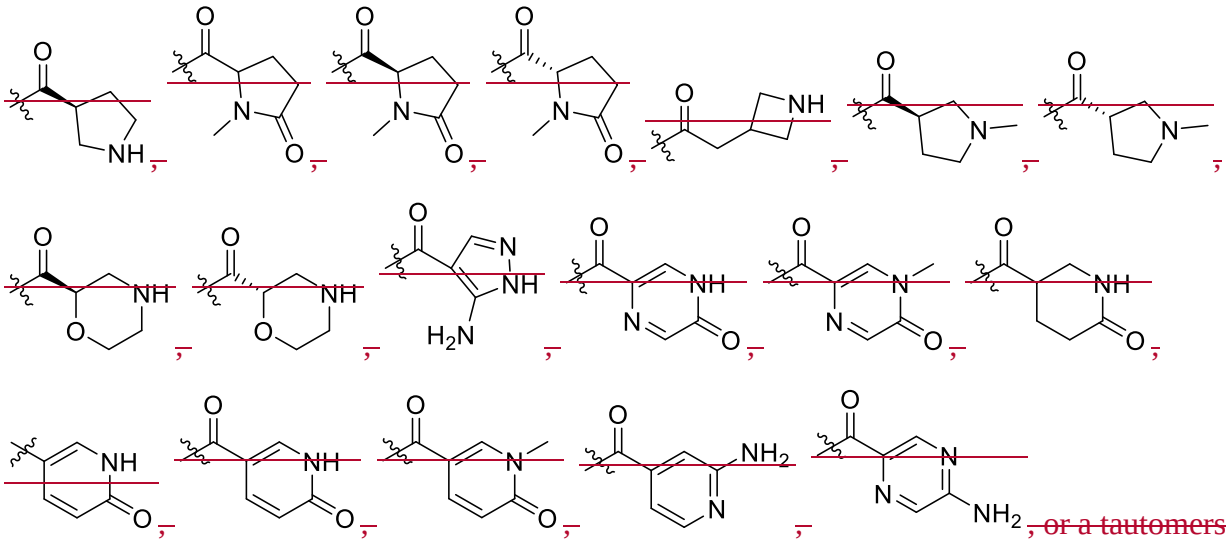


, and ; wherein the heterocycle is optionally substituted by one or more cyano, cycloalkyl, fluorinated alkyl, fluorinated cycloalkyl, halogen, OH, $NH_2$, oxo, or $(C=O)C_{1-4}$alkyl where valence permits.

23. The compound of claim 21, wherein $R_4$ is cycloalkyl optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits.

24. The compound of claim 23, wherein $R_4$ is , , , , , , , each optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits.

25. The compound of any one of claims 1-10, wherein $R_4$ is , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , 



, or a tautomers thereof.

26. The compound of any one of claims 1-25, wherein at least one occurrence of $R_5$ is H, alkyl or cycloalkyl.

27. The compound of any one of claims 1-25, wherein at least one occurrence of $R_5$ is oxo.

28. The compound of any one of claims 1-25, wherein two $R_5$ groups are connected to different carbon atoms on the ring and taken together form a bond or an alkyl chain containing 1-3 carbons.

29. The compound of any one of claims 1-25, wherein two $R_5$ groups taken together with the carbon atom(s) that they are connected to form a 3-7 membered optionally substituted saturated carbocycle.

30. The compound of any one of the proceeding claims, wherein at least one of $R_a$ and $R_b$ is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, or heteroaryl.

31. The compound of any one of claims 1-29, wherein $R_a$ and $R_b$ together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S.

32. The compound of any one of the proceeding claims, wherein each occurrence of $R_6$ and $R_7$ are independently H or alkyl.

33. The compound of any one of the preceding claims, wherein $R_9$ is H, alkyl, or halogen.

34. The compound of any one of claims 1-32, wherein $R_9$ is $(CR_6R_7)_{n4}OR_b$.

35. The compound of any one of claims 1-32, wherein $R_9$ is H, F, or OH.

36. The compound of any one of the preceding claims, wherein Z is $OR_a$, $NR_aR_b$, or $NR_b(C=O)R_a$.

37. The compound of claim 36, wherein Z is OH, OMe, $NH_2$, NHMe, or $NMe_2$.

38. The compound of claim 36, wherein Z is OH.

39. The compound of any one of the preceding claims, wherein $X_1$ is H, halogen, fluorinated alkyl or alkyl.

40. The compound of any one of the preceding claims, wherein $X_1$ is H, F, Cl, Br, Me, $CF_3$, or $CF_2Cl$.

41. The compound of claim 39, wherein $X_1$ is Me or Cl.

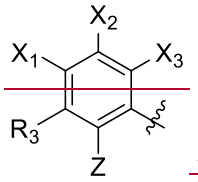
42. The compound of any one of the preceding claims, wherein $X_2$ is H, halogen, fluorinated alkyl or alkyl.

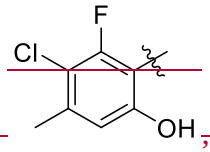
43. The compound of claim 42, wherein $X_2$ is H, F, Cl, Br, Me, $CF_3$, or $CF_2Cl$.

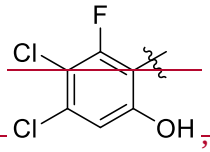
44. The compound of claim 42, wherein $X_2$ is Cl.

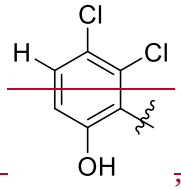
45. The compound of any one of the preceding claims, wherein $X_3$ is H, F, Cl, Br, fluorinated alkyl, or alkyl.

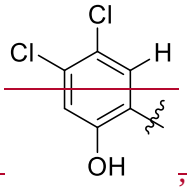
46. The compound of claim 45, wherein $X_3$ is H, F, Cl, or $CF_3$.

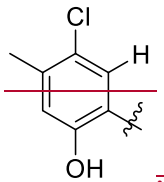
47. The compound of any one of claims 1-35, wherein the structural moiety 

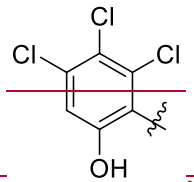
has the structure of 

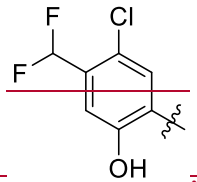
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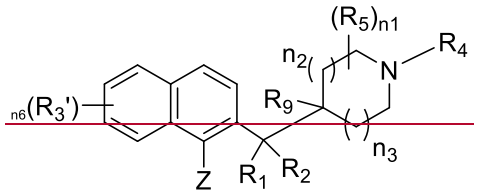
, or 

, each of which is substituted by $R_3$.

48. The compound of any one of claims 1-47, wherein $R_3$ is H or alkyl.

49. The compound of any one of claims 1-47, wherein $R_3$ is halogen.

50. The compound of any one of claims 1-38, wherein the compound has a structure of Formula II,



II ;

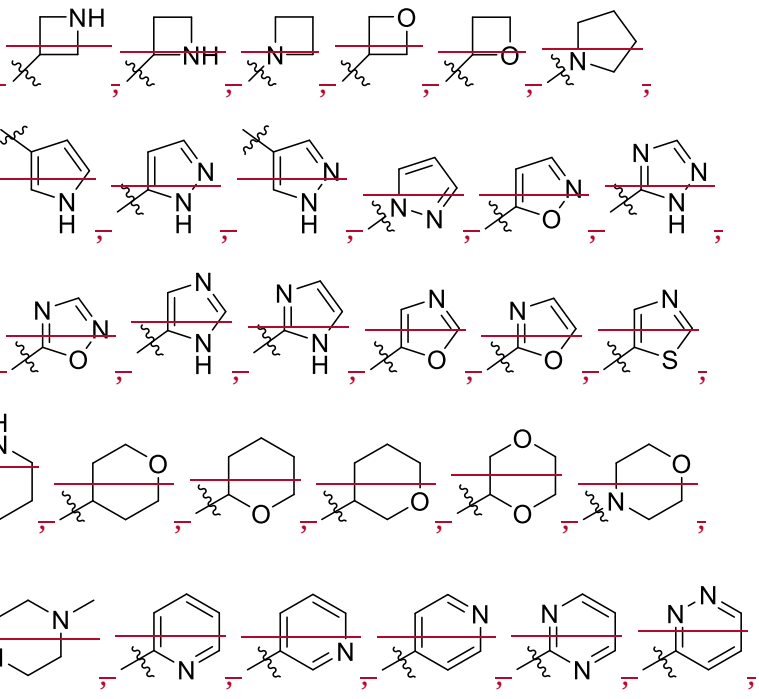
each occurrence of $R_{3'}$ is independently H, halogen, or alkyl; and

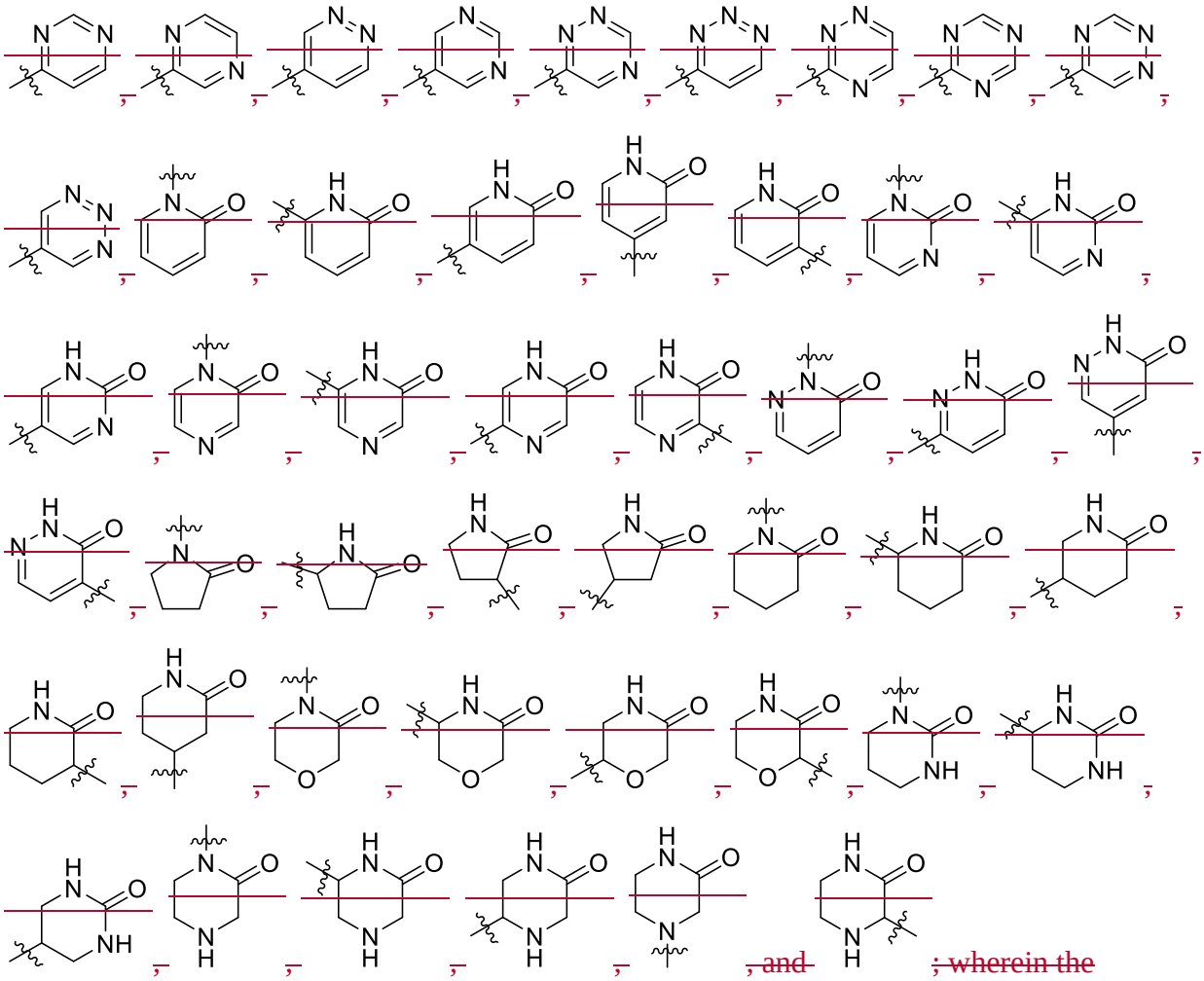
$n_6$ is an integer from 0-2.

51. The compound of claim 50, wherein at least one occurrence of $R_{3'}$ is H or alkyl.

52. The compound of claim 50, wherein at least one occurrence of $R_{3'}$ is halogen.

53. The compound of any one of the preceding claims, wherein at least one occurrence of $R_8$ is H, alkyl, or optionally substituted heterocycle.

54. The compound of claim 53, wherein $R_8$ is H, Me, Et, Pr, Bu, or a heterocycle selected from the group consisting of 



, and ; wherein the heterocycle is optionally substituted by one or more cyano, cycloalkyl, fluorinated alkyl, fluorinated cycloalkyl, halogen, OH, $NH_2$, oxo, or $(C=O)C_{1-4}$alkyl where valence permits.

55. The compound of any one of claims 1-52, wherein the two $R_8$ groups together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S.

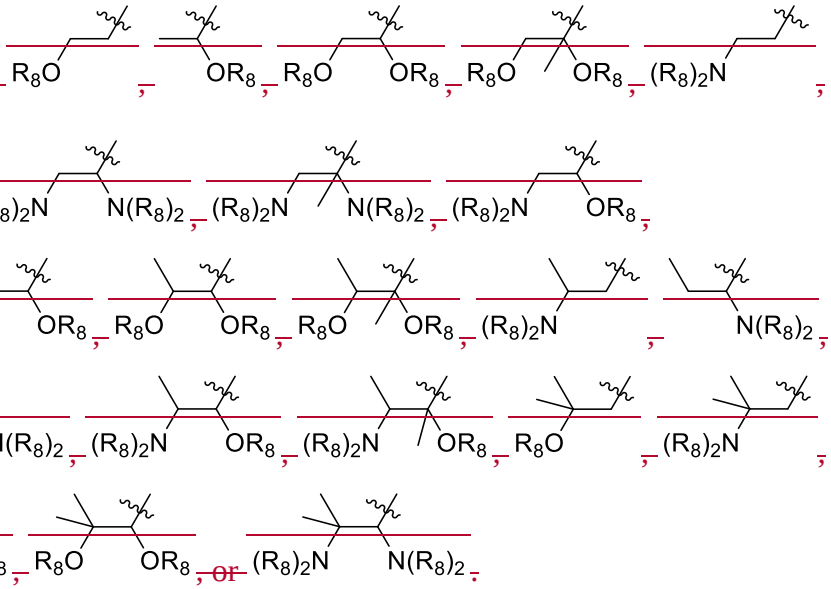
56. The compound of any one of the preceding claims, wherein $n_1$ is 0, 1, 2, or 3.

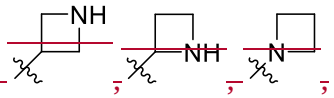
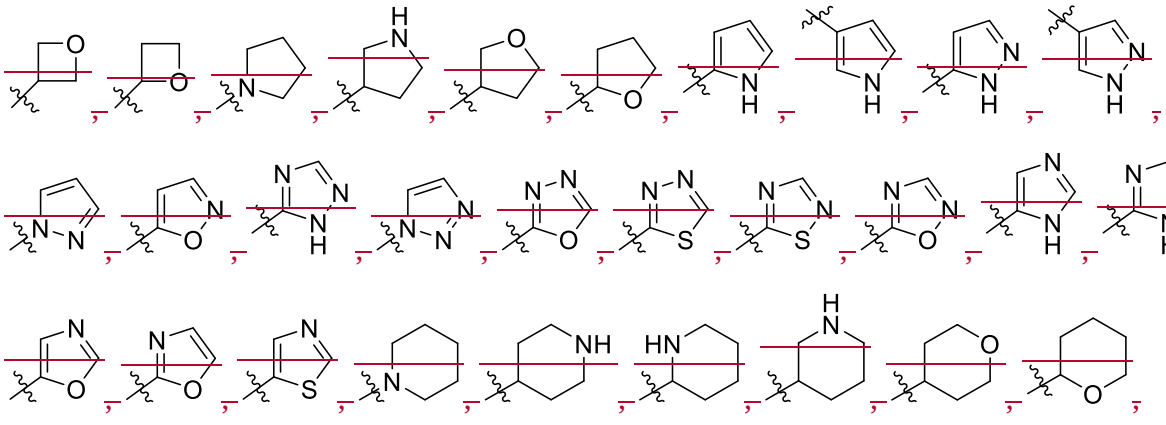
57. The compound of any one of claims 1-5, wherein $n_4$ is 0, 1, or 2.

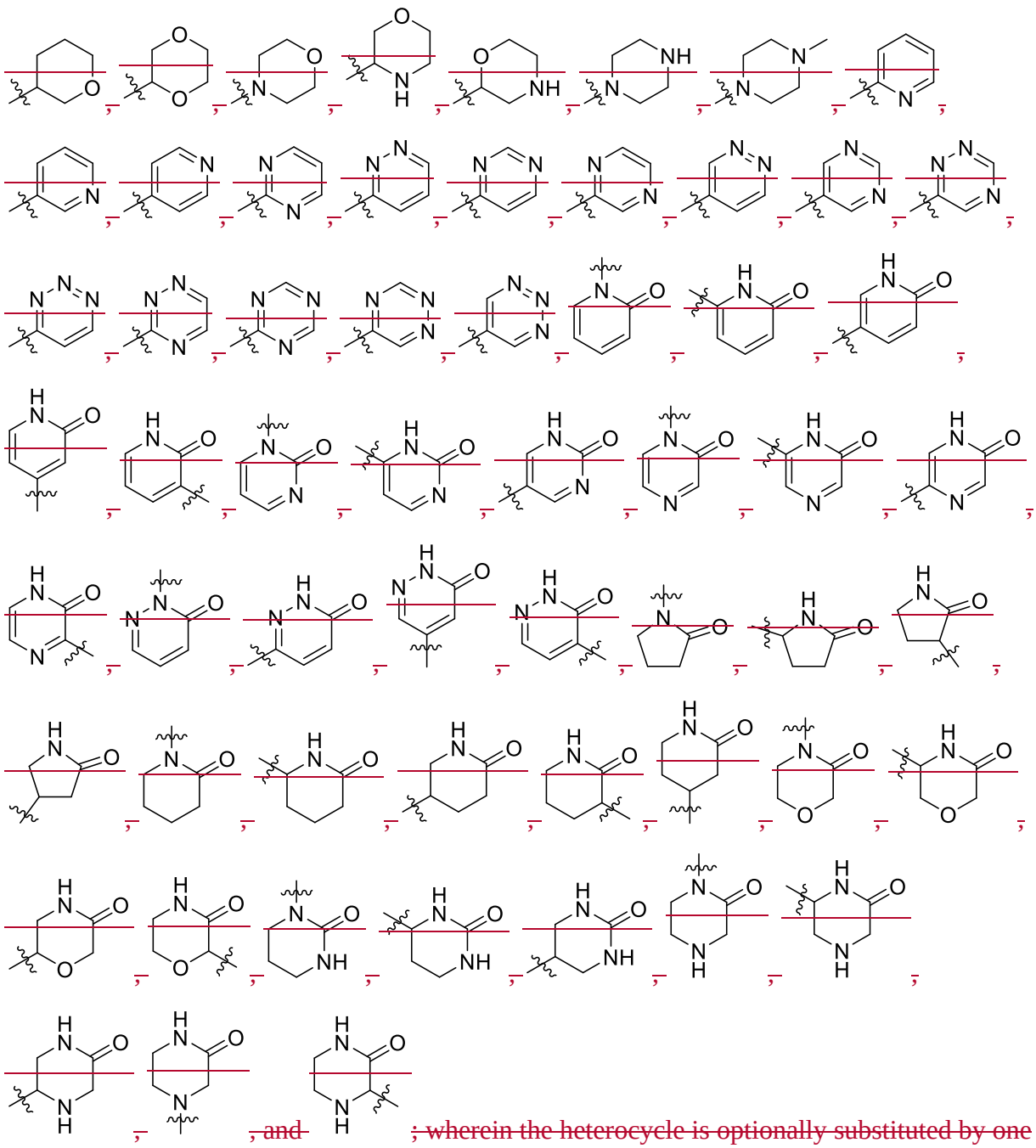
58. The compound of any one of claims 1-5, wherein at least one occurrence of $R_c$ or $R_d$ is independently H, alkyl, alkyl substituted by 1-4 substituents each independently selected from the group consisting of halogen, $OR_8$ and $N(R_8)_2$, alkenyl, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted spiroalkyl, optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl,

optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted -alkyl-cycloalkyl, or optionally substituted -cycloalkyl-alkyl.

59. The compound of any one of claims 1-5, wherein $R_c$ and $R_d$ together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S.

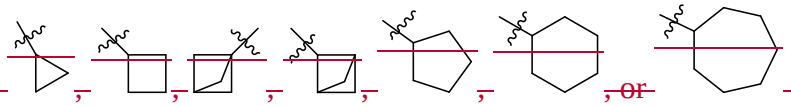
60. The compound of any one of claims 1-5, wherein at least one occurrence of $R_c$ or $R_d$ is independently H, Me, Et, .

61. The compound of any one of claims 1-5, wherein at least one occurrence of $R_c$ or $R_d$ is independently a heterocycle selected from the group consisting of , .



~~, and ; wherein the heterocycle is optionally substituted by one or more cyano, cycloalkyl, fluorinated alkyl, fluorinated cycloalkyl, halogen, OH, $NH_2$, oxo, or $(C=O)C_{1-4}$alkyl where valence permits.~~

~~62. The compound of any one of claims 1-5, wherein at least one occurrence of $R_c$ or $R_d$ is independently cycloalkyl, spiroalkyl, or bicycloalkyl each optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits.~~

63. The compound of any one of claims 1-5, wherein at least one occurrence of $R_c$ or $R_d$ is independently , each optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits.

64. The compound of claim 1, wherein the compound is selected from a group consisting of compounds 1-338 in Table 1.

65. A pharmaceutical composition comprising at least one compound according to any one of claims 1-64 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or diluent.

66. A method of treating a condition in a mammalian species in need thereof, comprising administering to the mammalian species a therapeutically effective amount of at least one compound according to any one of claims 1-64 or a pharmaceutically acceptable salt thereof, wherein the condition is selected from the group consisting of cancer, an immunological disorder, a Central Nerve System (CNS) disorder, an inflammatory disorder, a gastroenterological disorder, a metabolic disorder, a cardiovascular disorder, and a kidney disease.

67. The method of claim 66, wherein the immunological disorder is transplant rejection or an autoimmune disease.

68. The method of claim 67, wherein the autoimmune disease is rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, or Type I diabetes mellitus.

69. The method of claim 66, wherein the Central Nerve System (CNS) disorder is Alzheimer's disease.

70. The method of claim 66, wherein the inflammatory disorder is an inflammatory skin condition, arthritis, psoriasis, spondylitis, parodontitits, or an inflammatory neuropathy.

71. The method of claim 66, wherein the gastroenterological disorder is an inflammatory bowel disease.

72. The method of claim 66, wherein the metabolic disorder is obesity or Type II diabetes mellitus.

~~73. The method of claim 66, wherein the cardiovascular disorder is an ischemic stroke.~~

~~74. The method of claim 66, wherein the kidney disease is chronic kidney disease, nephritis, or chronic renal failure.~~

~~75. The method of claim 66, wherein the condition is selected from the group consisting of cancer, transplant rejection, rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, Type I diabetes mellitus, Alzheimer's disease, inflammatory skin condition, inflammatory neuropathy, psoriasis, spondylitis, parodontitis, Crohn's disease, ulcerative colitis, obesity, Type II diabetes mellitus, ischemic stroke, chronic kidney disease, nephritis, chronic renal failure, and a combination thereof.~~

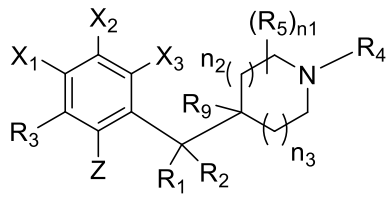
~~76. The method of claim 66, wherein the mammalian species is human.~~

~~77. A method of blocking Kv1.3 potassium channel in a mammalian species in need thereof, comprising administering to the mammalian species a therapeutically effective amount of at least one compound according to any one of claims 1-64 or a pharmaceutically acceptable salt thereof.~~

~~78. The method of claim 76, wherein the mammalian species is human.~~

CLAIMS

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




I ;

wherein

Z is $OR_a$, $NR_aR_b$, or $NR_b(C=O)R_a$;

$X_1$ is alkyl, halogenated alkyl, cycloalkyl, cycloalkenyl, halogenated cycloalkyl, H, halogen, or CN;

$X_2$ is halogen, CN, alkyl, halogenated alkyl, cycloalkyl, halogenated cycloalkyl, or H;

$X_3$ is H, halogen, fluorinated alkyl, or alkyl;

or alternatively $X_1$ and $X_2$ and the carbon atoms they are connected to taken together form an optionally substituted 6-membered aryl;

or alternatively $X_2$ and $X_3$ and the carbon atoms they are connected to taken together form an optionally substituted 6-membered aryl;

$R_3$ is H, halogen, or alkyl;

or alternatively $X_1$ and $R_3$ and the carbon atoms they are connected to taken together form an optionally substituted 6-membered aryl;

$R_1$ and $R_2$ are each independently H, alkyl, $(CR_6R_7)_{n4}OR_a$, $(CR_6R_7)_{n4}NR_aR_b$, $(CR_6R_7)_{n4}NR_a(C=O)R_b$, $(CR_6R_7)_{n4}NR_aSO_2R_b$, or $(CR_6R_7)_{n4}CONR_aR_b$, wherein at least one occurrence of $R_1$ and $R_2$ is $(CR_6R_7)_{n4}NR_aR_b$, $(CR_6R_7)_{n4}OR_a$, $(CR_6R_7)_{n4}NR_a(C=O)R_b$, $(CR_6R_7)_{n4}NR_aSO_2R_b$, or $(CR_6R_7)_{n4}CONR_aR_b$; or alternatively $R_1$, $R_2$ and the carbon atom they are connected to taken together form a 3-5 membered carbocycle;

$R_4$ is $(CR_6R_7)_{n4}(C=O)R_c$, $(C=O)(CR_6R_7)_{n4}R_c$, $(CR_6R_7)_{n4}OR_c$, $(CR_6R_7)_{n4}COOR_c$, $(CR_6R_7)_{n4}NR_c(C=O)R_d$, $(CR_6R_7)_{n4}(C=O)NR_cR_d$, $(C=O)(CR_6R_7)_{n4}NR_cR_d$, $(CR_6R_7)_{n4}(C=O)(C=O)NR_cR_d$, $(C=O)(CR_6R_7)_{n4}OR_c$, $(CR_6R_7)_{n4}SO_2R_c$, $(CR_6R_7)_{n4}SO_2NR_cR_d$, optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted cycloalkyl, optionally substituted -alkyl-cycloalkyl, or optionally substituted -cycloalkyl-alkyl;

each occurrence of $R_5$ is independently H, alkyl, cycloalkyl, or oxo;

or two $R_5$ groups taken together with the carbon atom(s) that they are connected to form a 3-7 membered optionally substituted saturated carbocycle;

or two $R_5$ groups are connected to different carbon atoms on the ring and taken together form a bond or an alkyl chain containing 1-3 carbons;

each occurrence of $R_6$ and $R_7$ are independently H, alkyl, or cycloalkyl;

each occurrence of $R_a$ and $R_b$ are independently H, alkyl, cycycloalkyl, saturated heterocycle, aryl, or heteroaryl; or alternatively $R_a$ and $R_b$ together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

each occurrence of $R_c$ and $R_d$ are independently H, alkyl, alkyl substituted by 1-4 substituents each of which is independently halogen, $OR_8$ or $N(R_8)_2$, alkenyl, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted spiroalkyl, optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted -alkyl-cycloalkyl, or optionally substituted -cycloalkyl-alkyl; or alternatively $R_c$ and $R_d$ together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

each occurrence of $R_8$ is independently H, alkyl, or an optionally substituted heterocycle; or alternatively the two $R_8$ groups together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

$R_9$ is H, alkyl, halogen, or $(CR_6R_7)_{n4}OR_b$;

the alkyl, cycloalkyl, spiroalkyl, bicycloalkyl, heterocycle, aryl, and heteroaryl in $X_1$, $X_2$, $X_3$, $R_1$, $R_2$, $R_3$, $R_4$, $R_5$, $R_6$, $R_7$, $R_9$, $R_a$, $R_b$, $R_c$, and $R_d$, where applicable, are optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)C_{1-4}$alkyl, $(C=O)N(R_8)_2$, and oxo where valence permits;

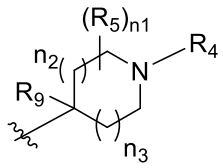
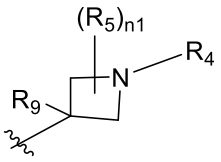
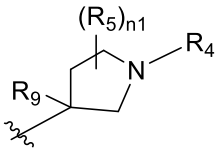
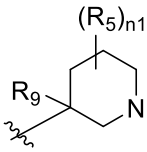
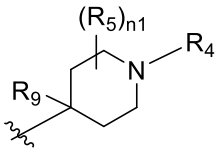
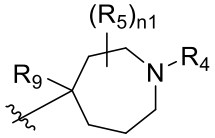
each occurrence of $n_1$ is independently an integer from 0-3 where valence permits;

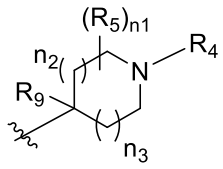
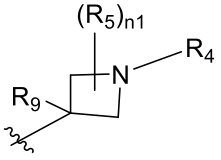
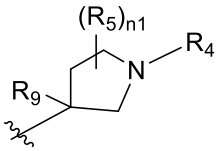
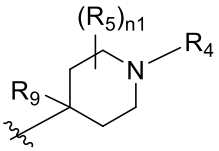
each occurrence of $n_2$ and $n_3$ is independently an integer that is 1, 2 or 0; and

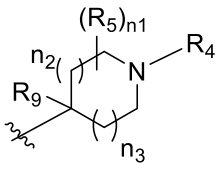
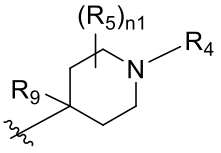
each occurrence of $n_4$ is independently an integer from 0-3.

2. The compound of claim 1, wherein:

(a) each occurrence of $n_2$ and $n_3$ is independently an integer from 0-1; or

(b) the structural motif  has the structure of , , , , or ; or

(c) the structural motif  has the structure of , , or ; or

(d) the structural motif  has the structure of .

3. The compound of claim 1 or 2, wherein at least one occurrence of $R_1$ and $R_2$ is $(CR_6R_7)_{n4}OR_a$, $(CR_6R_7)_{n4}NR_aR_b$, $(CR_6R_7)_{n4}NR_a(C=O)R_b$, $(CR_6R_7)_{n4}NR_aSO_2R_b$, or $(CR_6R_7)_{n4}CONR_aR_b$.

4. The compound of claim 3, wherein at least one occurrence of $R_1$ and $R_2$ is $OR_a$ or $NR_aR_b$.

5. The compound of claim 1 or 2, wherein $R_1$, $R_2$, and the carbon atom they are connected to taken together form a 3-5 membered carbocycle.

6. The compound of any one of claims 1-5, wherein:

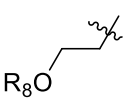
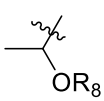
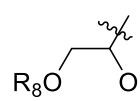
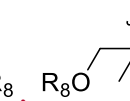
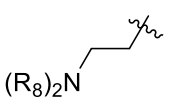
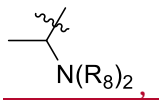
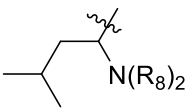
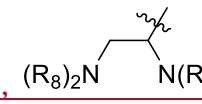
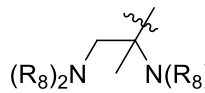
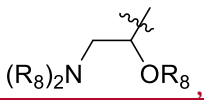
(a) $R_4$ is $(CR_6R_7)_{n4}OR_c$, $(CR_6R_7)_{n4}COR_c$, $(C=O)(CR_6R_7)_{n4}R_c$, $(CR_6R_7)_{n4}COOR_c$, $(CR_6R_7)_{n4}NR_c(C=O)R_d$, $(CR_6R_7)_{n4}(C=O)NR_cR_d$, $(CR_6R_7)_{n4}(C=O)(C=O)NR_cR_d$, $(C=O)(CR_6R_7)_{n4}OR_c$, $(CR_6R_7)_{n4}SO_2R_c$, or $(CR_6R_7)_{n4}SO_2NR_cR_d$; or

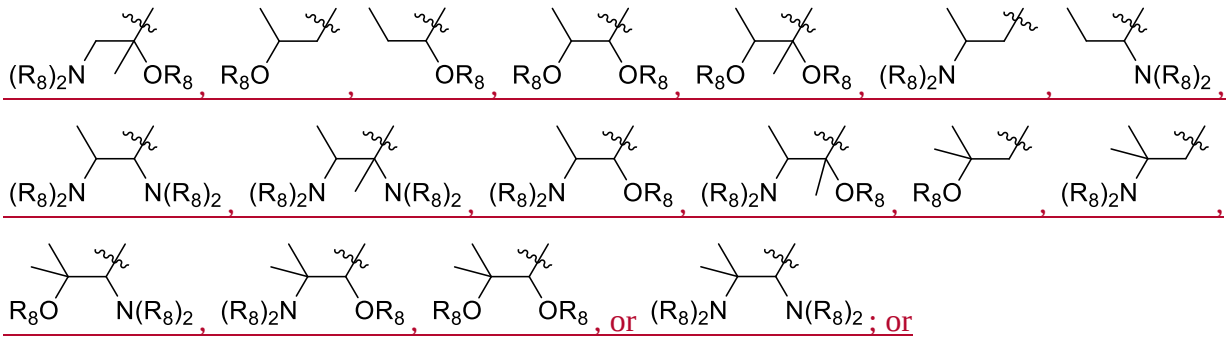
(b) $R_4$ is $(CR_6R_7)_2OR_c$, $(C=O)R_c$, $(C=O)(CR_6R_7)_{1-2}R_c$, $COOR_c$, $(CR_6R_7)_{1-2}NR_c(C=O)R_d$, $(C=O)NR_cR_d$, $(CR_6R_7)_{n4}(C=O)(C=O)NR_cR_d$, $(C=O)(CR_6R_7)_{1-2}OR_c$, $SO_2R_c$, or $SO_2NR_cR_d$; or

(c) $R_4$ is $(CH_2)_2OH$, $(CH_2)_2OMe$, $(C=O)H$, $(C=O)Me$, $(C=O)CH_2OH$, $(C=O)CH_2OMe$, $(C=O)Et$, $(C=O)Ph$, $(C=O)$isopropyl, $(C=O)NH_2$, $(C=O)NHMe$, $(C=O)NMe_2$, $(C=O)CH_2NH_2$, $(C=O)CH_2NHMe$, $(C=O)CH(OH)CH_2OH$, $(C=O)CH(OMe)CH_2OH$, $(C=O)CH(OH)CH_2OMe$, $(C=O)(C=O)NMe_2$, $(C=O)OMe$, $SO_2Me$, $SO_2Et$, $SO_2CH_2OH$, $SO_2CH_2OMe$, $SO_2NH_2$, $SO_2NHMe$, or $SO_2NMe_2$; or

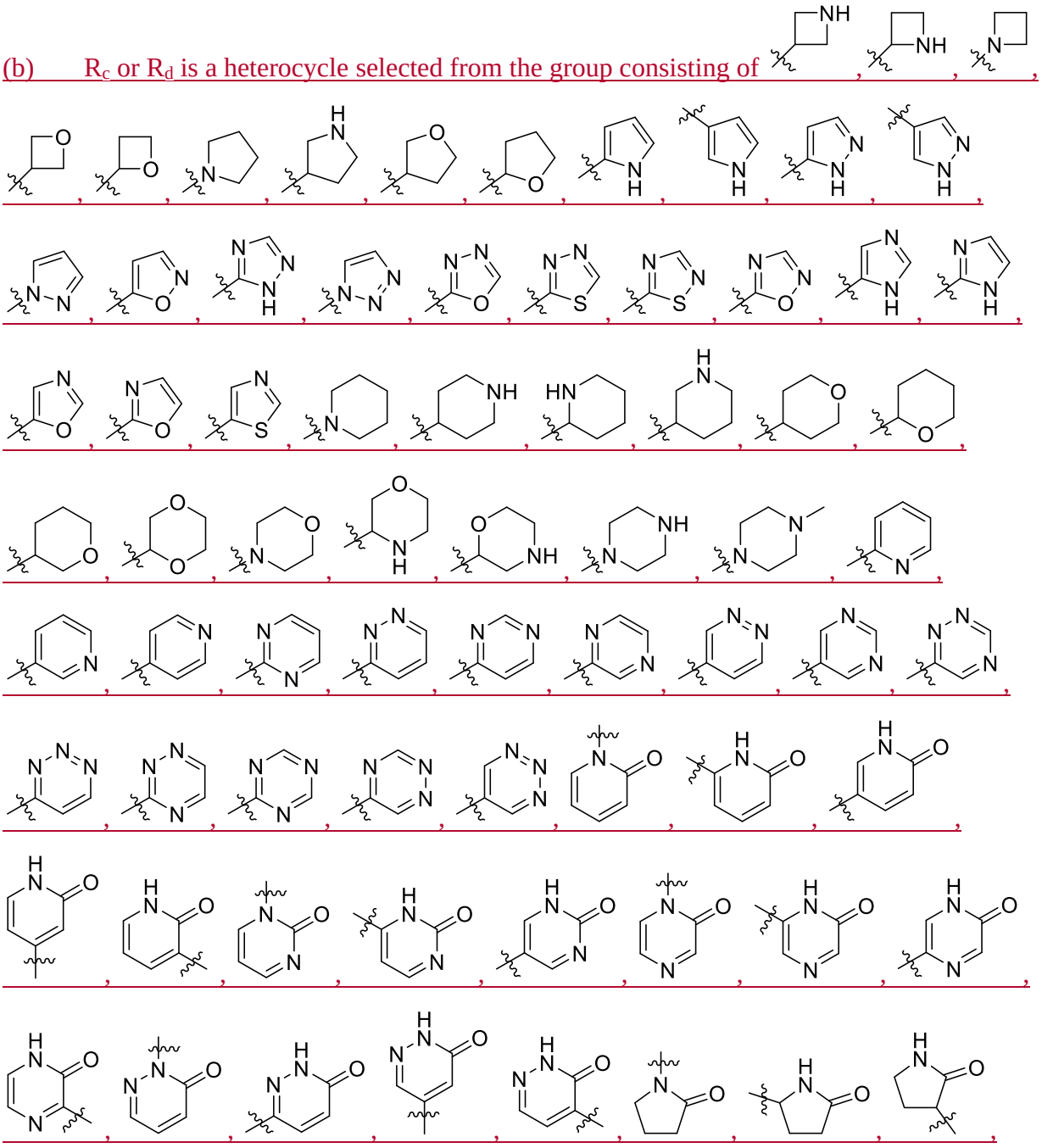
(d) $R_4$ is $(C=O)R_c$, $(C=O)(CR_6R_7)_{1-2}R_c$, $(C=O)(CR_6R_7)_{1-2}OR_c$, or $SO_2R_c$; and wherein $R_c$ is selected from the group consisting of H, alkyl, alkyl substituted by 1-4 substituents each independently selected from the group consisting of halogen, $OR_8$ and $N(R_8)_2$, alkenyl, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted spiroalkyl, optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted -alkyl-cycloalkyl, and optionally substituted -cycloalkyl-alkyl.

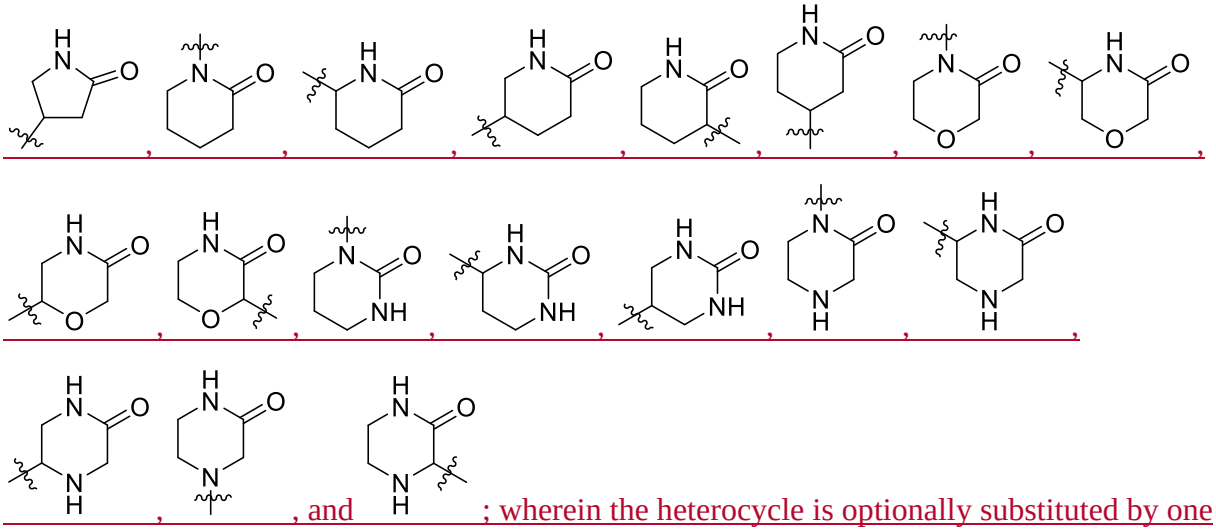
7. The compound of any one of claims 1-5, wherein $R_4$ is $(CR_6R_7)_2OR_c$, $(C=O)R_c$, $(C=O)(CR_6R_7)_{1-2}R_c$, $COOR_c$, $(CR_6R_7)_{1-2}NR_c(C=O)R_d$, $(C=O)NR_cR_d$, $(CR_6R_7)_{n4}(C=O)(C=O)NR_cR_d$, $(C=O)(CR_6R_7)_{1-2}OR_c$, $SO_2R_c$, or $SO_2NR_cR_d$, and:

(a) $R_c$ or $R_d$ is H, Me, Et, , , , , , , , , , 



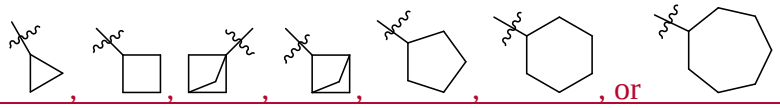
(b) $R_c$ or $R_d$ is a heterocycle selected from the group consisting of





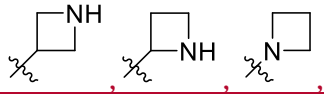
; wherein the heterocycle is optionally substituted by one or more cyano, cycloalkyl, fluorinated alkyl, fluorinated cycloalkyl, halogen, OH, $NH_2$, oxo, or $(C=O)C_{1-4}$alkyl where valence permits; or

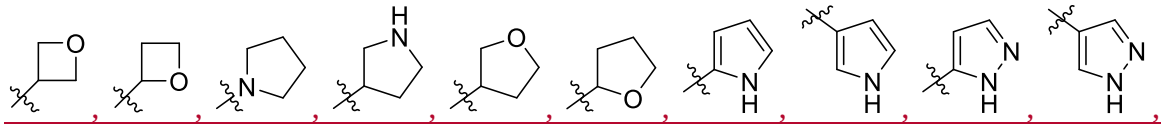
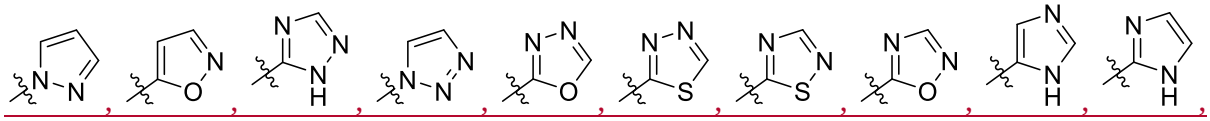
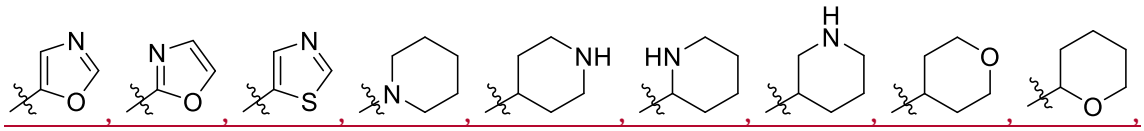
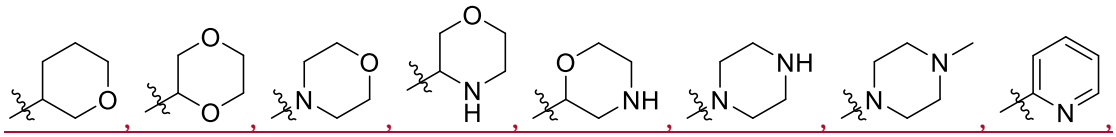
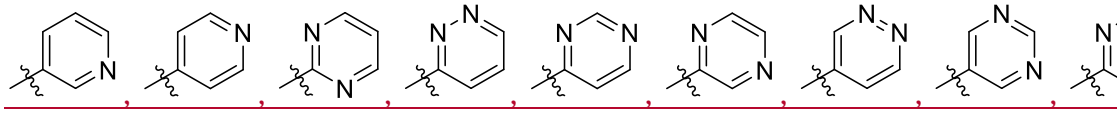
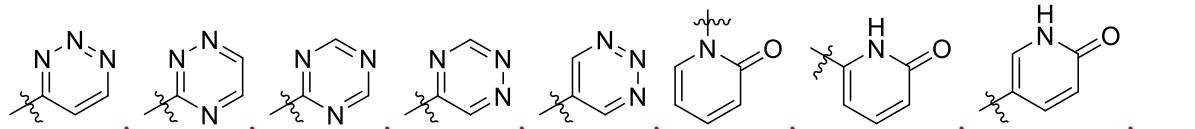
(c) $R_c$ is cycloalkyl, spiroalkyl, or bicycloalkyl each optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits; or

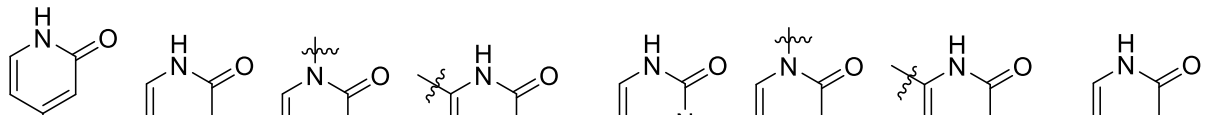
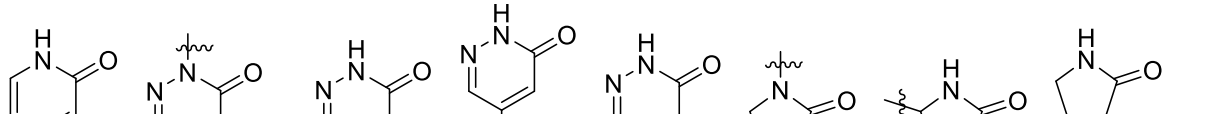
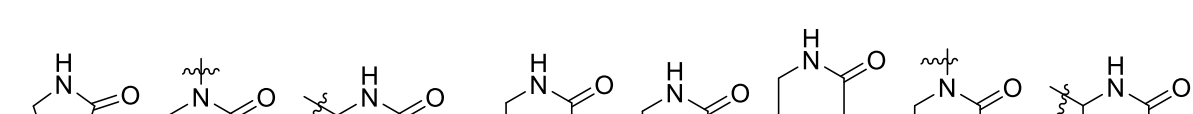
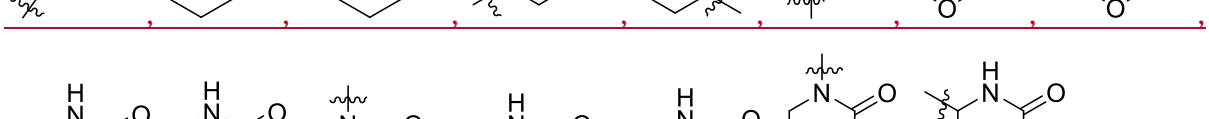
(d) $R_c$ is  each optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits.

8. The compound of any one of claims 1-5, wherein:

(a) $R_4$ is optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted cycloalkyl, optionally substituted -alkyl-cycloalkyl, or optionally substituted -cycloalkyl-alkyl; or

(b) $R_4$ is a heterocycle selected from the group consisting of 

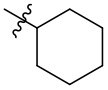
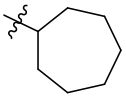







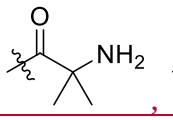
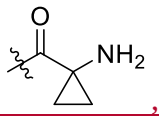
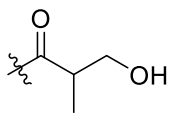
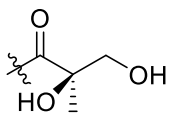
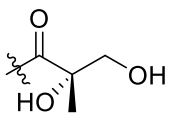
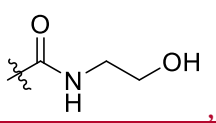
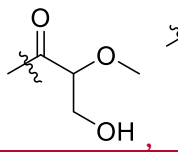
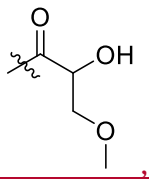
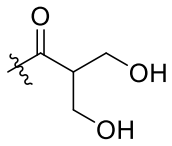
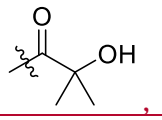
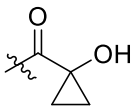
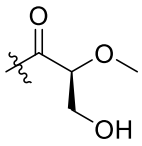
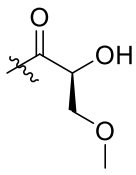
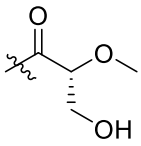
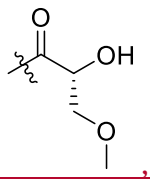
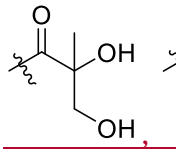
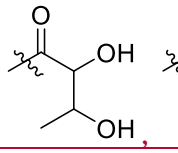
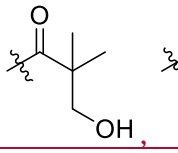
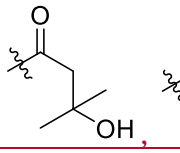
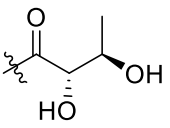
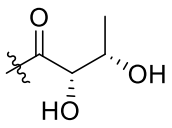
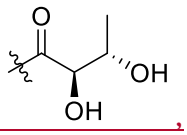
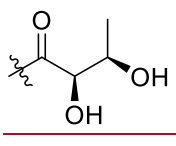
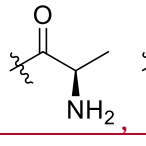
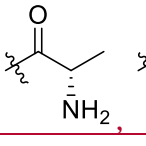
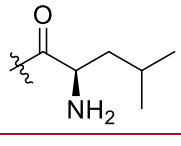
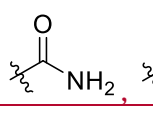
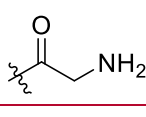
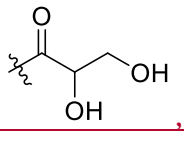
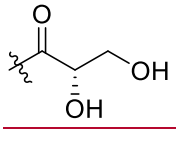
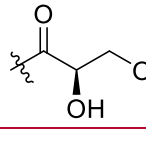
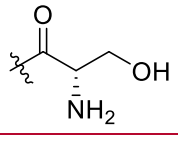
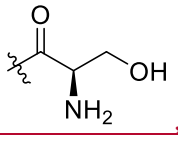





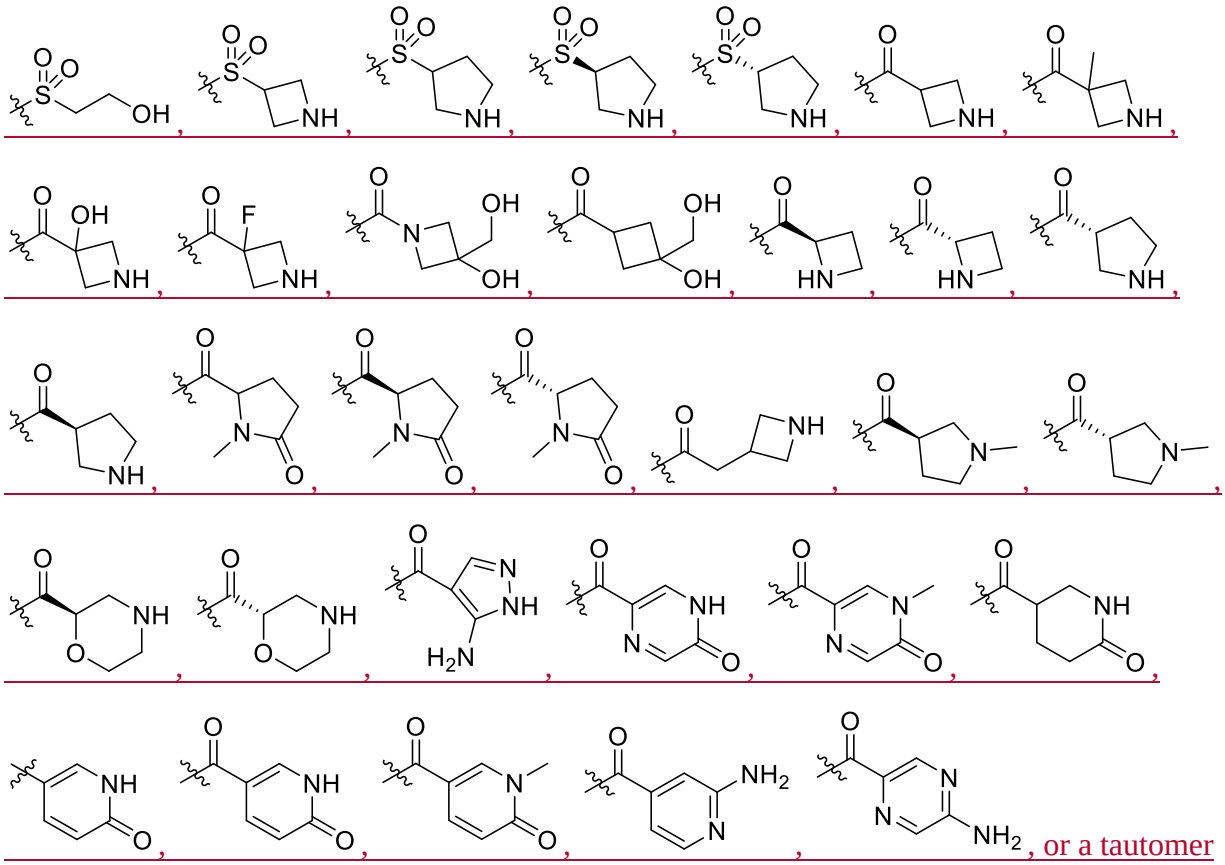
, and ; wherein the heterocycle is optionally substituted by one

or more cyano, cycloalkyl, fluorinated alkyl, fluorinated cycloalkyl, halogen, OH, $NH_2$, oxo, or $(C=O)C_{1-4}$alkyl where valence permits; or

(c) $R_4$ is cycloalkyl optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits; or

(d) $R_4$ is , , , , , , or  each optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, halogen, CN, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, and oxo where valence permits.

9. The compound of any one of claims 1-5, wherein $R_4$ is , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , .



, or a tautomer thereof.

10. The compound of any one of claims 1-9, wherein:

(a) at least one occurrence of $R_5$ is H, alkyl or cycloalkyl; or

(b) at least one occurrence of $R_5$ is oxo; or

(c) two $R_5$ groups are connected to different carbon atoms on the ring and taken together form a bond or an alkyl chain containing 1-3 carbons; or

(d) two $R_5$ groups taken together with the carbon atom(s) that they are connected to form a 3-7 membered optionally substituted saturated carbocycle.

11. The compound of any one of the preceding claims, wherein:

(a) at least one of $R_a$ and $R_b$ is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, or heteroaryl; or

(b) $R_a$ and $R_b$ together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each

selected from the group consisting of N, O, and S.

12. The compound of any one of the preceding claims, wherein:

(a) each occurrence of $R_6$ and $R_7$ are independently H or alkyl; and/or

(b) $R_9$ is (i) H, alkyl, or halogen, or (ii) $(CR_6R_7)_{n4}OR_b$; or (iii) H, F, or OH.

13. The compound of any one of the preceding claims, wherein:

(a) Z is OH, OMe, $NH_2$, NHMe, or $NMe_2$; or

(b) Z is OH.

14. The compound of any one of the preceding claims, wherein:

(a) $X_1$ is Me or Cl; or

(b) $X_1$ is H, halogen, fluorinated alkyl or alkyl; or

(c) $X_1$ is H, F, Cl, Br, Me, $CF_3$, or $CF_2Cl$.

15. The compound of any one of the preceding claims, wherein:

(a) $X_2$ is Cl; or

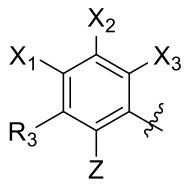
(b) $X_2$ is H, halogen, fluorinated alkyl or alkyl; or

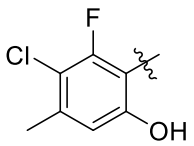
(c) $X_2$ is H, F, Cl, Br, Me, $CF_3$, or $CF_2Cl$.

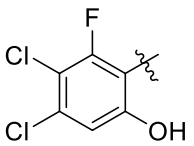
16. The compound of any one of the preceding claims, wherein:

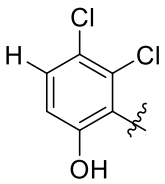
(a) $X_3$ is H, F, Cl, Br, fluorinated alkyl, or alkyl; or

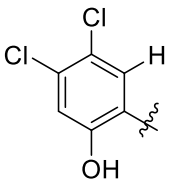
(b) $X_3$ is H, F, Cl, or $CF_3$.

17. The compound of any one of claims 1-12, wherein the structural moiety 

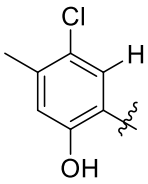
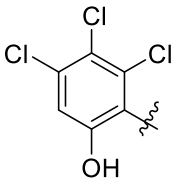
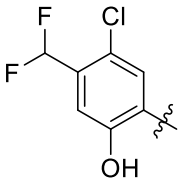
has the structure of 

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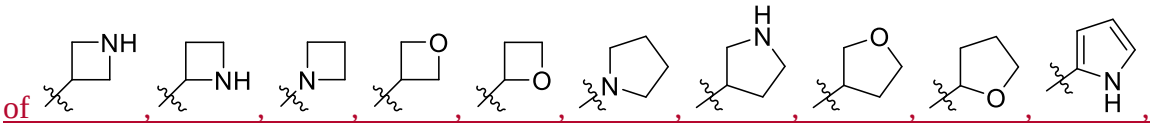
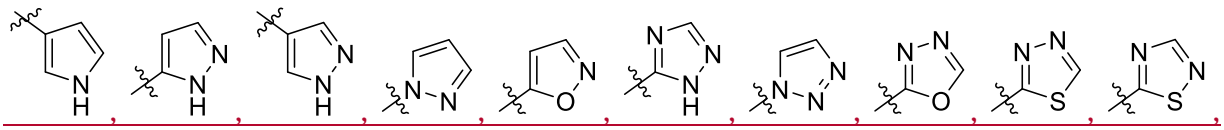
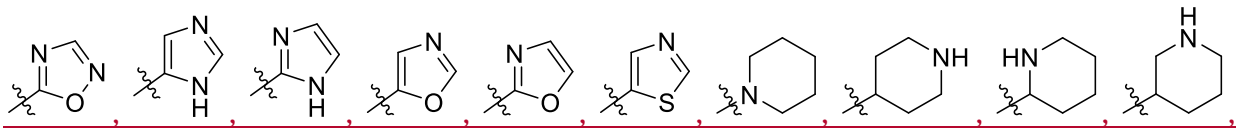
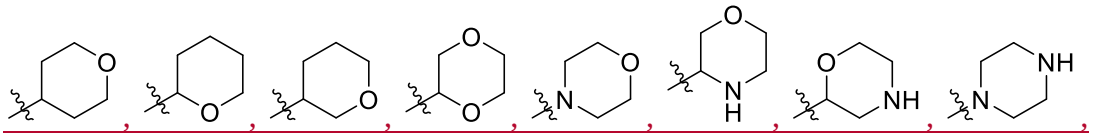
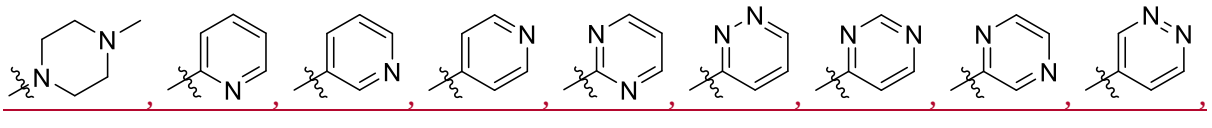
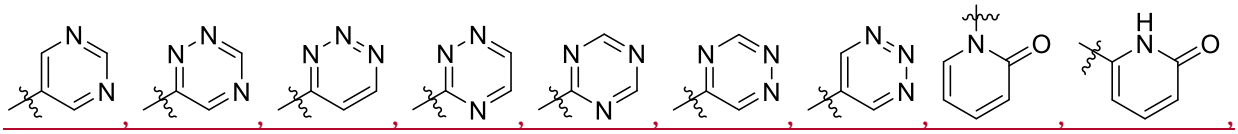
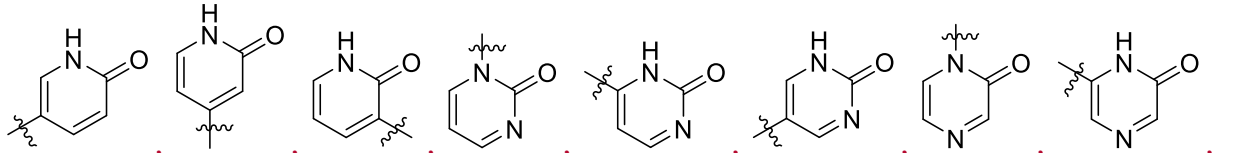
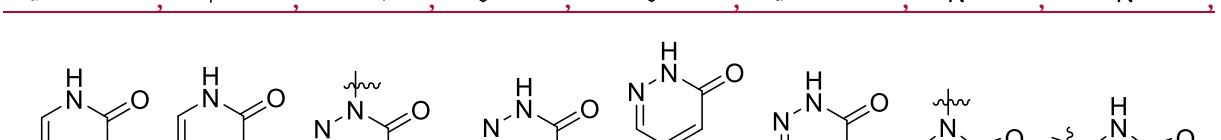
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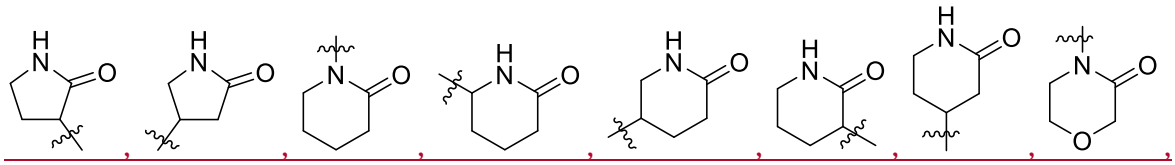
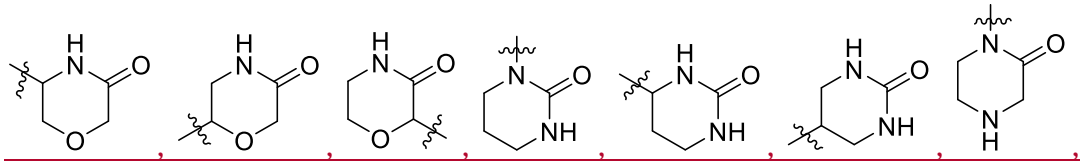
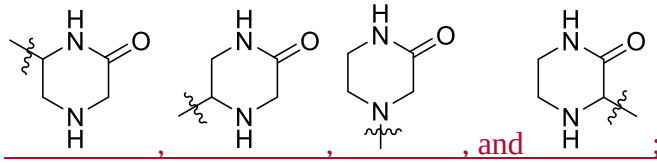
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, , or , each of which is substituted by $R_3$, optionally wherein $R_3$ is (a) H or alkyl or (b) halogen.

18. The compound of any one of the preceding claims, wherein:

(a) at least one occurrence of $R_8$ is H, alkyl, or optionally substituted heterocycle, optionally wherein $R_8$ is H, Me, Et, Pr, Bu, or a heterocycle selected from the group consisting of

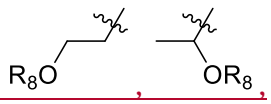
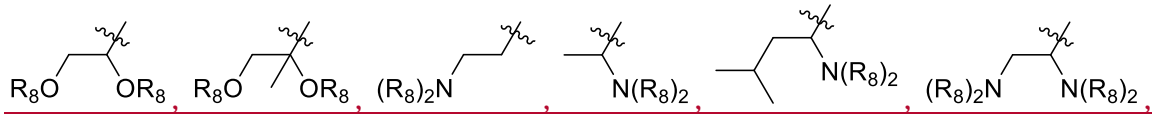









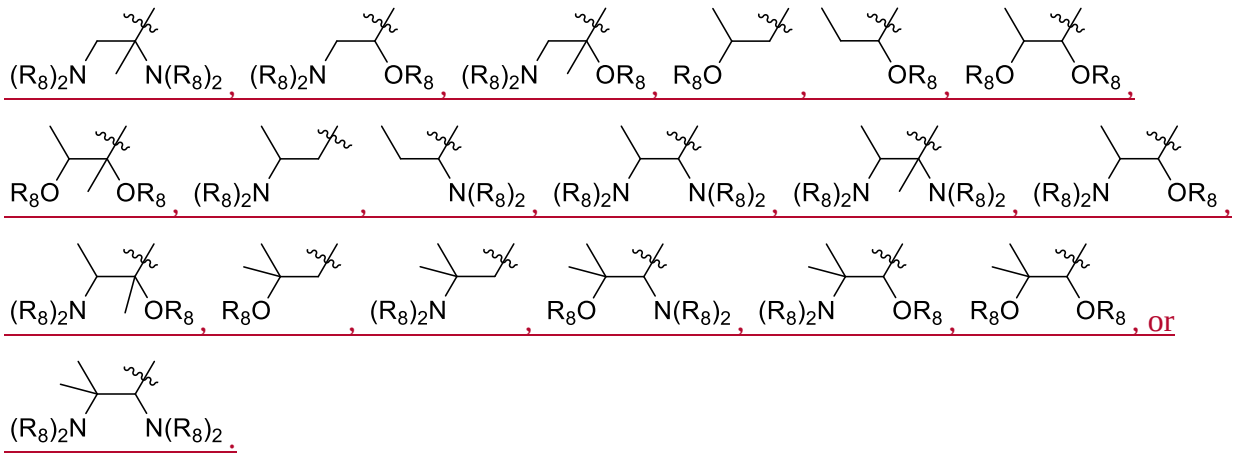




, and ; wherein the heterocycle is optionally substituted by one or more cyano, cycloalkyl, fluorinated alkyl, fluorinated cycloalkyl, halogen, OH, $NH_2$, oxo, or $(C=O)C_{1\text{-}4}$alkyl where valence permits; or

(b) the two $R_8$ groups together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S.

19. The compound of any one of claim 1-5, wherein:

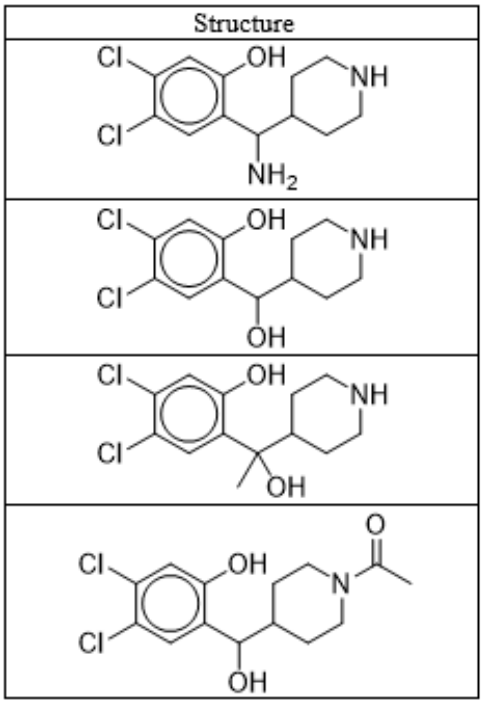
(a) at least one occurrence of $R_c$ or $R_d$ is independently H, alkyl, alkyl substituted by 1-4 substituents each independently selected from the group consisting of halogen, $OR_8$ and $N(R_8)_2$, alkenyl, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted spiroalkyl, optionally substituted saturated heterocycle, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted -alkyl-aryl, optionally substituted -alkyl-heteroaryl, optionally substituted -alkyl-heterocycle, optionally substituted -alkyl-cycloalkyl, or optionally substituted -cycloalkyl-alkyl; or

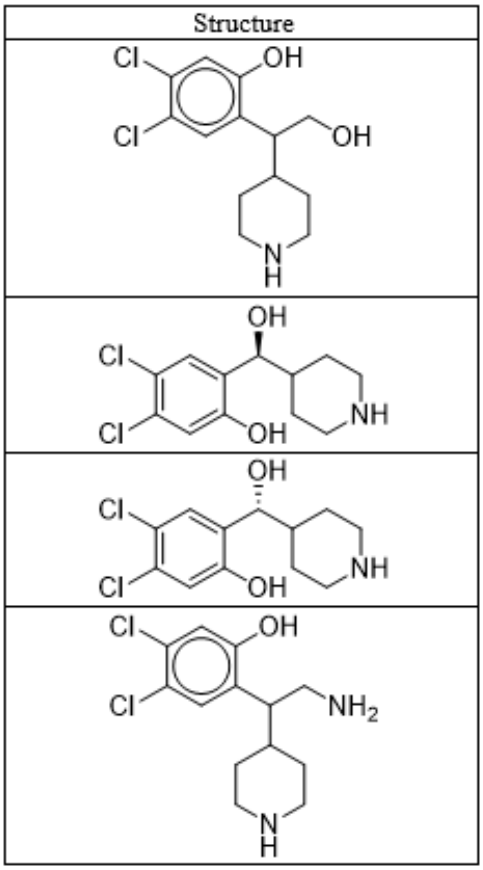
(b) at least one occurrence of $R_c$ or $R_d$ is independently H, Me, Et, 


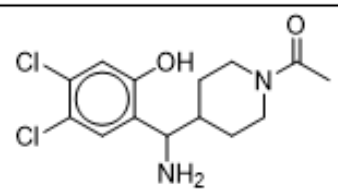
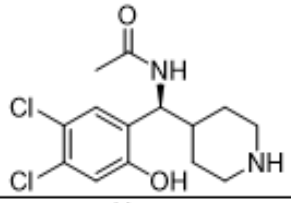
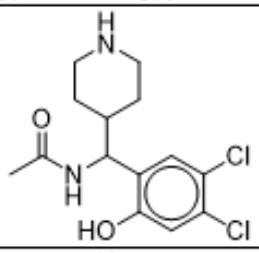
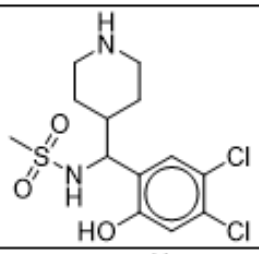
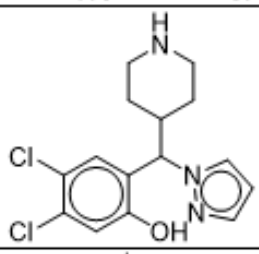
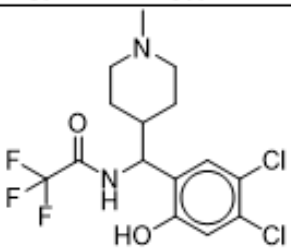
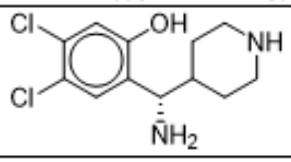
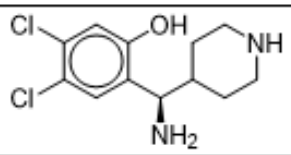


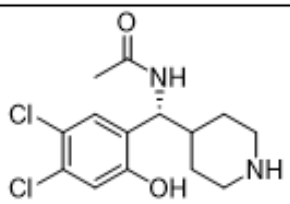
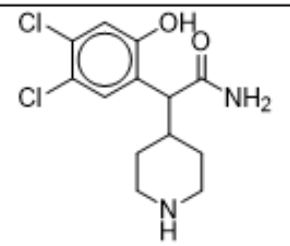
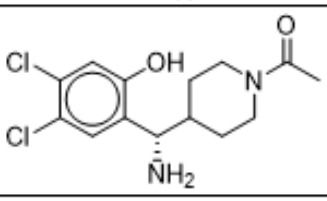
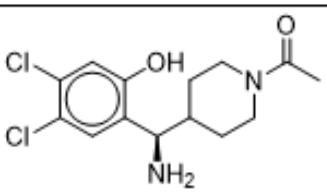
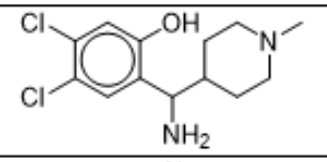
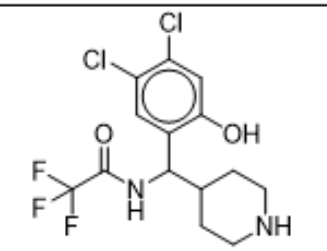
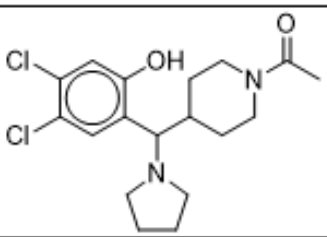
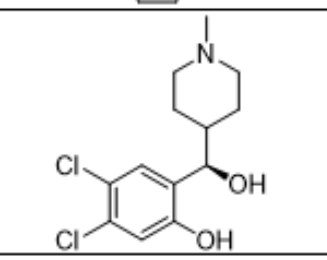
20. The compound of claim 1, wherein the compound is selected from a group consisting of compounds 1-338 in Table 1.

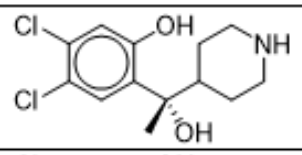
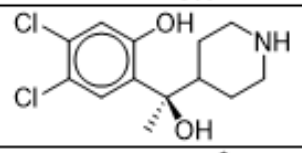
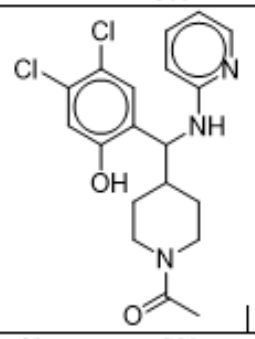
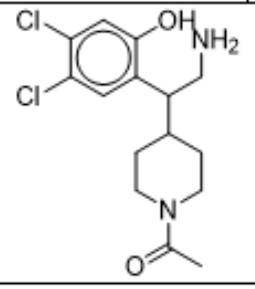
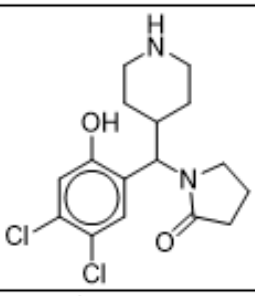
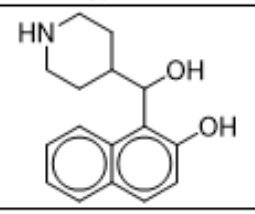
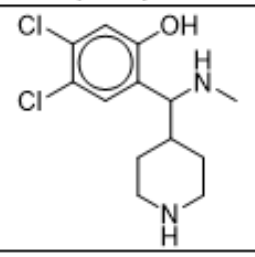
21. The compound of claim 1, wherein the compound is selected from the group consisting of the following compounds and pharmaceutically acceptable salts thereof

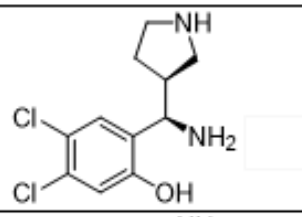
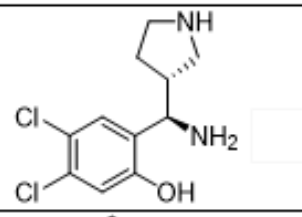
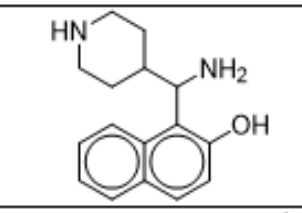
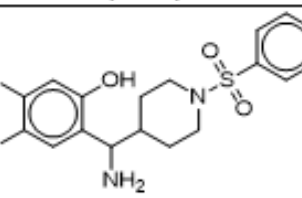
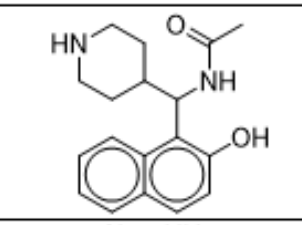
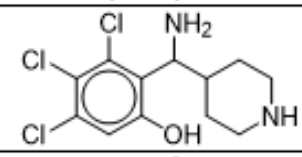
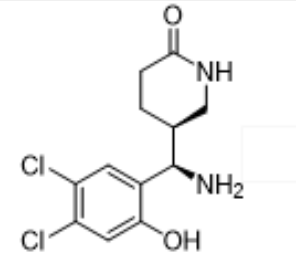
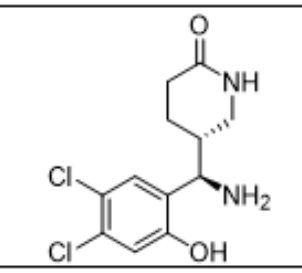


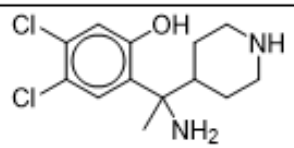
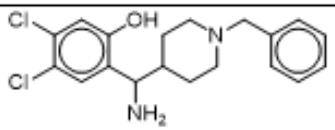
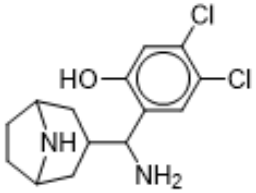
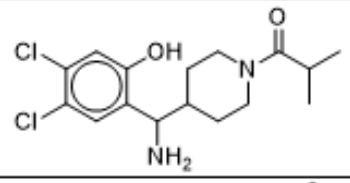
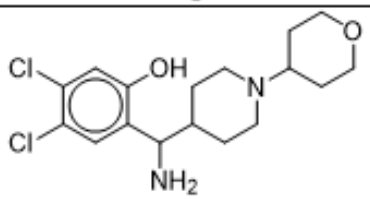
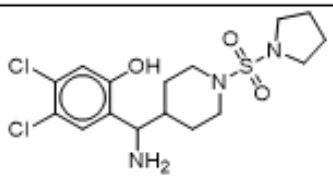
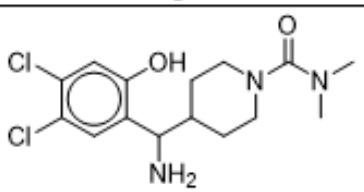
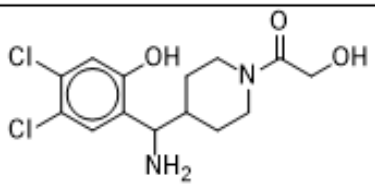
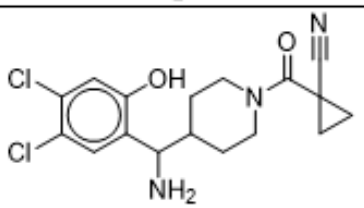
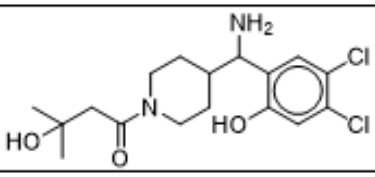



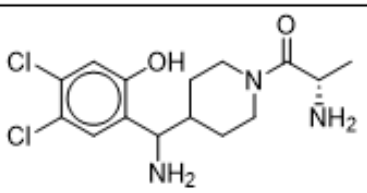
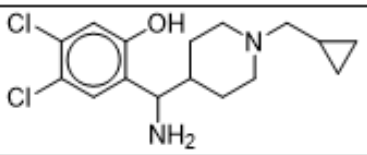
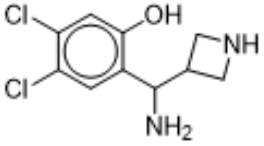
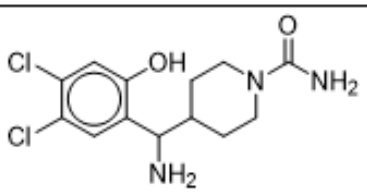
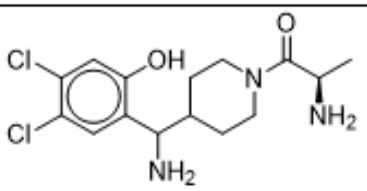
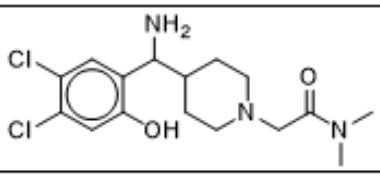
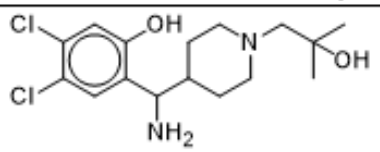
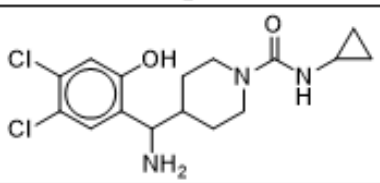
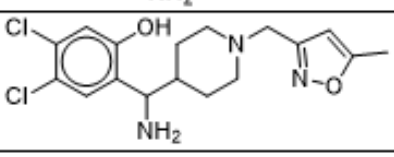
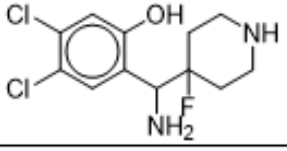
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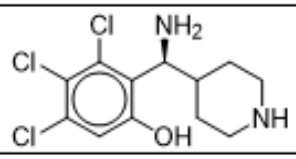
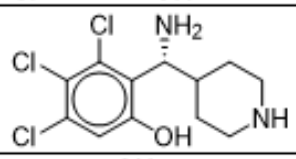
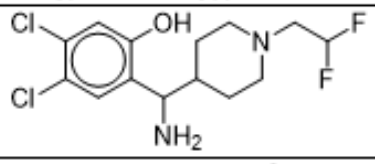
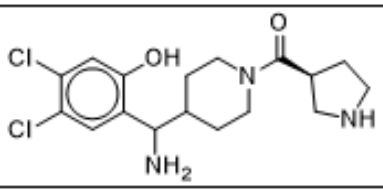
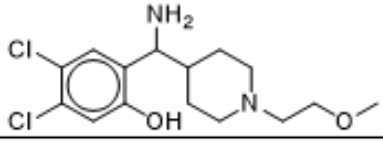
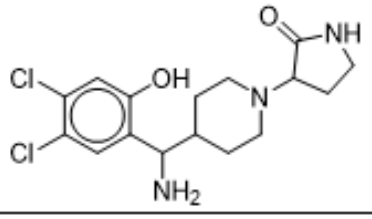
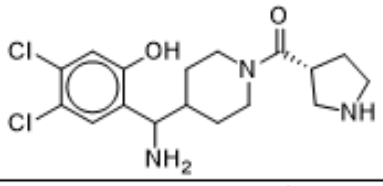
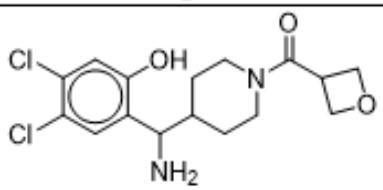
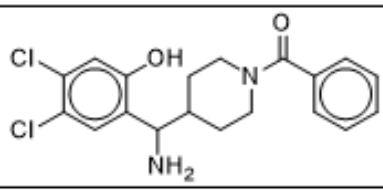
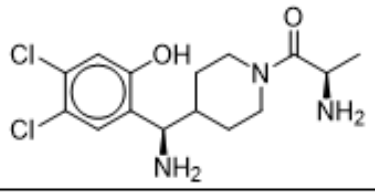
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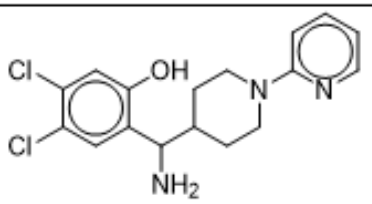
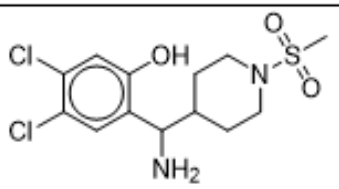
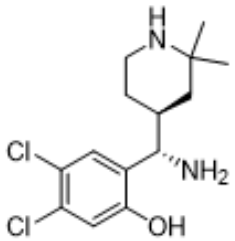
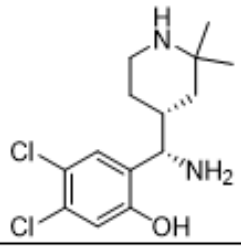
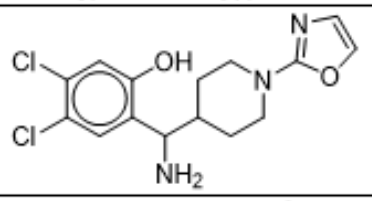
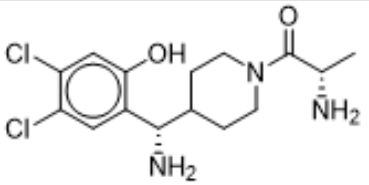
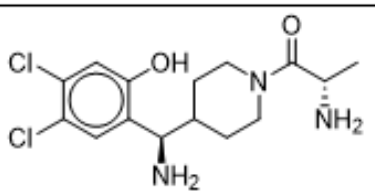
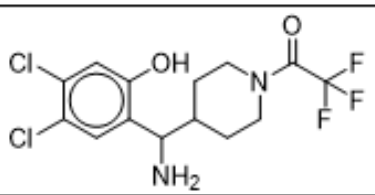
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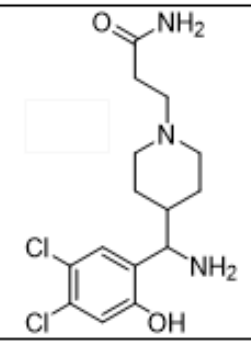
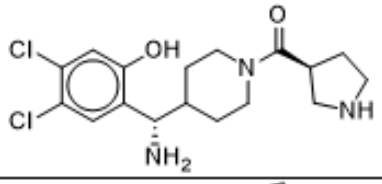
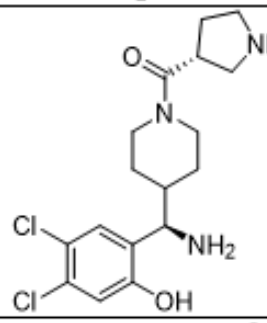
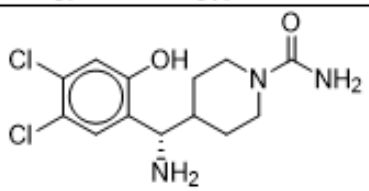
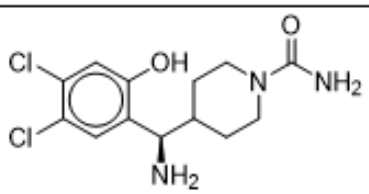
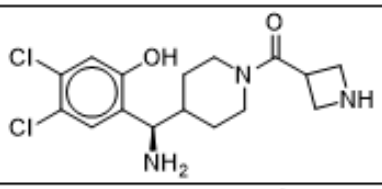
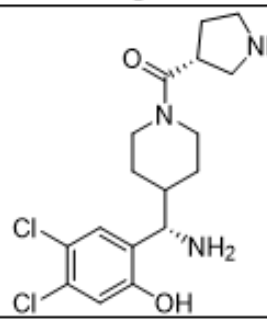
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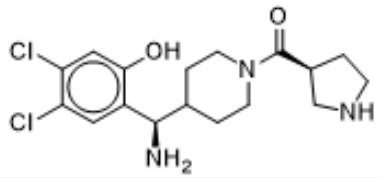
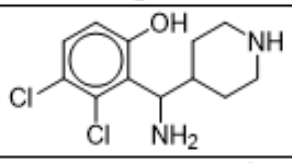
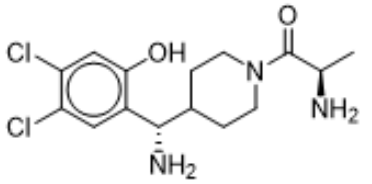
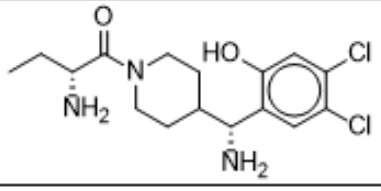
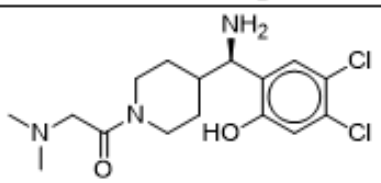
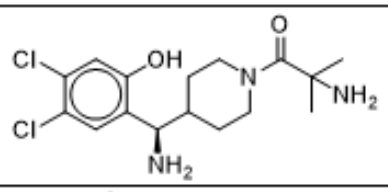
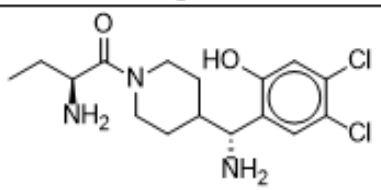
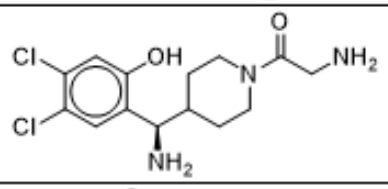
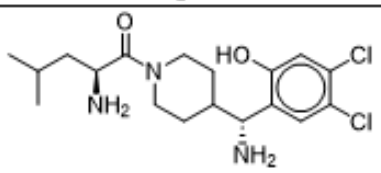
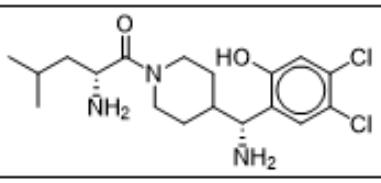
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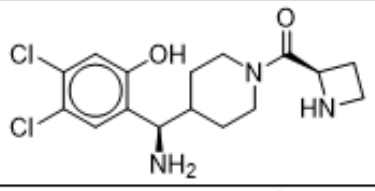
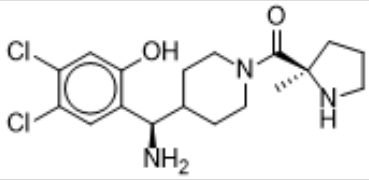
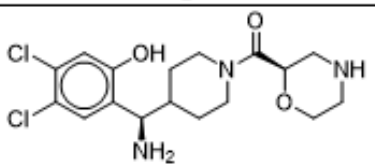
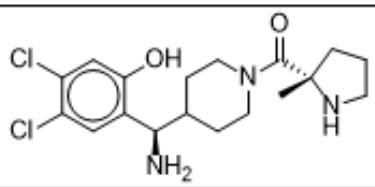
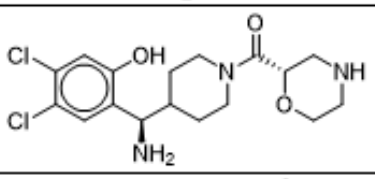
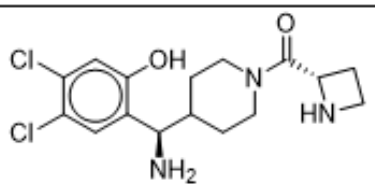
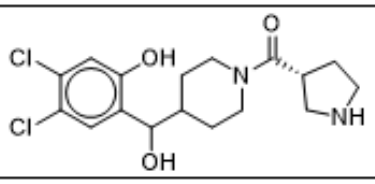
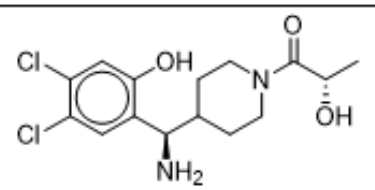
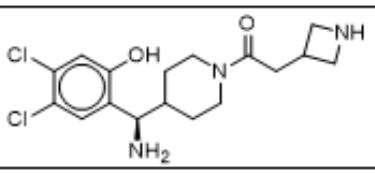
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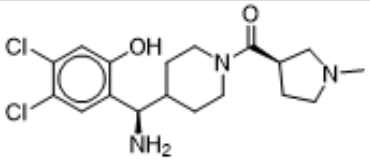
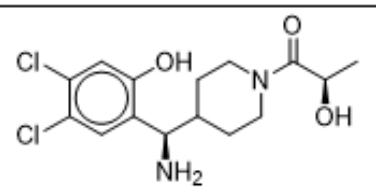
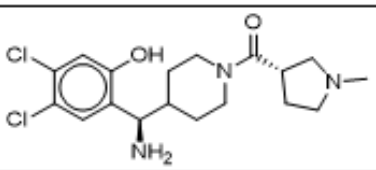
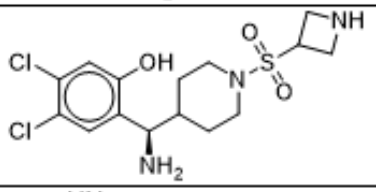
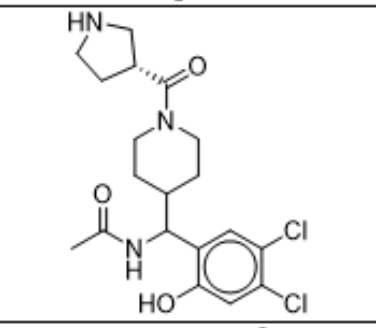
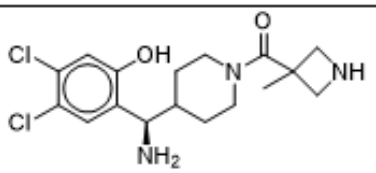
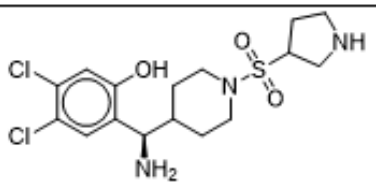
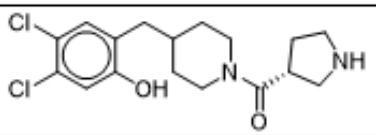
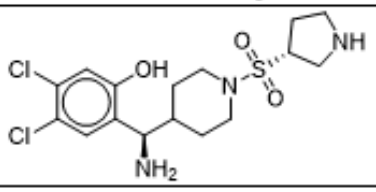
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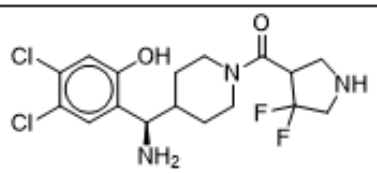
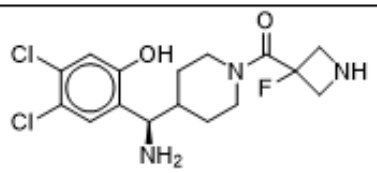
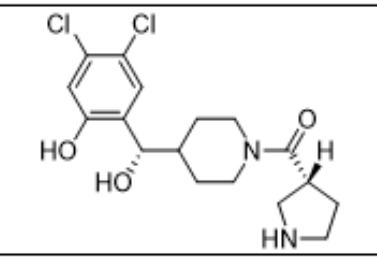
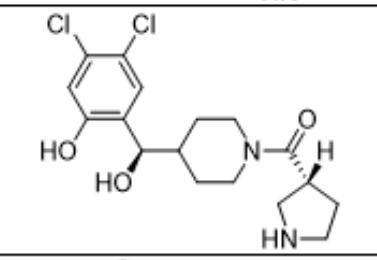
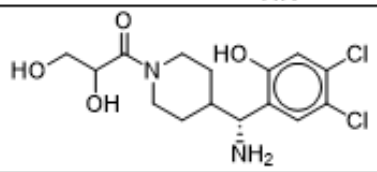
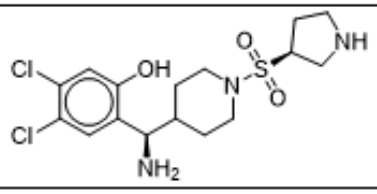
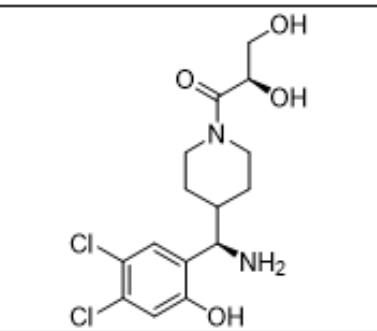
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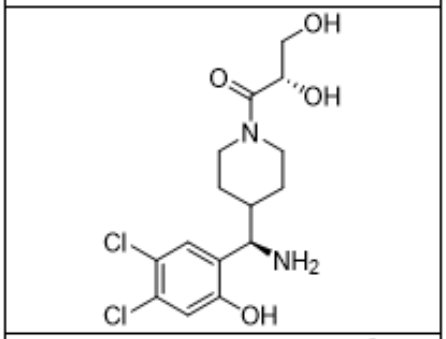
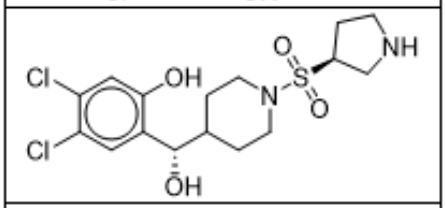
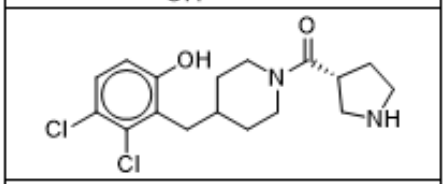
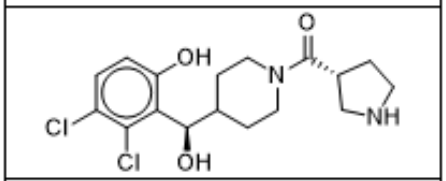
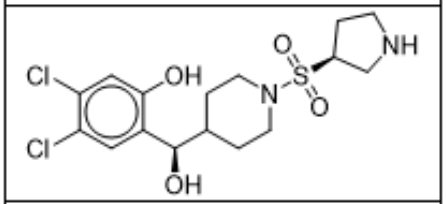
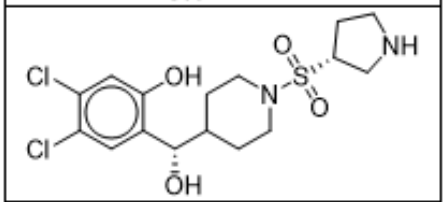
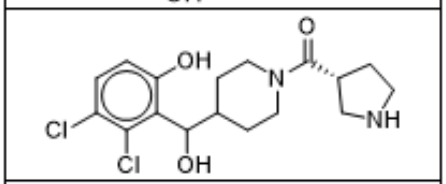
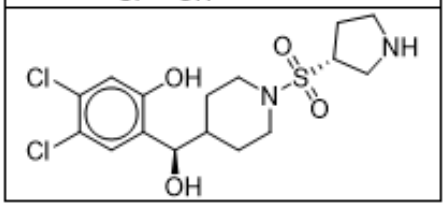
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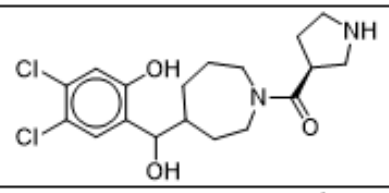
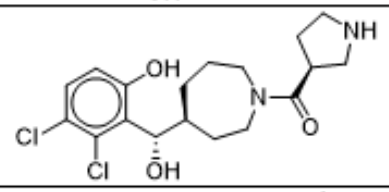
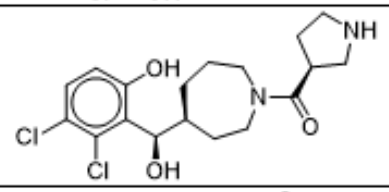
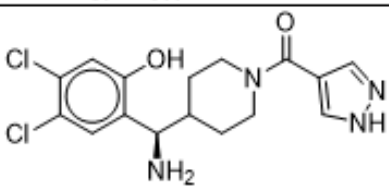
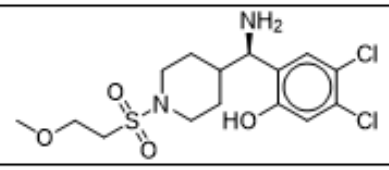
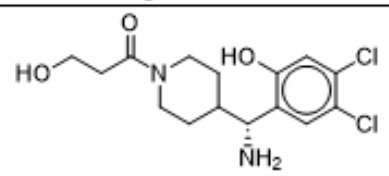
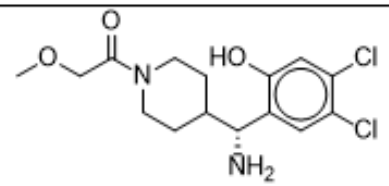
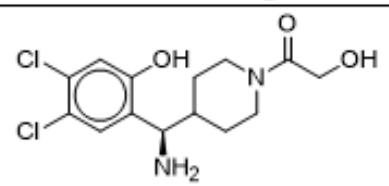
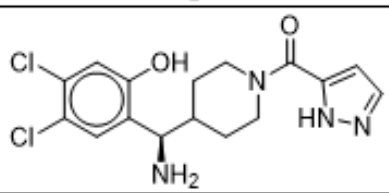
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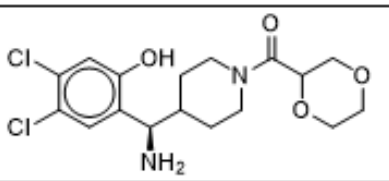
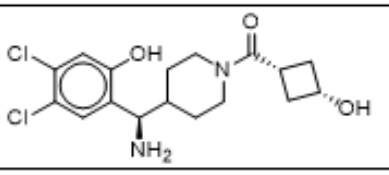
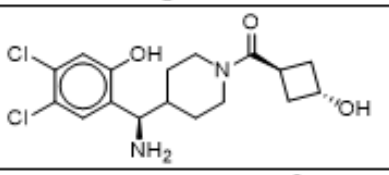
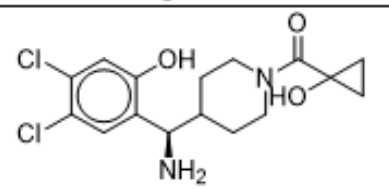
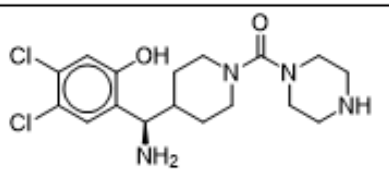
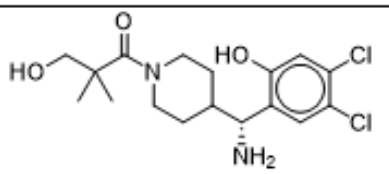
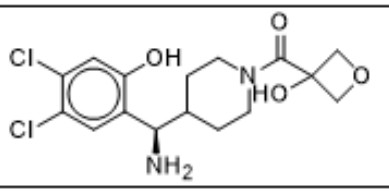
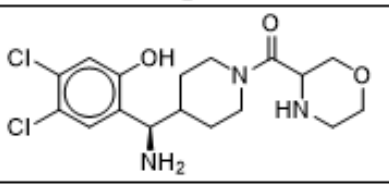
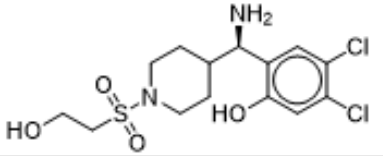
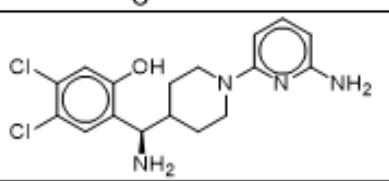
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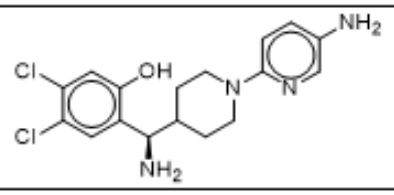
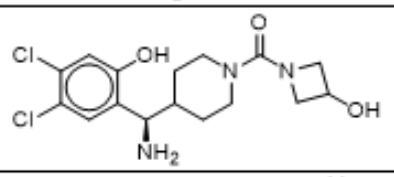
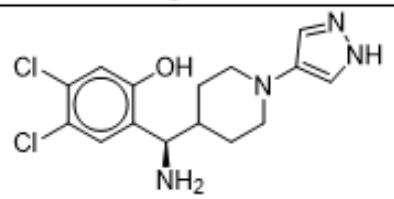
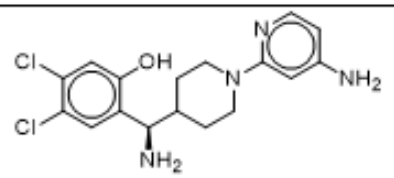
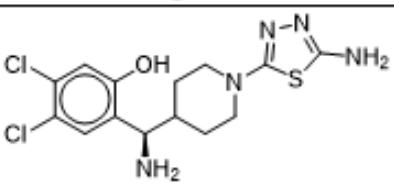
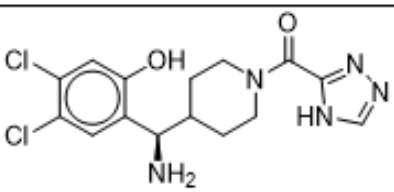
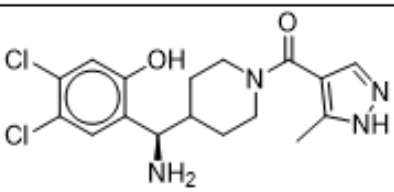
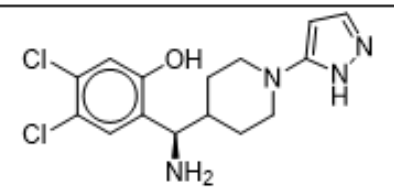
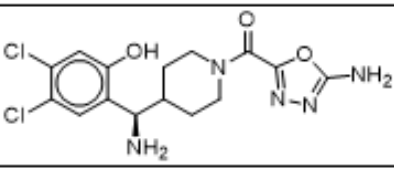
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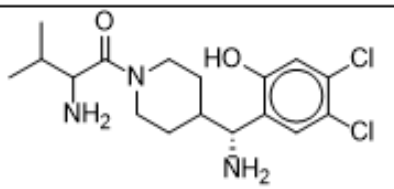
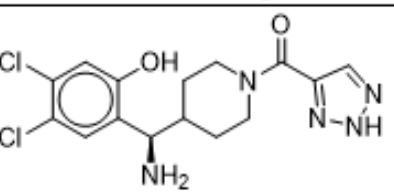
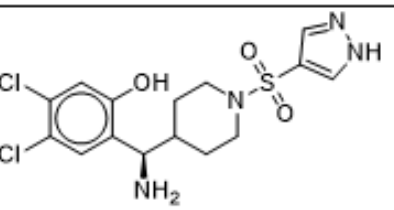
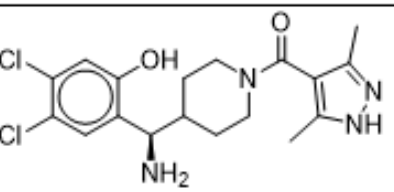
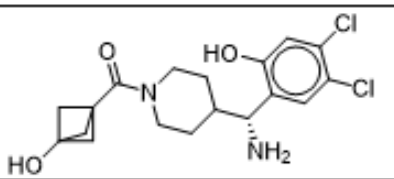
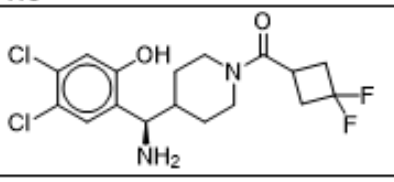
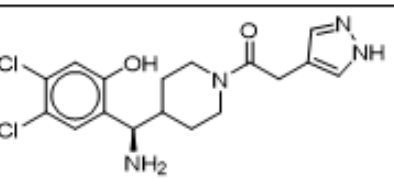
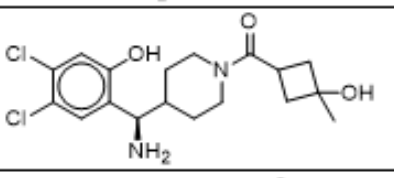
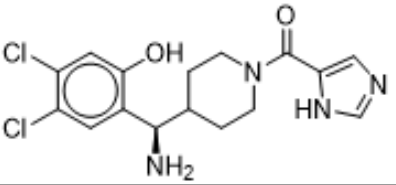
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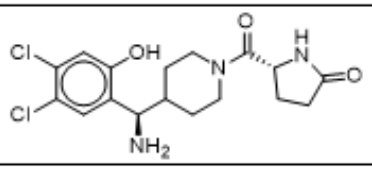
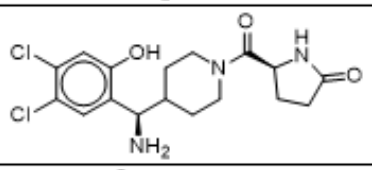
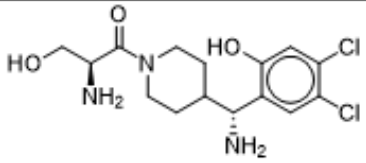
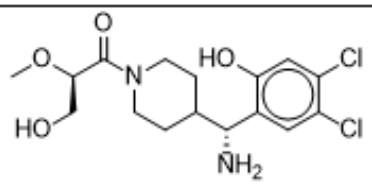
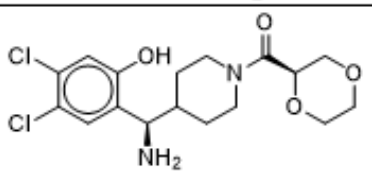
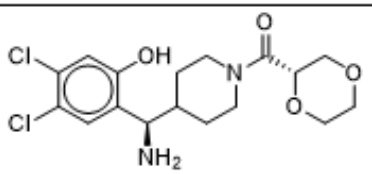
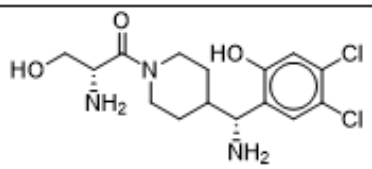
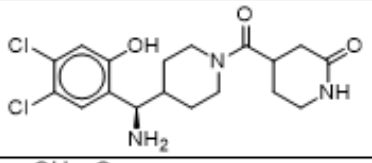
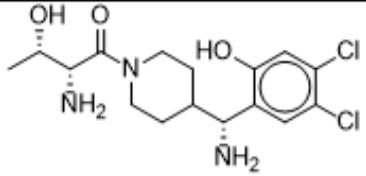
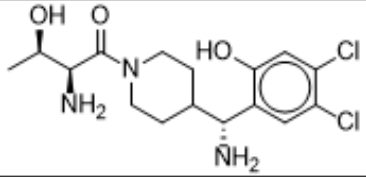
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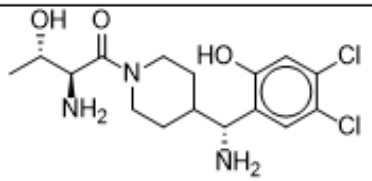
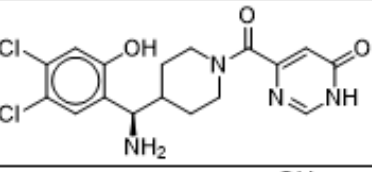
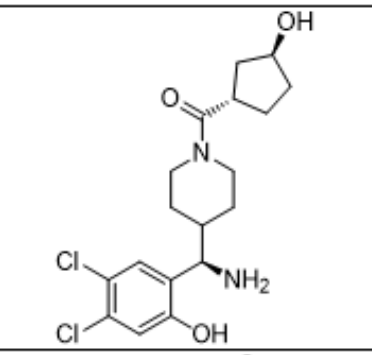
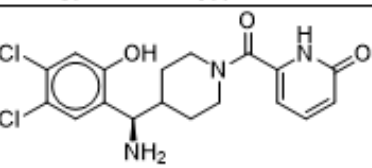
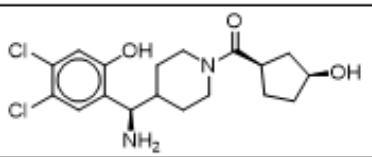
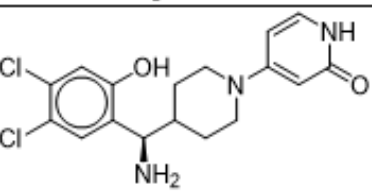
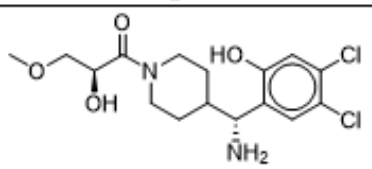
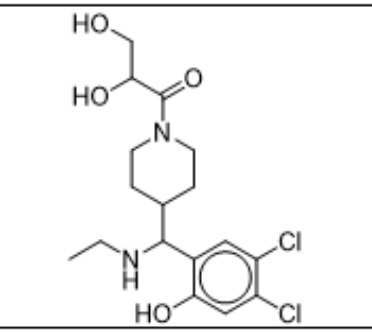
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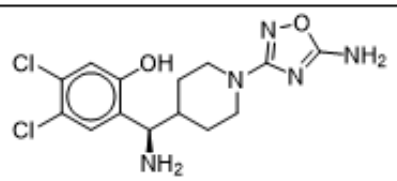
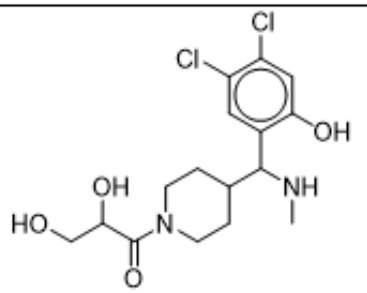
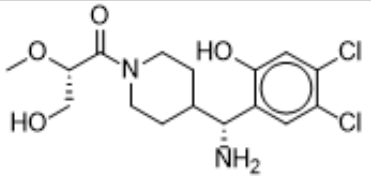
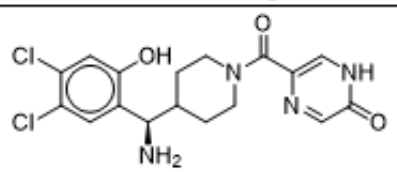
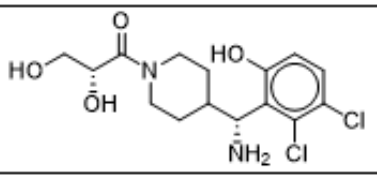
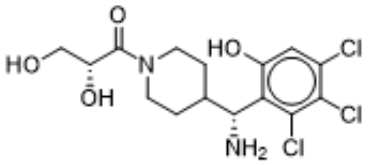
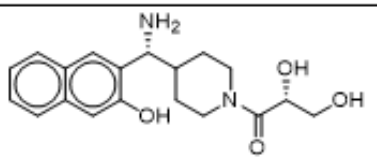
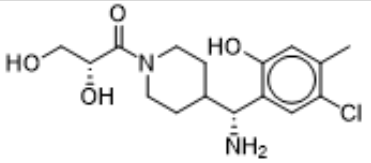
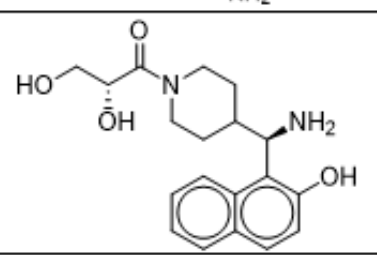
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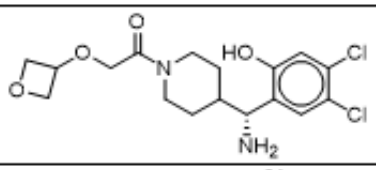
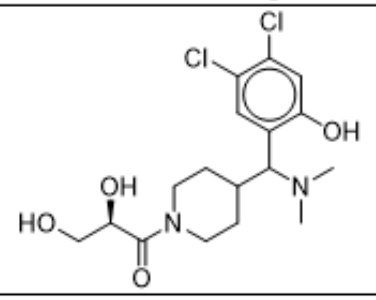
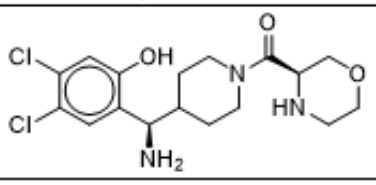
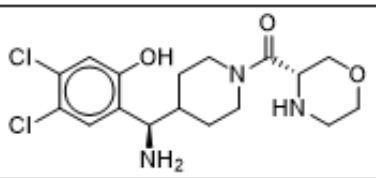
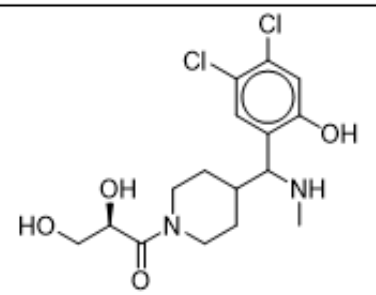
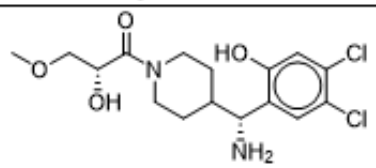
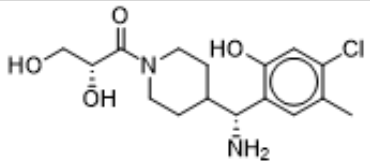
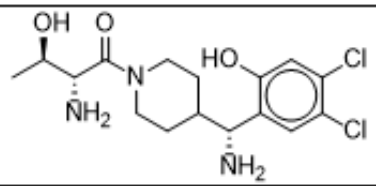
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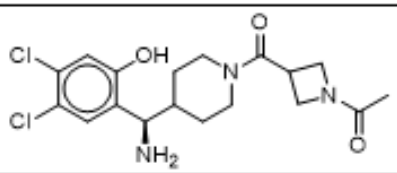
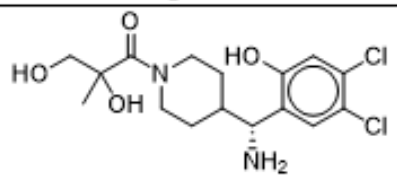
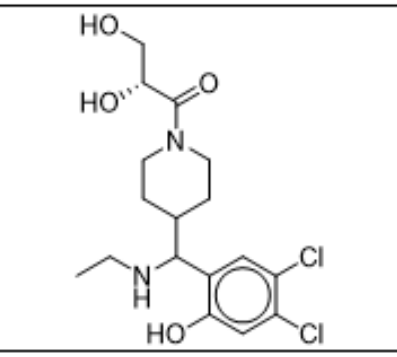
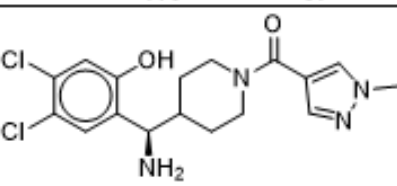
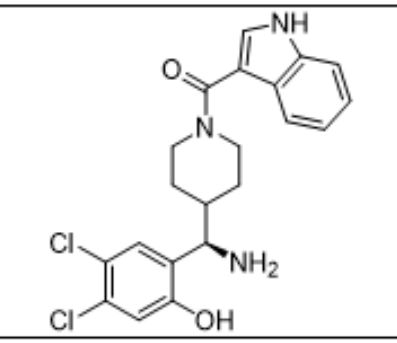
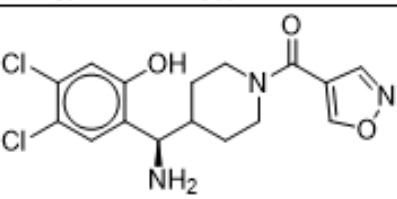
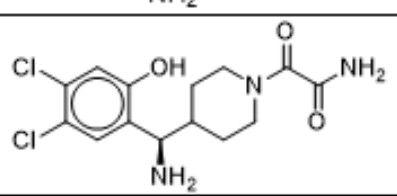
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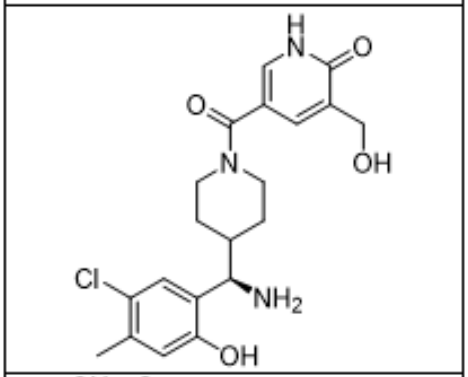
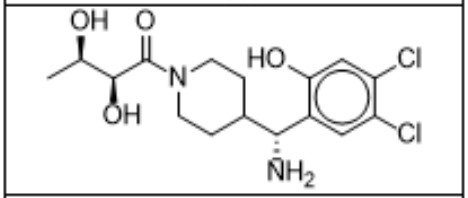
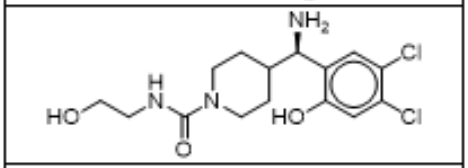
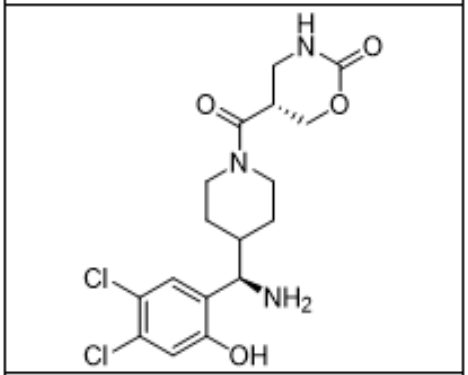
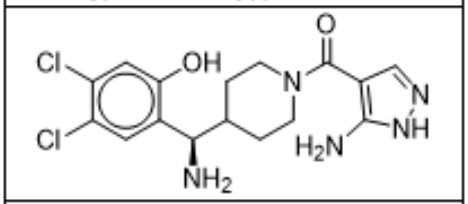
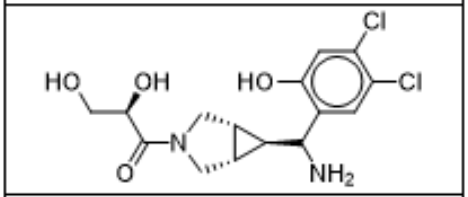
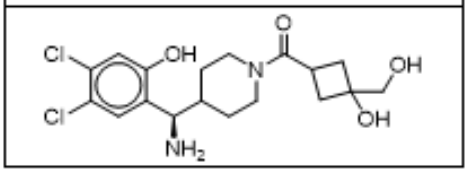
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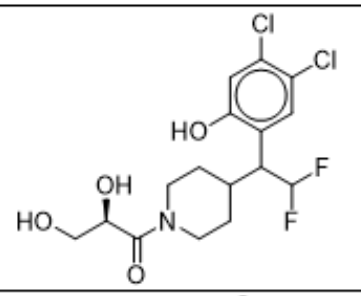
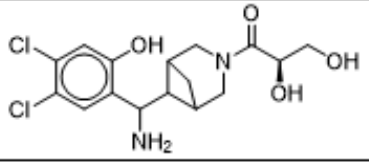
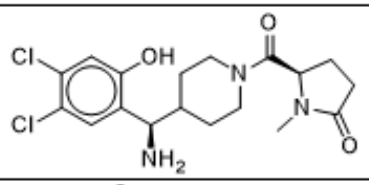
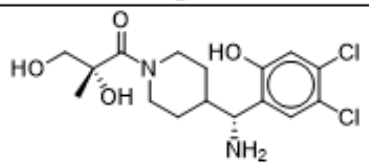
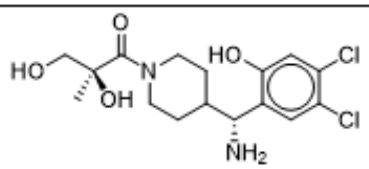
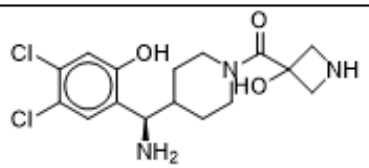
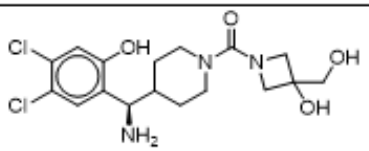
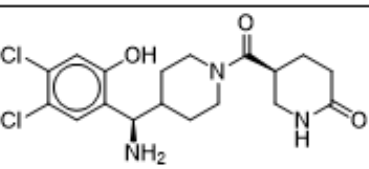
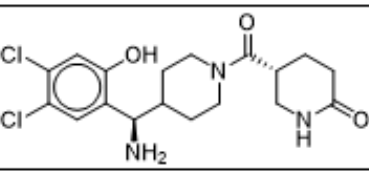
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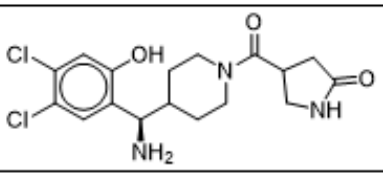
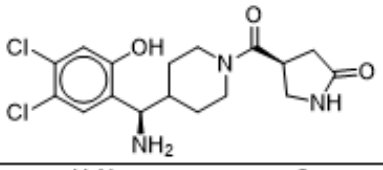
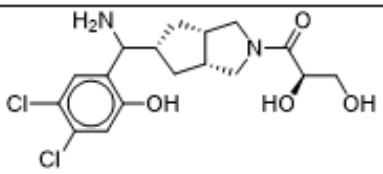
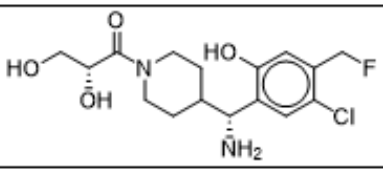
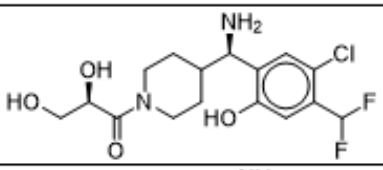
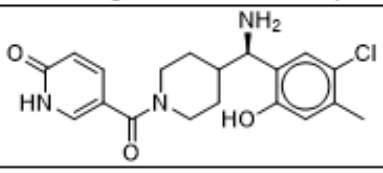
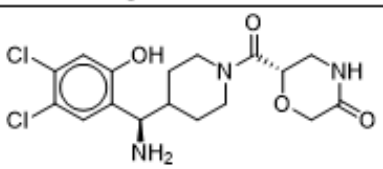
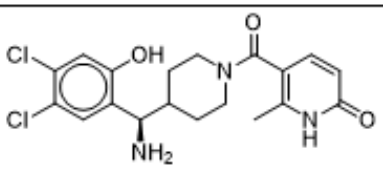
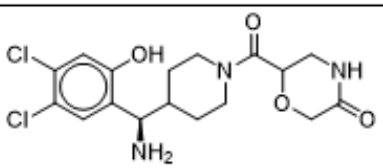
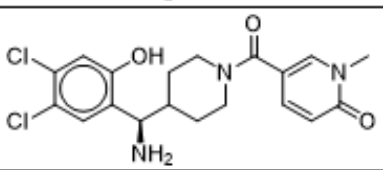
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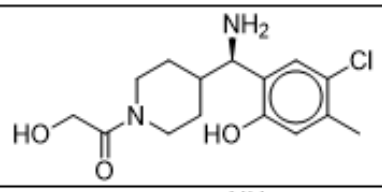
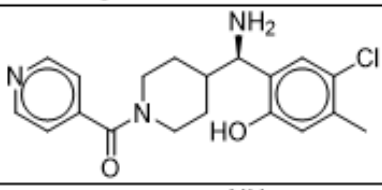
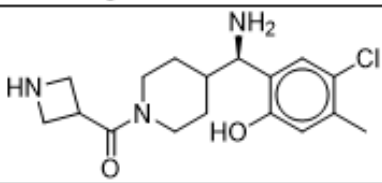
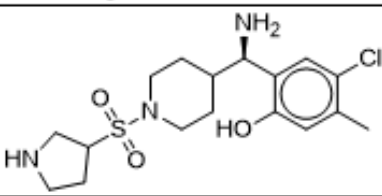
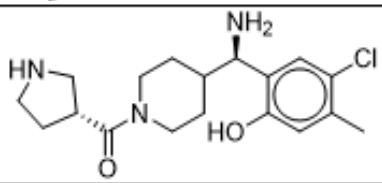
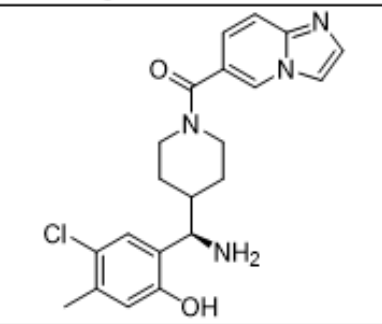
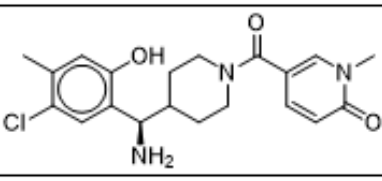
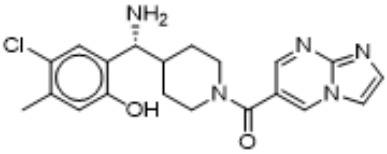
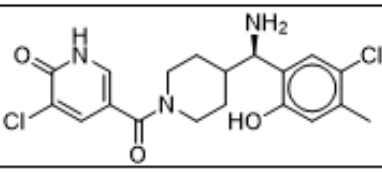
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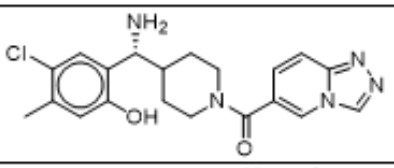
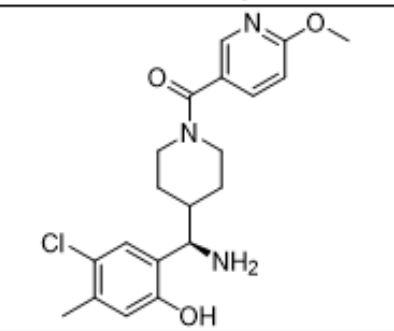
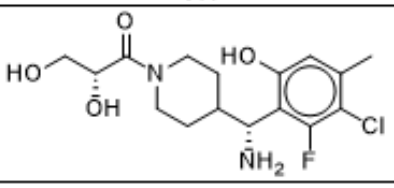
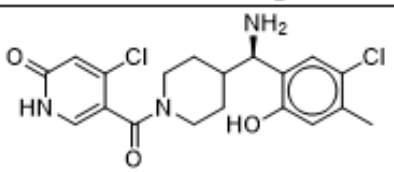
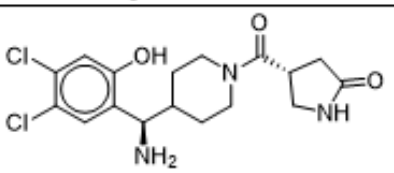
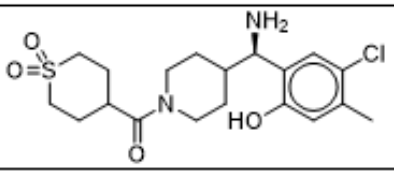
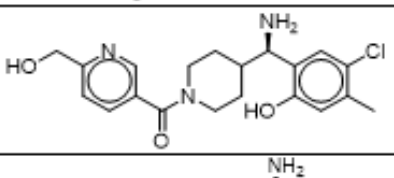
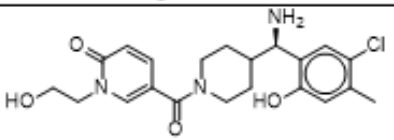
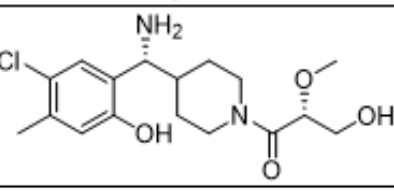
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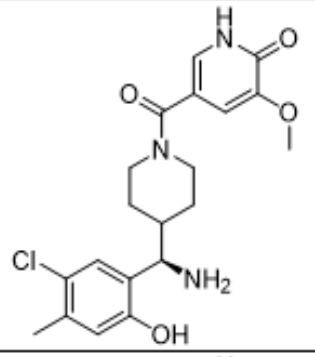
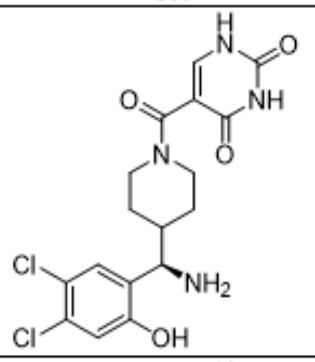
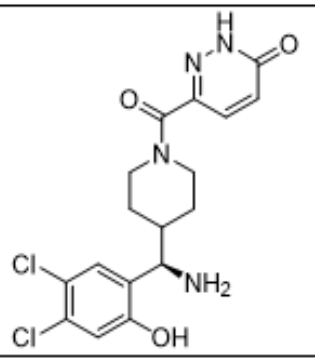
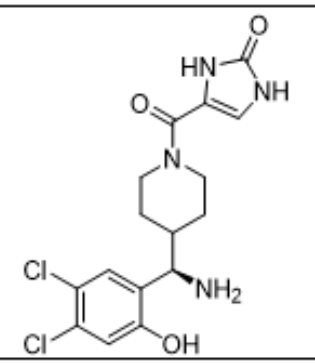
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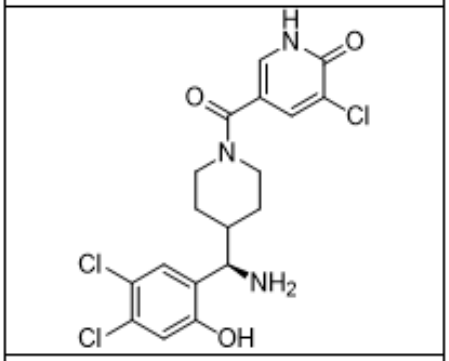
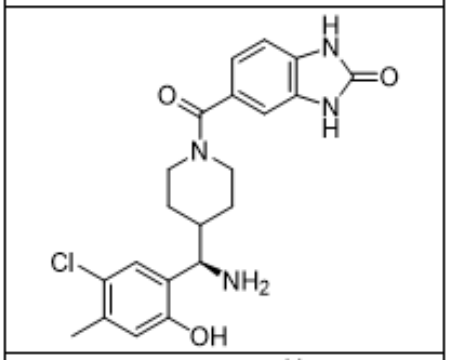
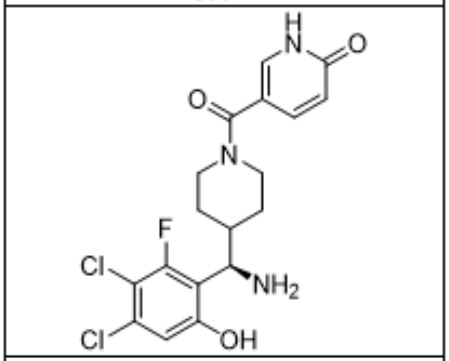
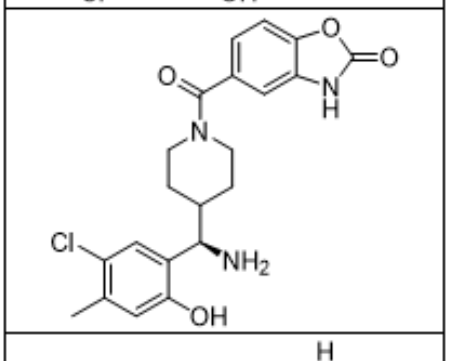
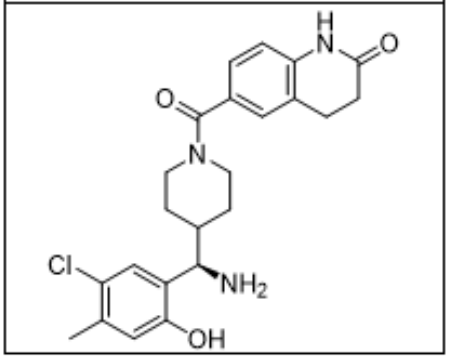
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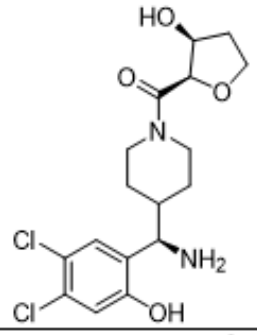
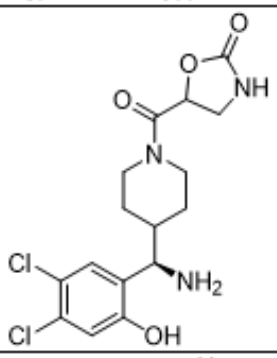
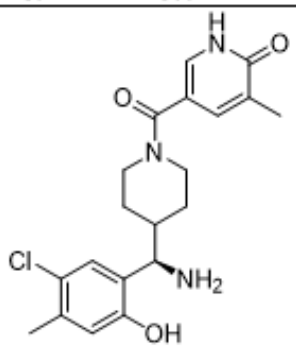
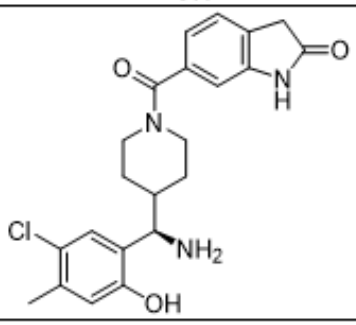
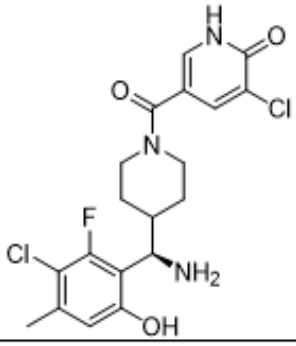
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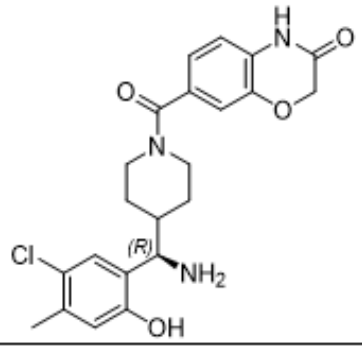
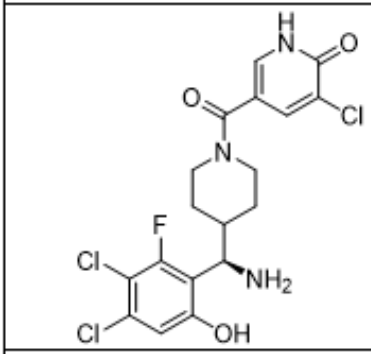
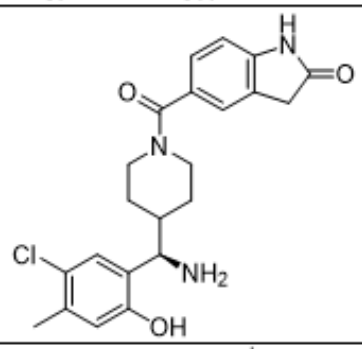
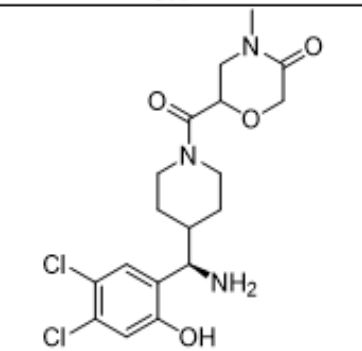
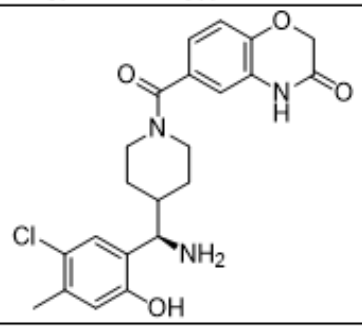
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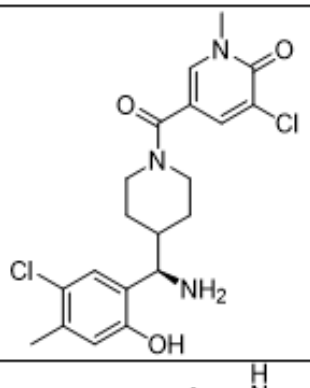
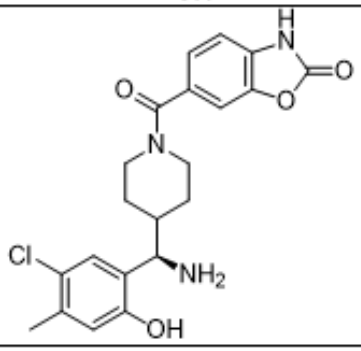
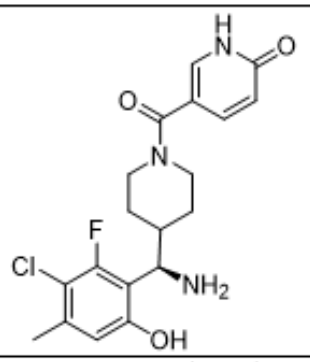
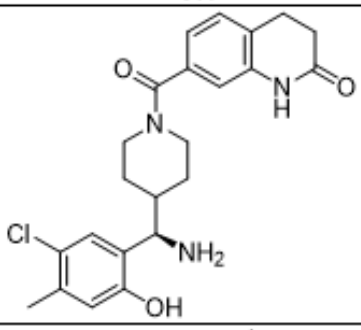
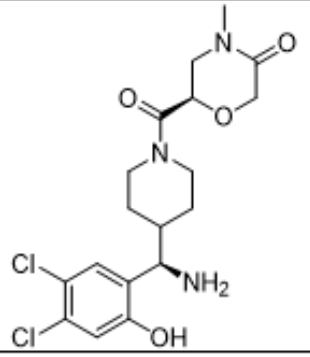
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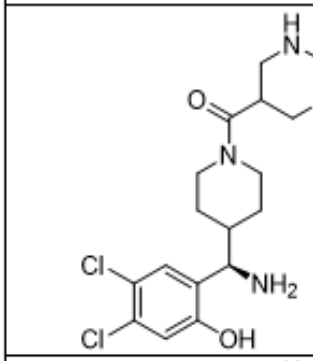
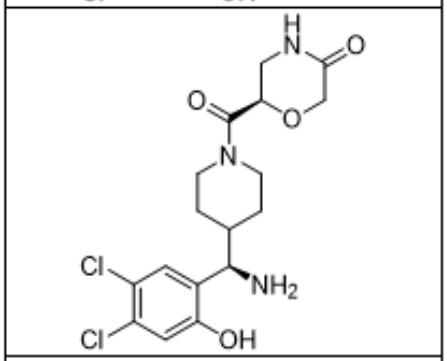
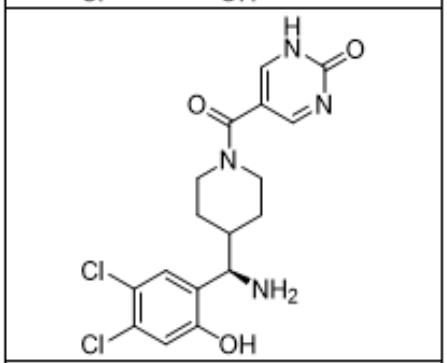
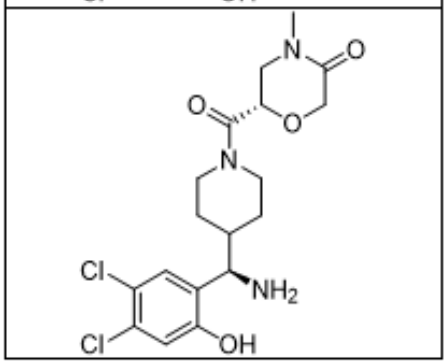
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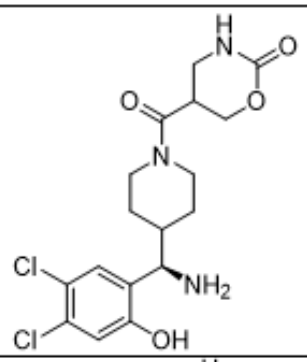
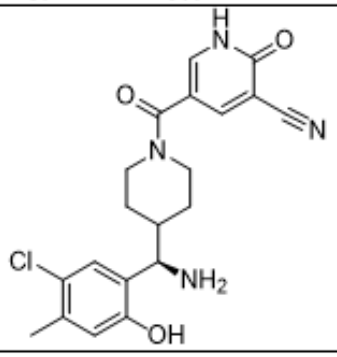
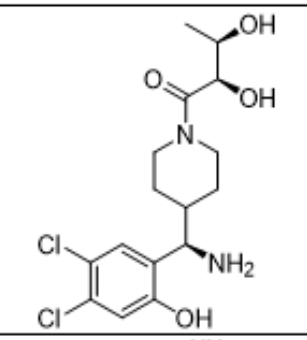
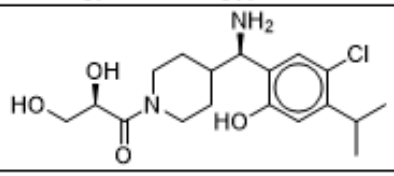
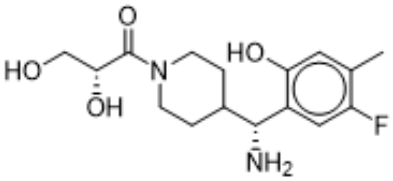
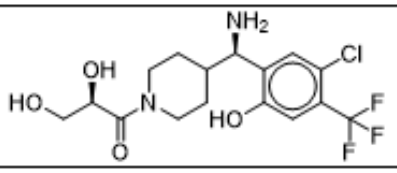
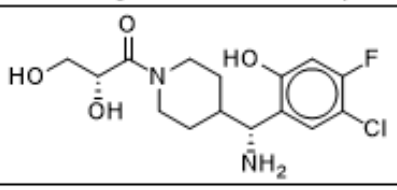
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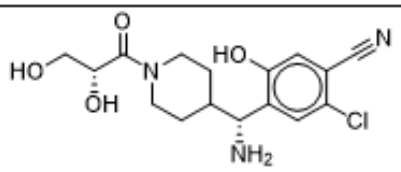
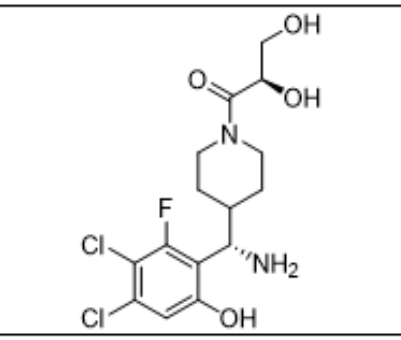
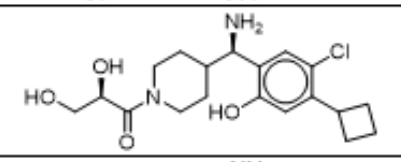
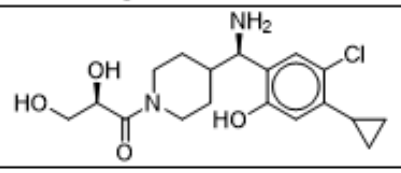
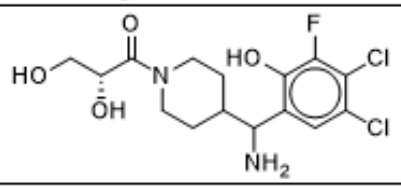
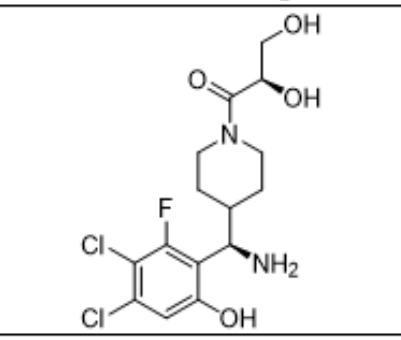
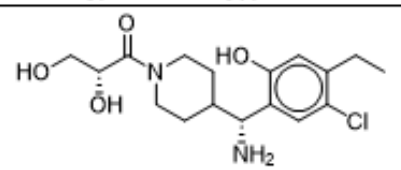
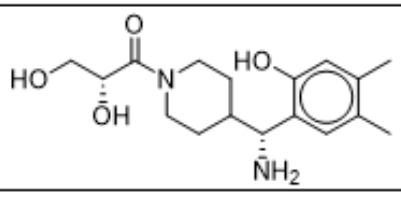
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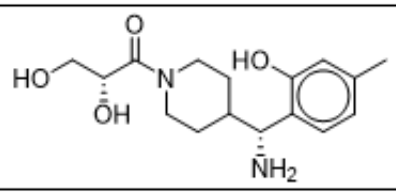
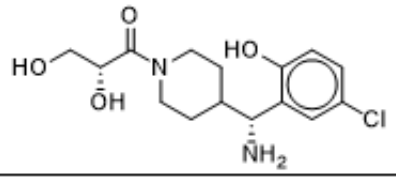
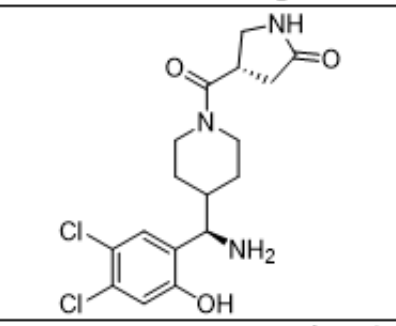
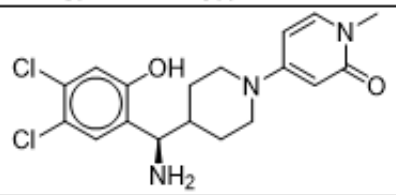
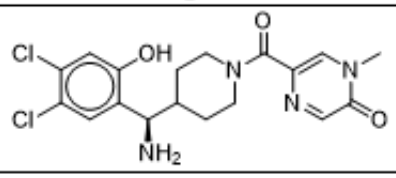
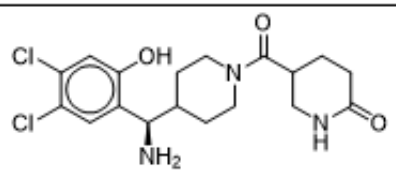
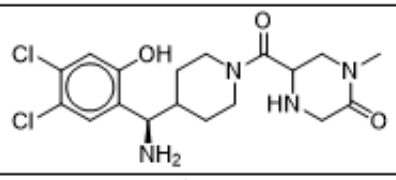
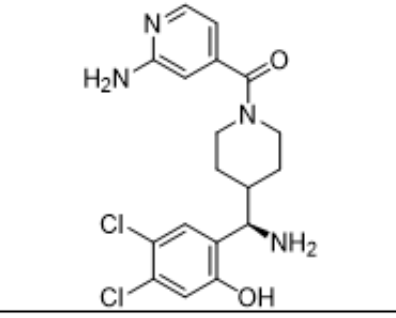
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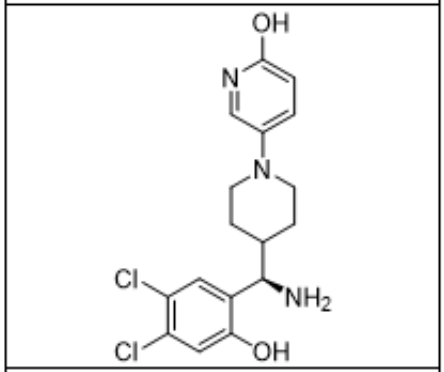
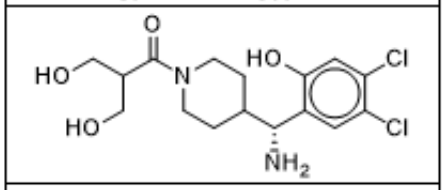
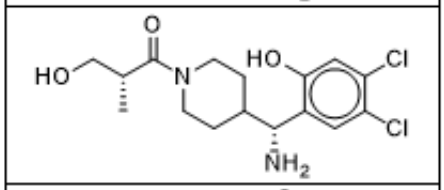
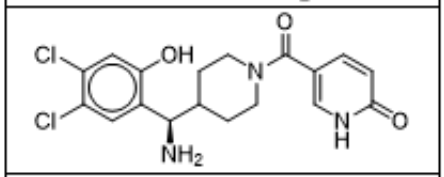
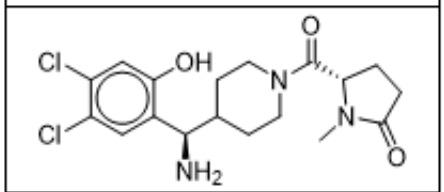
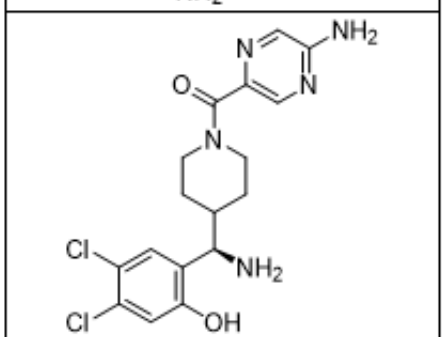
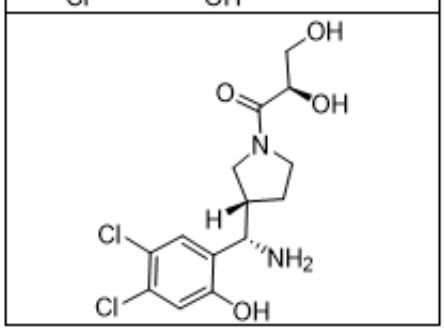
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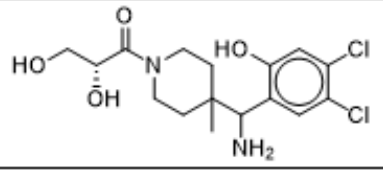
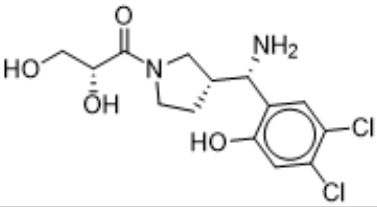
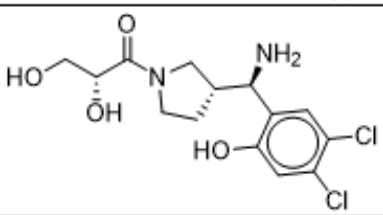
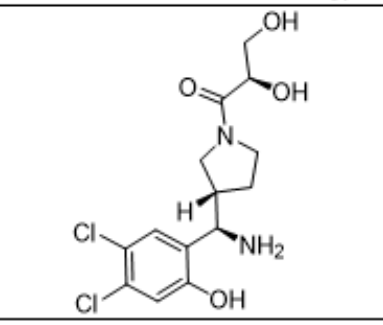
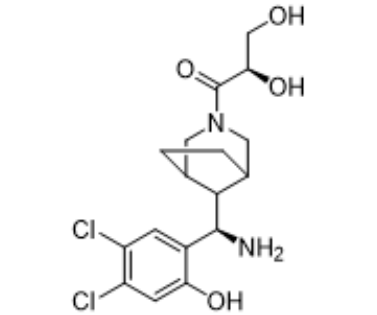
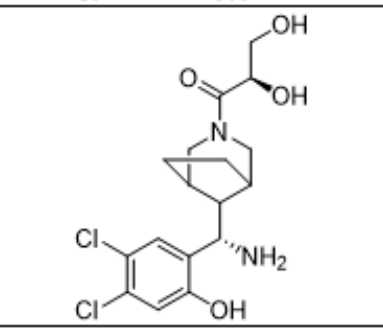
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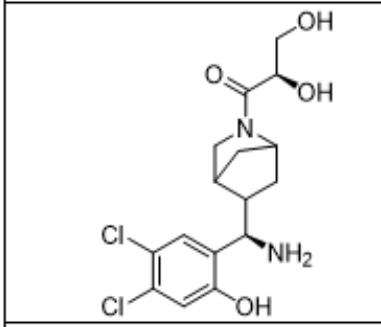
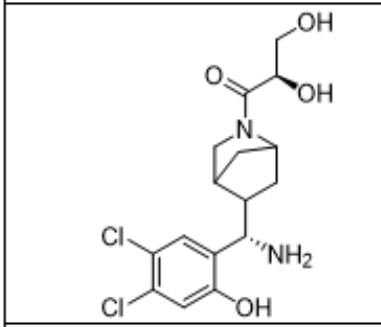
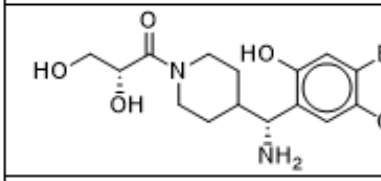
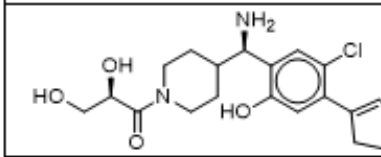
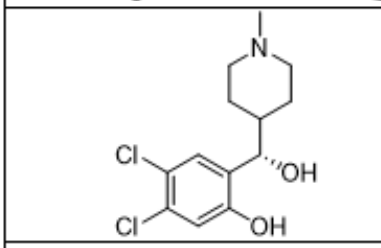
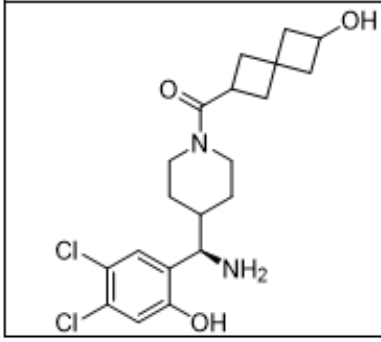
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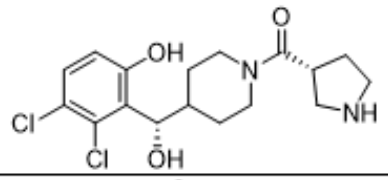
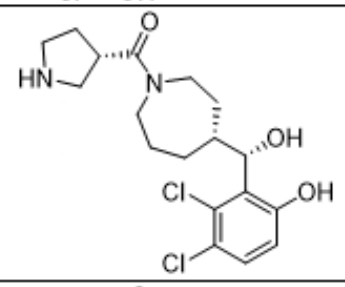
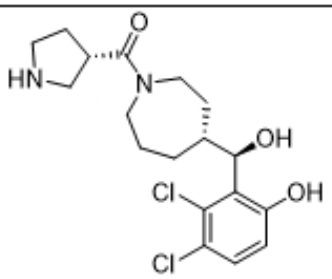
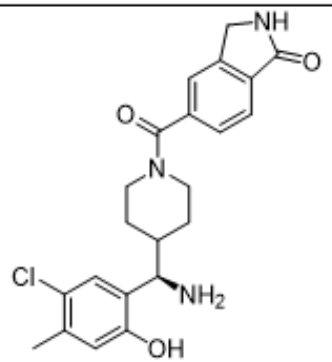
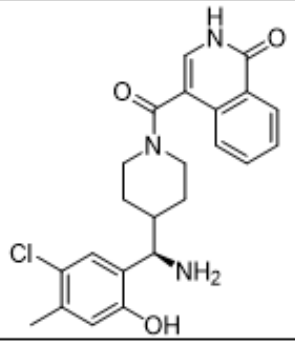
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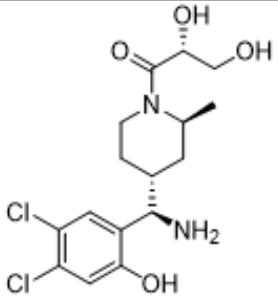
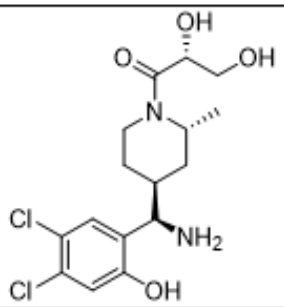
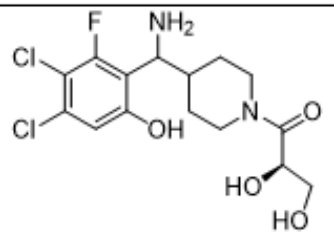
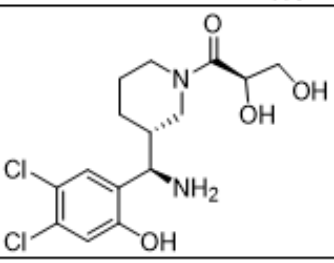
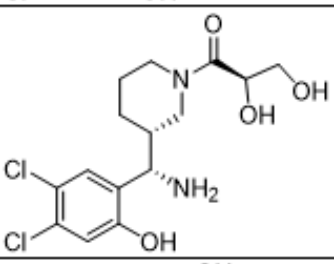
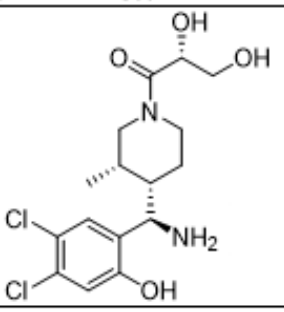
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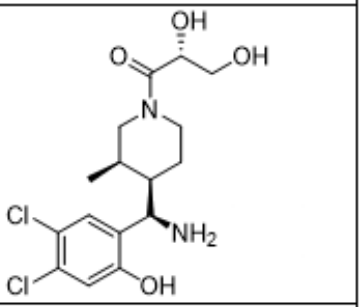
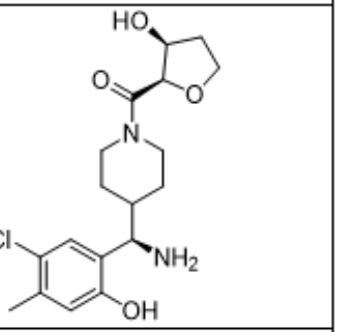
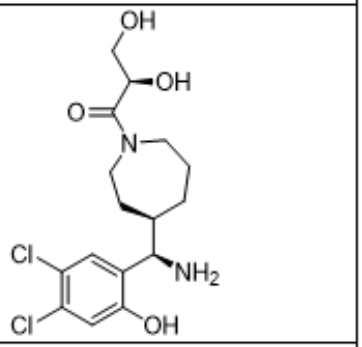
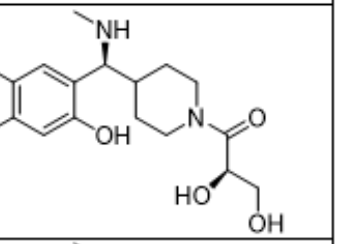
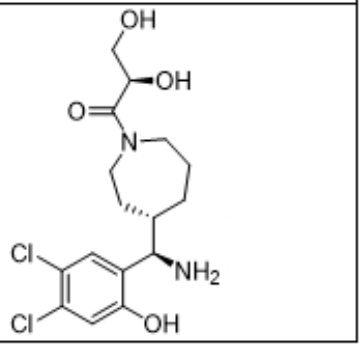
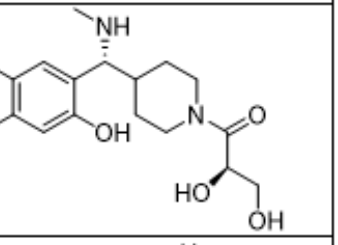
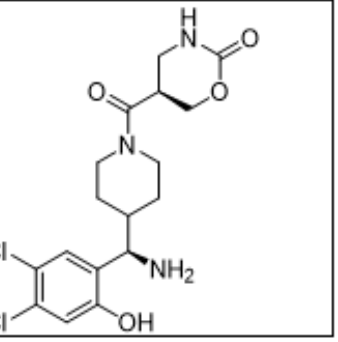
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22. A pharmaceutical composition comprising at least one compound according to any one of claims 1-21 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier or diluent.

23. A compound according to any one of claims 1-21 for use as a medicament.

24. Use of a compound according to any one of claims 1-21 in the manufacture of a medicament for treating a condition in a mammalian species in need thereof, the medicament comprising a therapeutically effective amount of the compound or a pharmaceutically acceptable

salt thereof, wherein the condition is selected from the group consisting of cancer, an immunological disorder, a Central Nerve System (CNS) disorder, an inflammatory disorder, a gastroenterological disorder, a metabolic disorder, a cardiovascular disorder, and a kidney disease;

optionally wherein the condition is:

(a) an immunological disorder that is transplant rejection or an autoimmune disease, wherein the autoimmune disease is optionally rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, or Type I diabetes mellitus; or

(b) a Central Nerve System (CNS) disorder that is Alzheimer's disease;

(c) an inflammatory disorder that is an inflammatory skin condition, arthritis, psoriasis, spondylitis, parodontitits, or an inflammatory neuropathy;

(d) an gastroenterological disorder that is an inflammatory bowel disease; or

(e) a metabolic disorder that is obesity or Type II diabetes mellitus; or

(f) a cardiovascular disorder that is an ischemic stroke; or

(g) a kidney disease that is chronic kidney disease, nephritis, or chronic renal failure; or

(h) selected from the group consisting of cancer, transplant rejection, rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, Type I diabetes mellitus, Alzheimer's disease, inflammatory skin condition, inflammatory neuropathy, psoriasis, spondylitis, parodontitis, Crohn's disease, ulcerative colitis, obesity, Type II diabetes mellitus, ischemic stroke, chronic kidney disease, nephritis, chronic renal failure, and a combination thereof;

and optionally wherein the mammalian species is human.