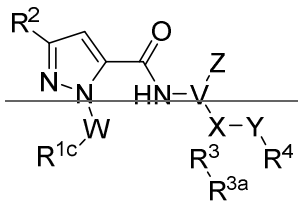
# CLAIMS

What is claimed is:

1. A compound, or a pharmaceutically acceptable salt thereof, represented by formula I:



(I)

wherein:

V is optionally substituted aryl or heteroaryl;

W is optionally substituted aryl or heteroaryl;

X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), -C($NH_2$), -C($NR^aR^b$), -C($N_3$), -C(CN), -C($NO_2$), -C($S(O)_nR^a$), -C[-C(=O)$R^e$], -C[-C(=O)$R^e$], -C[-C(=O)$NR^eR^d$], -C[-C(=O)$SR^e$], -C[-S(O)$R^e$], -C[-$S(O)_2R^e$], -C[S(O)($OR^e$)], -C[-$S(O)_2$($OR^e$)], -C[-$SO_2NR^eR^d$], -C(halogen), -C[($C_1$-$C_8$)alkyl], -C[($C_4$-$C_8$)carbocyclylalkyl], -C[($C_1$-$C_8$)substituted alkyl], -C[($C_2$-$C_8$)alkenyl], -C[($C_2$-$C_8$)substituted alkenyl], -C[($C_2$-$C_8$)alkynyl], -C[($C_2$-$C_8$)substituted alkynyl], -C[aryl($C_1$-$C_8$)alkyl], C(O)N, $CH_2$N, N, C(O), P(O), -O-, S(O)N, or $S(O)_2$N; provided that:

if X represents CH, then -Y-$R^4$ represents -H or -OH, or both Y and $R^4$ are present;

if X represents C(OH), C(O($C_1$-$C_6$)alkyl), -C($NH_2$), -C($NR^aR^b$), -C($N_3$), -C(CN), -C($NO_2$), -C($S(O)_nR^a$), -C[-C(=O)$R^e$], -C[-C(=O)$R^e$], -C[-C(=O)$NR^eR^d$], -C[-C(=O)$SR^e$], -C[-S(O)$R^e$], -C[-$S(O)_2R^e$], -C[S(O)($OR^e$)], -C[-$S(O)_2$($OR^e$)], -C[-$SO_2NR^eR^d$], -C(halogen), -C[($C_1$-$C_8$)alkyl], -C[($C_4$-$C_8$)carbocyclylalkyl], -C[($C_1$-$C_8$)substituted alkyl], -C[($C_2$-$C_8$)alkenyl], -C[($C_2$-$C_8$)substituted alkenyl], -C[($C_2$-$C_8$)alkynyl], -C[($C_2$-$C_8$)substituted alkynyl], or -C[aryl($C_1$-$C_8$)alkyl], then -Y-$R^4$ is present;

if X represents C(O)N, then -Y-$R^4$ represents H; or -Y-$R^4$ represents H, and -$R^3$-$R^{3a}$ represents H;

if X represents $CH_2$N, then -Y-$R^4$ represents ($C_1$-$C_6$)alkyl;

if X represents N, then -Y-$R^4$ represents H, or both Y and $R^4$ are present; and

if X represents C(O) or -O-, then -Y-$R^4$ is absent;

~~-Y-$R^4$, when present, represents -$((C_1-C_6)$alkyl)-$R^4$, -$CH_2C(O)-R^4$, -$CH_2NH-R^4$, -$CH_2N((C_1-C_6)$alkyl)-$R^4$, -$CR^aR^b-R^4$, -$NH-R^4$, -$NHCH_2-R^4$, -$NHC(O)-R^4$, -$N((C_1-C_6)$alkyl)-$R^4$, -$N((C_1-C_6)$alkyl)$CH_2-R^4$, -$N((CH_2)_2OH)-R^4$, -$N[(C_3-C_8)$cycloalkyl$(C_1-C_6)$alkyl$]R^4$, -heterocyclyl-$R^4$, -$OR^4$, -$OCH_2-R^4$, -$OC(O)-R^4$, -$OC(O)NR^aR^b$, -$SCH_2R^4$, or -$SR^4$, wherein the $(C_1-C_6)$alkyl moiety of -$((C_1-C_6)$alkyl)-$R^4$ is optionally substituted;~~

~~Z is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, $(C_1-C_6)$alkyl, -$CF_3$, -$OCF_3$, $(C_1-C_6)$alkoxy, aryl, aryloxy, amino, amino$(C_1-C_6)$alkyl, -$C(O)NH_2$, cyano, -$NHC(O)(C_1-C_6)$alkyl, -$SO_2(C_1-C_6)$alkyl, -$SO_2NH_2$, $(C_3-C_8)$cycloalkyl, $(CH_2)_rOR^a$, $NO_2$, $(CH_2)_r-NR^aR^b$, $(CH_2)_rC(O)R^a$, $NR^aC(O)R^b$, $C(O)NR^cR^d$, $NR^aC(O)NR^cR^d$, -$C(=NR^a)NR^cR^d$, $NHC(=NR^a)NR^cR^d$, $NR^aR^b$, $SO_2NR^cR^d$, $NR^aSO_2NR^cR^d$, $NR^aSO_2-(C_1-C_6)$alkyl, $NR^aSO_2R^a$, $S(O)_pR^a$, $(CF_2)_rCF_3$, $NHCH_2R^a$, $OCH_2R^a$, $SCH_2R^a$, $NH(CH_2)_2(CH_2)_rR^a$, $O(CH_2)_2(CH_2)_rR^a$, and $S(CH_2)_2(CH_2)_rR^a$; or alternatively Z is a 5- or 6-membered aromatic heterocycle containing from 1 to 4 heteroatoms selected from the group consisting of N, O, and S;~~

~~$R^{1c}$ represents halo, amino$(C_1-C_6)$alkyl, $(C_1-C_6)$alkoxy, cyano, -$C(=NH)NH_2$, -$CONR^aR^b$, -$(C_1-C_6)$alkylCONR$^aR^b$, -$SO_2CH_3$, formyl, acyl, -$NH_2$, -$C(=NH)NH(OH)$, -$C(=NH)NH(C(O)O-(C_1-C_6)$alkyl), -$C(=NH)NH(C(O)O-(C_1-C_6)$haloalkyl), -$C(=NH)NH(C(O)S-(C_1-C_6)$alkyl), -$C(=NH)NH(C(O)(OCH(C_1-C_6)$alkyl)$OC(O)(C_1-C_6)$alkyl), optionally substituted aryl, or optionally substituted heteroaryl;~~

~~$R^2$ represents halo, $(C_1-C_6)$alkyl, $(C_3-C_8)$cycloalkyl, $(C_1-C_6)$fluoroalkyl, -$OCH_3$, -$Si(CH_3)_3$, -$CONH_2$, -$C(O)OH$, cyano, or phenyl;~~

~~$R^3$, when present, represents -NH-, -O-, optionally substituted aryl, heteroaryl, phenyl, carbocyclyl, or heterocyclyl;~~

~~$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, $(C_1-C_6)$alkyl, -$CF_3$, -$OCF_3$, $(C_1-C_6)$alkoxy, aryl, aryloxy, amino, amino$(C_1-C_6)$alkyl, -$C(O)NH_2$, cyano, -$NHC(O)(C_1-C_6)$alkyl, -$SO_2(C_1-C_6)$alkyl, -$SO_2NH_2$, $(C_3-C_8)$cycloalkyl, $(CH_2)_rOR^a$, $NO_2$, $(CH_2)_r-NR^aR^b$, $(CH_2)_rC(O)R^a$, $NR^aC(O)R^b$, $C(O)NR^cR^d$, $NR^aC(O)NR^cR^d$, -$C(=NR^a)NR^cR^d$, $NHC(=NR^a)NR^cR^d$, $NR^aR^b$, $SO_2NR^cR^d$, $NR^aSO_2NR^cR^d$, $NR^aSO_2-(C_1-C_6)$alkyl, $NR^aSO_2R^a$, $S(O)_pR^a$, $(CF_2)_rCF_3$, $NHCH_2R^a$, $OCH_2R^a$, $SCH_2R^a$, $NH(CH_2)_2(CH_2)_rR^a$, $O(CH_2)_2(CH_2)_rR^a$, or~~

~~$S(CH_2)_2(CH_2)_rR^a$; or alternatively $R^{3a}$ is a 5- or 6-membered aromatic heterocycle containing from 1 to 4 heteroatoms selected from the group consisting of N, O, and S;~~

~~$R^4$ represents hydrogen, hydroxy, optionally substituted $(C_1$-$C_6)$alkyl, optionally substituted $(C_3$-$C_8)$cycloalkyl, heterocyclyl$(C_1$-$C_6)$alkyl, $(C_3$-$C_8)$cycloalkyl$(C_1$-$C_6)$alkyl, $CH_2OH$, $CH((C_1$-$C_6)$alkyl)OH, $CH(NH_2)CH((C_1$-$C_6)$alkyl)$_2$, optionally substituted aryl, optionally substituted aryl$(C_1$-$C_6)$alkyl, heteroaryl, optionally substituted heteroaryl$(C_1$-$C_6)$alkyl, $CH_2S(C_1$-$C_6)$alkyl, amino, or cyano; or $(CR^aR^b)_r(CR^aR^b)_p$ fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent $NR^a$ fused to the position *ortho* to X on that phenyl;~~

~~each $R^a$ and $R^b$ is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, aryl$(C_1$-$C_8)$alkyl, $(C_3$-$C_8)$carbocyclylalkyl, $C(=O)R^e$, $C(=O)OR^e$, $C(=O)NR^eR^d$, $C(=O)SR^e$, $S(O)R^e$, $S(O)_2R^e$, $S(O)(OR^e)$, or $SO_2NR^eR^d$;~~

~~each $R^e$ and $R^d$ is independently H, $(C_1$-$C_8)$alkyl, $(C_2$-$C_8)$alkenyl, $(C_2$-$C_8)$alkynyl, $(C_4$-$C_8)$carbocyclylalkyl, optionally substituted aryl, optionally substituted heteroaryl, $C(=O)(C_1$-$C_8)$alkyl, $S(O)_n(C_1$-$C_8)$alkyl, or aryl$(C_1$-$C_8)$alkyl; or when $R^e$ and $R^d$ are bonded to a common nitrogen atom, then they may form a 3- to 7-membered heterocyclic ring wherein optionally a carbon atom of said heterocyclic ring may be replaced with -O-, -S- or $-NR^a$-;~~

~~$X-Y$ $R^3$ $R^4$ $R^{3a}$~~ ~~can represent~~ ~~$C=CH$ $R^3$ $R^4$ $R^{3a}$~~, ~~$C=CH$ $R^3$ $R^4$ $R^{3a}$~~, ~~or~~ ~~$C=N$ $R^3$ $R^4$ $R^{3a}$~~;

~~n is 2 or 3;~~

~~r is independently for each occurrence 0, 1, 2, or 3;~~

~~p is independently for each occurrence 0, 1, or 2; and~~

~~the stereochemical configuration at any chiral center is *R*, *S*, or a mixture of *R* and *S*.~~

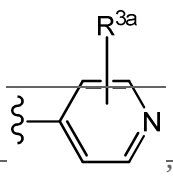
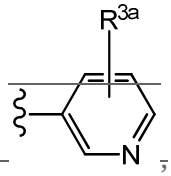
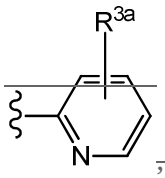
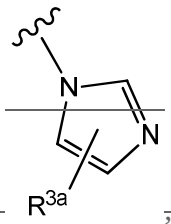
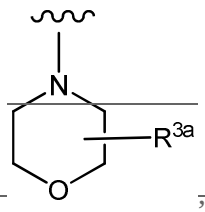
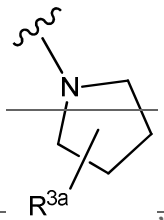
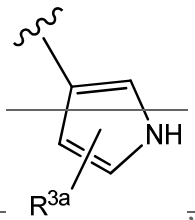
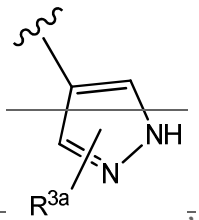
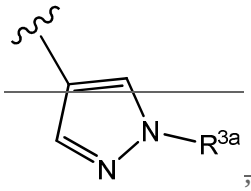
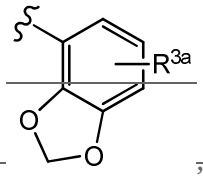
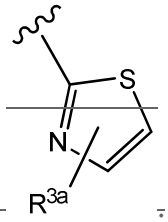
~~2. The compound of claim 1, wherein X represents CH, and both Y and $R^4$ are present.~~

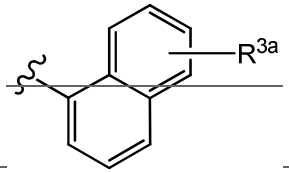
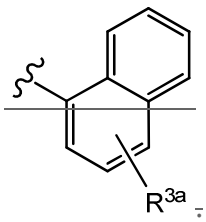
~~3. The compound of claim 1, wherein -X-Y- represents $-CHNHCH_2-$.~~

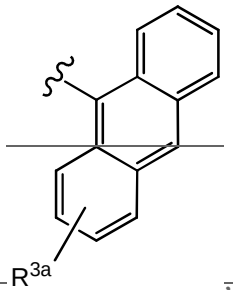
~~4. The compound of claim 1, wherein -X-Y- represents $-C(OH)CH_2CH_2-$.~~

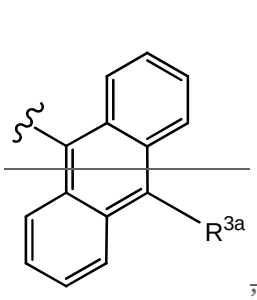
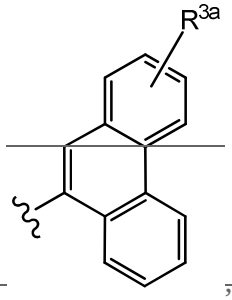
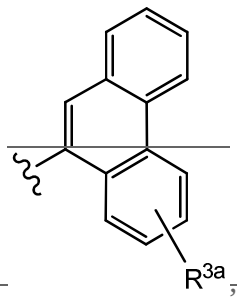
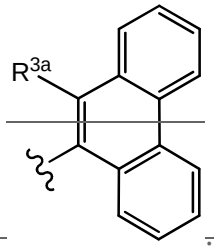
~~5. The compound of claim 1, wherein -X-Y- represents $-CHOCH_2-$.~~

~~6. The compound of claim 1, wherein $R^3$ represents phenylene-$R^{3a}$.~~

7. The compound of claim 1, wherein $R^3$-$R^{3a}$ represents , , , , , , , , , , , or .

8. The compound of claim 1, wherein $R^3$-$R^{3a}$ represents  or .

9. The compound of claim 1, wherein $R^3$ $R^{3a}$ represents ,

, , , or .

10. The compound of claim 1, wherein $R^{3a}$ is absent.

11. The compound of claim 1, wherein $R^4$ is cyclopropyl.

12. The compound of claim 1, wherein $R^3$ is phenyl, and $R^{3a}$ is *ortho*, *meta*, or *para* -OH.

13. The compound of claim 1, wherein $R^3$ is phenyl, and $R^{3a}$ is *meta* or *para* $-NH_2$.

14. The compound of claim 1, wherein $R^3$ is phenyl, and $R^{3a}$ is *meta* or *para* -CN.

15. The compound of claim 1, wherein Z is absent.

16. The compound of claim 1, wherein Z represents fluoro.

17. The compound of claim 1, wherein Z represents chloro.

18. The compound of claim 1, wherein Z represents 2-F, 4-F, 5-F, 6-F, 6-Cl, or 5-($C_3$-$C_8$)cycloalkyl.

19. The compound of claim 1, wherein Z represents 6-F.

20. The compound of claim 1, wherein $R^{1c}$ represents aminomethyl.

21. The compound of claim 1, wherein $R^{1c}$ represents cyano.

22. The compound of claim 1, wherein $R^{1c}$ represents $-SO_2CH_3$.

23. The compound of any one of claims 1-22, wherein $R^2$ is $-CH_3$ or $-CF_3$.

24. The compound of any one of claims 1-22, wherein $R^2$ is $-CF_3$.

25. The compound of any one of claims 1-22, wherein $R^2$ is *tert*-butyl.

26. The compound of any one of claims 1-22, wherein $R^2$ is cyclopropyl.

27. The compound of any one of claims 1-22, wherein $R^2$ is $-OCH_3$.

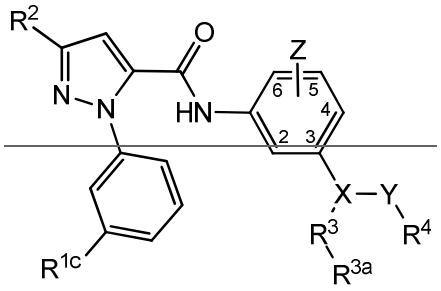
28. The compound of any one of claims 1-22, wherein $R^2$ is $-Si(CH_3)_3$.

29. The compound of any one of claims 1-22, wherein $R^2$ is $-CONH_2$.

30. The compound of any one of claims 1-22, wherein $R^2$ is cyano.

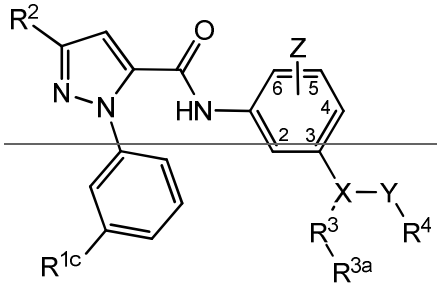
31. The compound of any one of claims 1-22, wherein $R^2$ is phenyl.

32. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula II:




(II).

33. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula III:




(III)

wherein:

X represents CH, C(OH), $C(O(C_1-C_6)alkyl)$, C(O)N, $CH_2N$, N, C(O), or O;

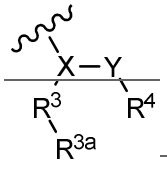
Y $R^4$, when present, represents $((C_1-C_6)alkyl)-R^4$, $-CH_2C(O)-R^4$, $-CH_2NH-R^4$, $-CH_2N((C_1-C_6)alkyl)-R^4$, $-CR^aR^b-R^4$, $-NH-R^4$, $-NHCH_2-R^4$, $-NHC(O)-R^4$, $-N((C_1-C_6)alkyl)-R^4$, $-N((C_1-C_6)alkyl)CH_2-R^4$, $-N((CH_2)_2OH)-R^4$, $-N[(C_3-C_8)cycloalkyl(C_1-C_6)alkyl]R^4$, heterocyclyl $R^4$, $-OR^4$, $-OCH_2-R^4$, $-OC(O)-R^4$, $-OC(O)NR^aR^b$, $-SCH_2R^4$, or $-SR^4$, wherein the $(C_1-C_6)$alkyl moiety of $((C_1-C_6)alkyl)-R^4$ is optionally substituted;

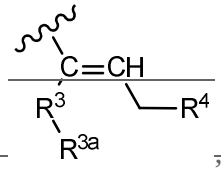
Z is absent or represents halo, hydroxy, $(C_1-C_6)$alkyl, $-CF_3$, $-OCF_3$, $(C_1-C_6)$alkoxy, aryl, aryloxy, amino, amino$(C_1-C_6)$alkyl, $-C(O)NH_2$, cyano, $-NHC(O)(C_1-C_6)$alkyl, $-SO_2(C_1-C_6)$alkyl, $-SO_2NH_2$, or $(C_3-C_8)$cycloalkyl;

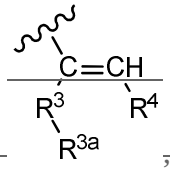
$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, $-SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

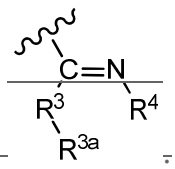
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, $-CF_3$, $-OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, $-C(O)NH_2$, cyano, $-NHC(O)$($C_1$-$C_6$)alkyl, $-SO_2$($C_1$-$C_6$)alkyl, and $-SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, $-CH_2OH$, $-CH$(($C_1$-$C_6$)alkyl)OH, $-CH(NH_2)CH$(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, $-CH_2S$($C_1$-$C_6$)alkyl, amino, or cyano; or $-CH_2-$ fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent $-NH-$ fused to the position *ortho* to X on that phenyl; and



can represent


,


, or


.

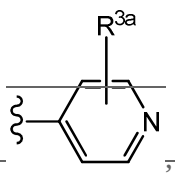
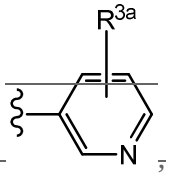
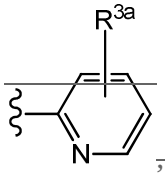
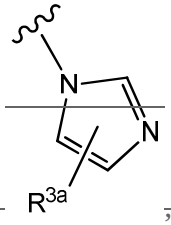
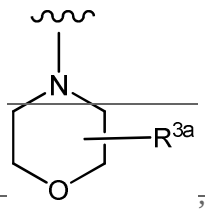
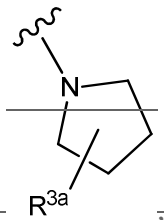
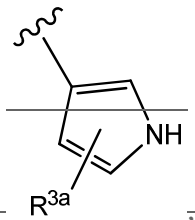
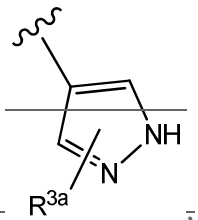
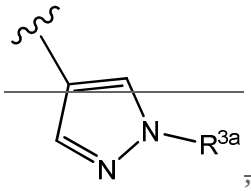
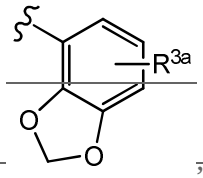
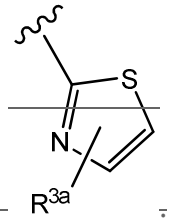
34. The compound of claim 33, wherein X represents CH, and both Y and $R^4$ are present.

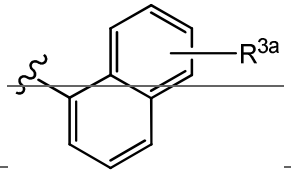
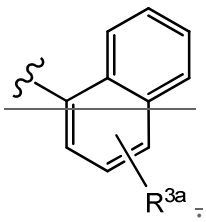
35. The compound of claim 33, wherein $-X-Y-$ represents $-CHNHCH_2-$.

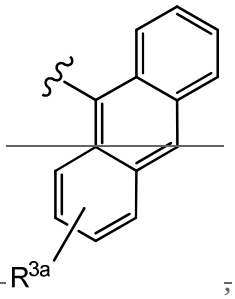
36. The compound of claim 33, wherein $-X-Y-$ represents $-C(OH)CH_2CH_2-$.

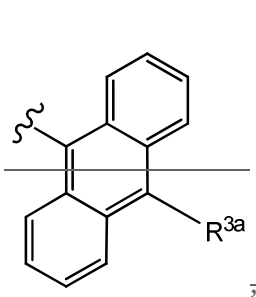
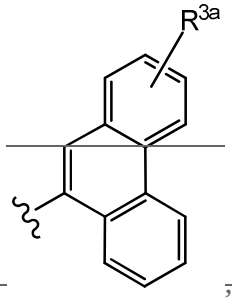
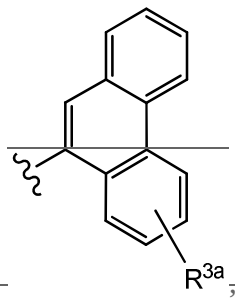
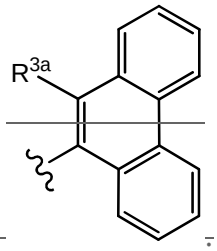
37. The compound of claim 33, wherein $-X-Y-$ represents $-CHOCH_2-$.

38. The compound of claim 33, wherein $R^3$ represents phenylene-$R^{3a}$.

39. The compound of claim 33, wherein $R^3$-$R^{3a}$ represents , , , , , , , , , , , or .

40. The compound of claim 33, wherein $R^3$-$R^{3a}$ represents  or .

41. The compound of claim 33, wherein -$R^3$-$R^{3a}$ represents ;

, , , or .

42. The compound of claim 33, wherein $R^{3a}$ is absent.

43. The compound of claim 33, wherein $R^4$ is cyclopropyl.

44. The compound of claim 33, wherein $R^3$ is phenyl, and $R^{3a}$ is *ortho*, *meta*, or *para* -OH.

45. The compound of claim 33, wherein $R^3$ is phenyl, and $R^{3a}$ is *meta* or *para* -$NH_2$.

46. The compound of claim 33, wherein $R^3$ is phenyl, and $R^{3a}$ is *meta* or *para* -CN.

47. The compound of claim 33, wherein Z is absent.

48. The compound of claim 33, wherein Z represents fluoro.

49. The compound of claim 33, wherein Z represents chloro.

50. The compound of claim 33, wherein Z represents 2-F, 4-F, 5-F, 6-F, 6-Cl, or 5-($C_3$-$C_8$)cycloalkyl.

51. The compound of claim 33, wherein Z represents 6-F.

52. The compound of claim 33, wherein $R^{1c}$ represents aminomethyl.

53. The compound of claim 33, wherein $R^{1c}$ represents cyano.

54. The compound of claim 33, wherein $R^{1c}$ represents -$SO_2CH_3$.

55. The compound of any one of claims 33-54, wherein $R^2$ is -$CH_3$ or -$CF_3$.

56. The compound of any one of claims 33-54, wherein $R^2$ is -$CF_3$.

57. The compound of any one of claims 33-54, wherein $R^2$ is *tert*-butyl.

58. The compound of any one of claims 33-54, wherein $R^2$ is cyclopropyl.

59. The compound of any one of claims 33-54, wherein $R^2$ is -$OCH_3$.

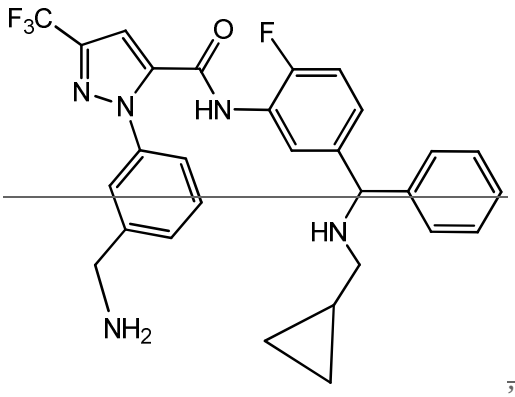
~~60. The compound of any one of claims 33-54, wherein $R^2$ is $-Si(CH_3)_3$.~~

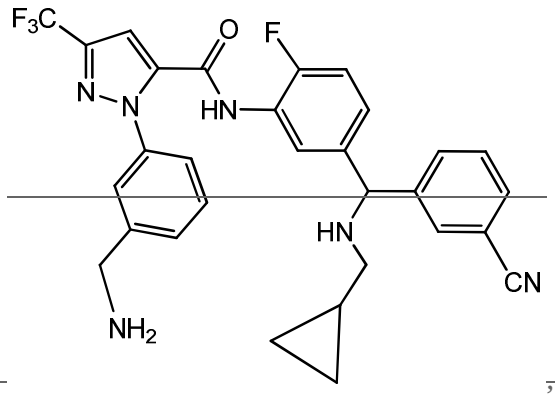
~~61. The compound of any one of claims 33-54, wherein $R^2$ is $-CONH_2$.~~

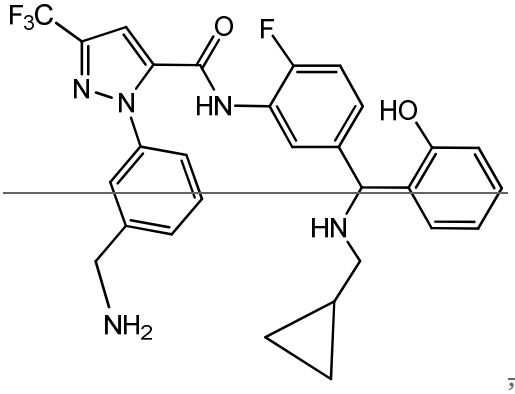
~~62. The compound of any one of claims 33-54, wherein $R^2$ is cyano.~~

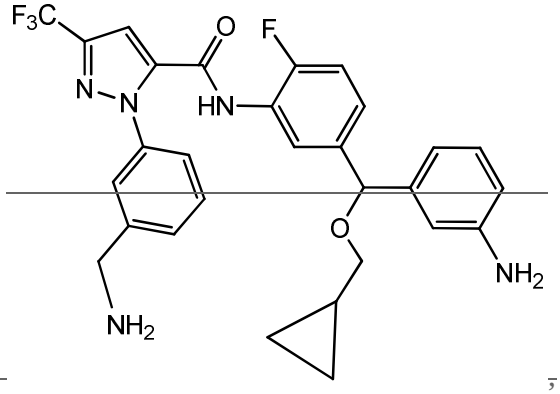
~~63. The compound of any one of claims 33-54, wherein $R^2$ is phenyl.~~

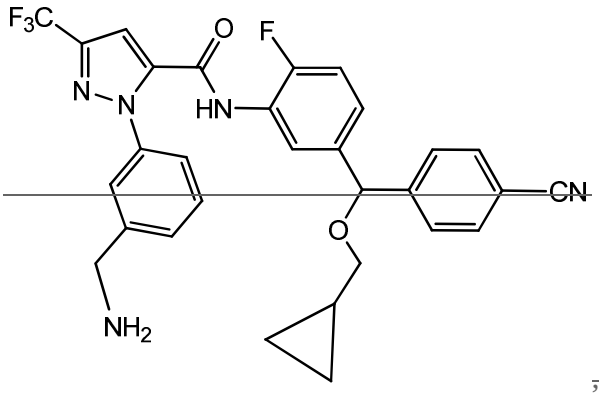
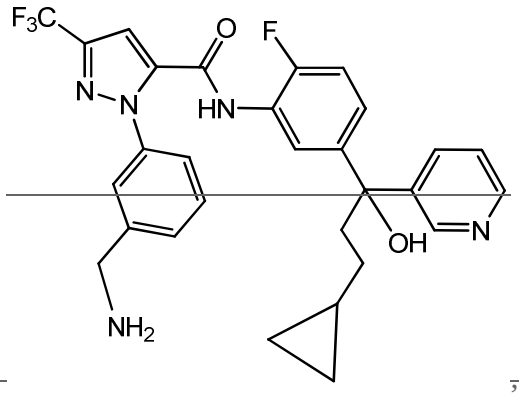
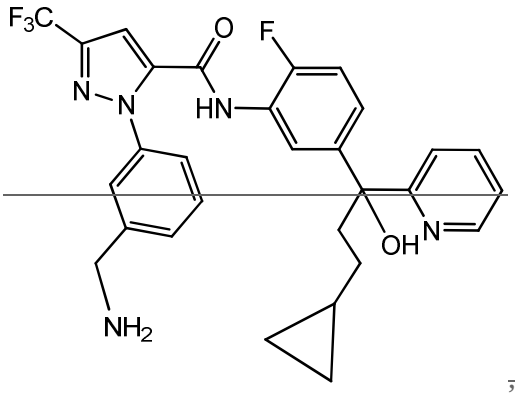
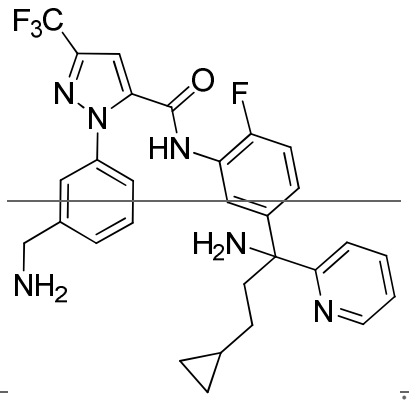
~~64. The compound of claim 33, wherein said compound is selected from the group consisting of:~~



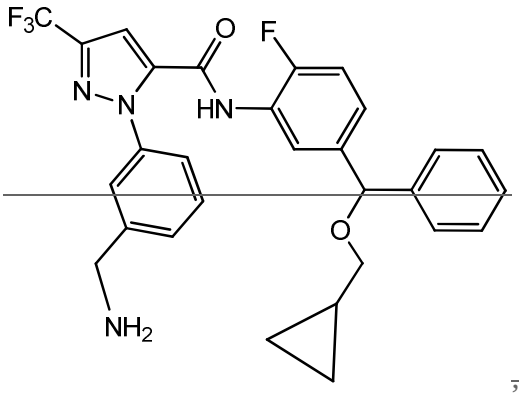



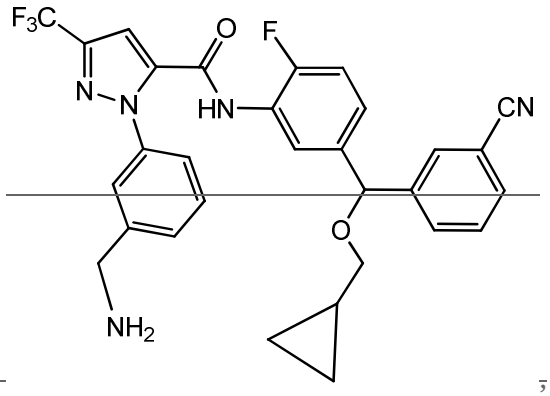



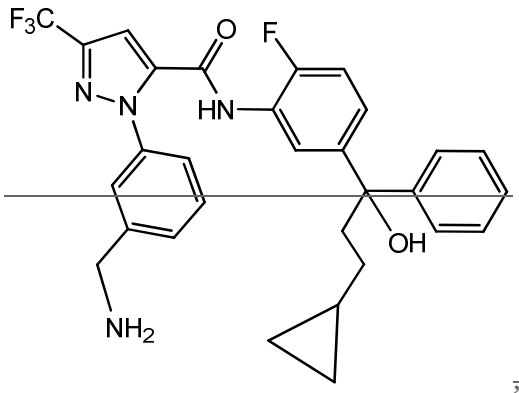



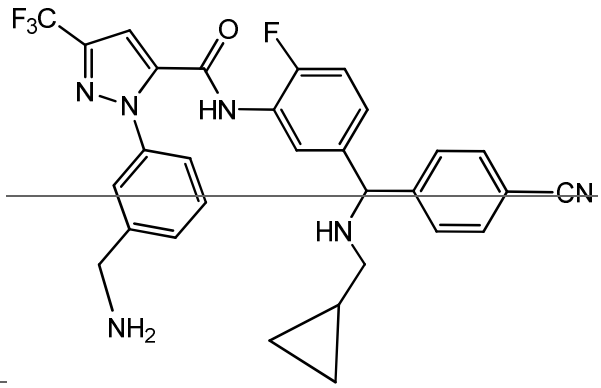





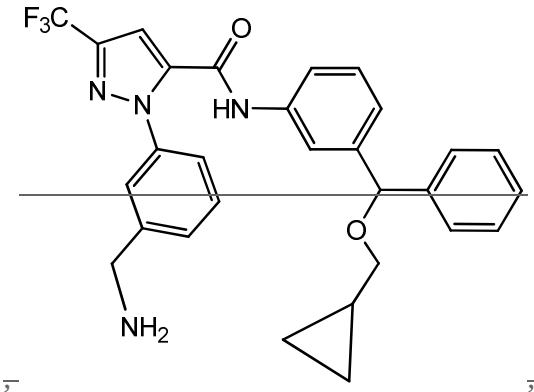
65. The compound of claim 33, wherein said compound is selected from the group consisting of:

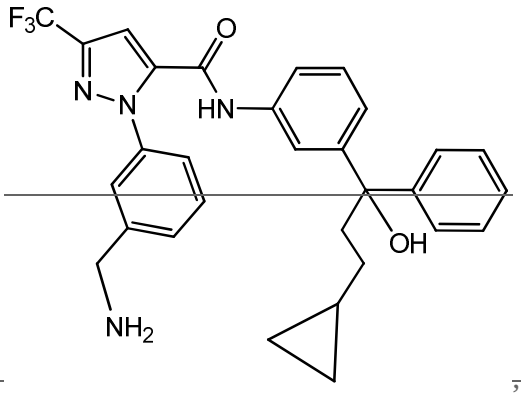

F3C
O
F
N
N
HN
O
NH2
,

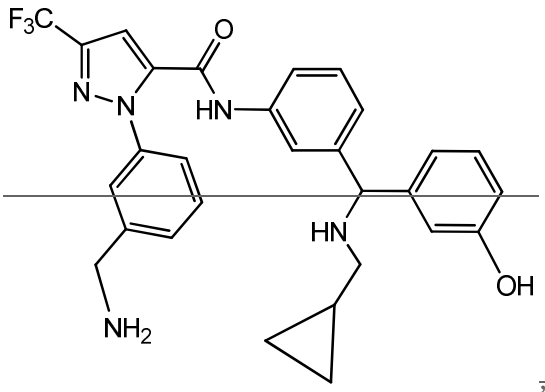

F3C
O
F
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HN
CN
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NH2
,

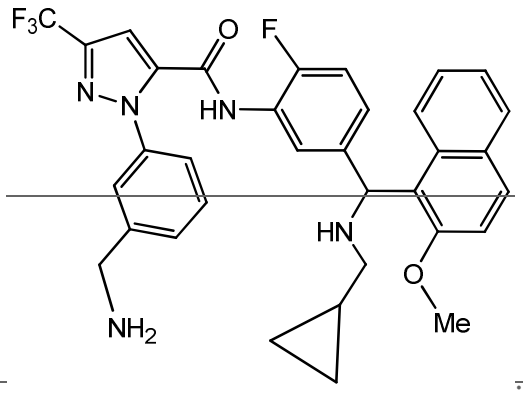

F3C
O
F
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HN
OH
NH2
,


F3C
O
F
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HN
CN
HN
NH2
,

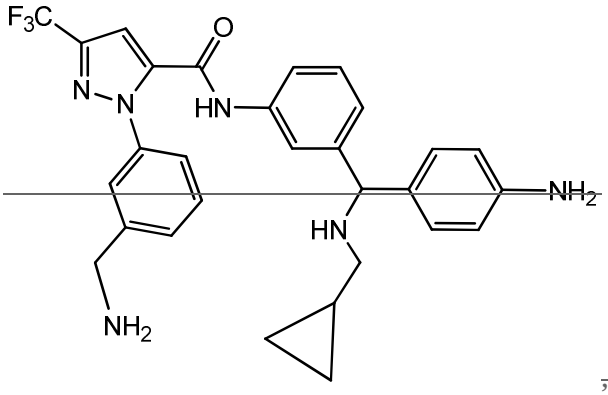

F3C
O
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O
NH2
,


F3C
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N
HN
OH
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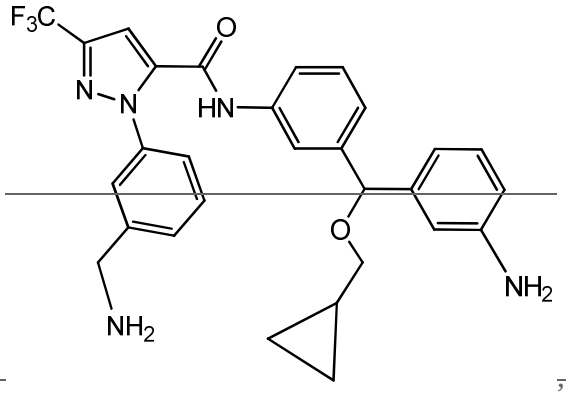

F3C
O
N
N
HN
HN
OH
NH2
, ~~and~~


F3C
O
F
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HN
O
Me
NH2
,

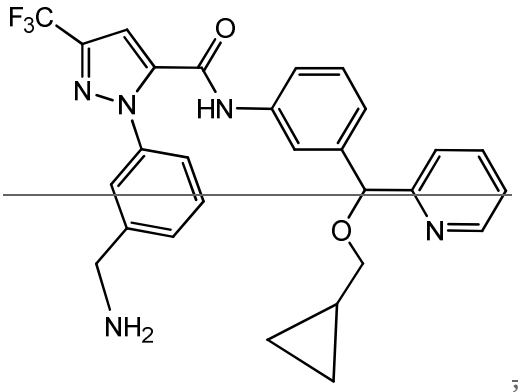
66. The compound of claim 33, wherein said compound is selected from the group consisting of:



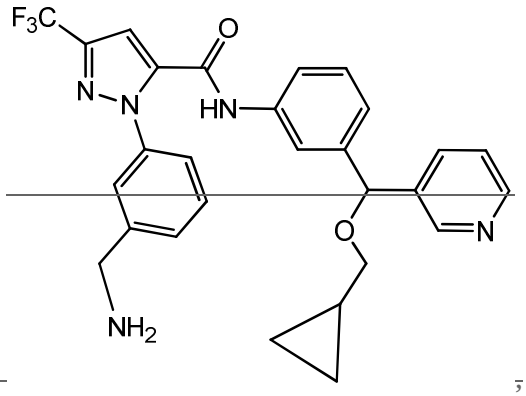
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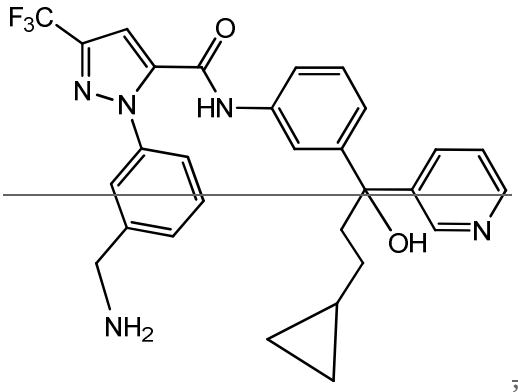
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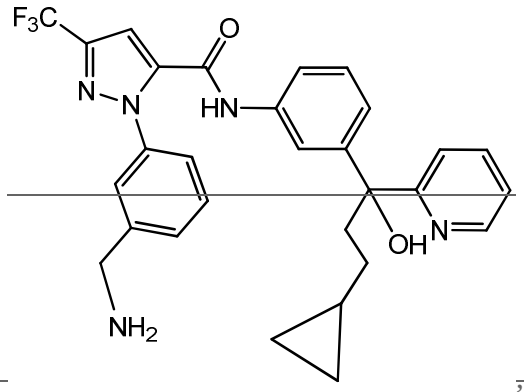
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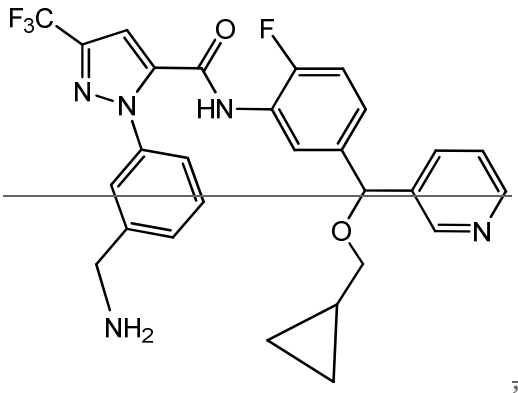
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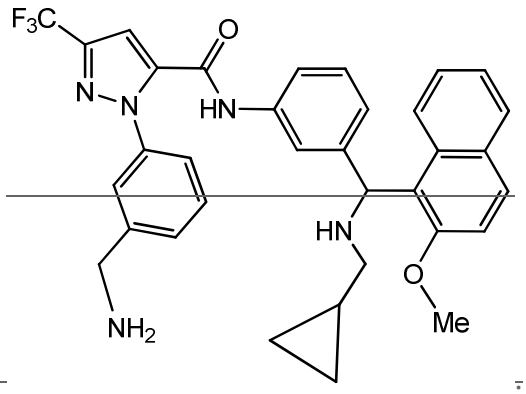


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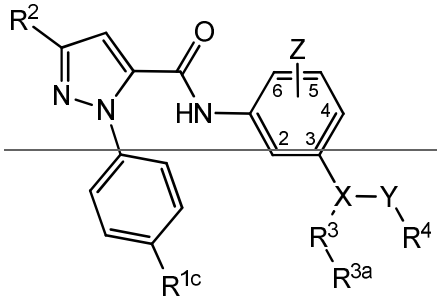
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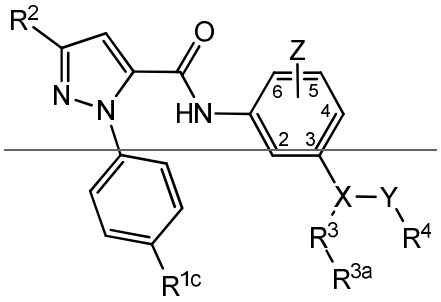
~~, and~~ .

~~67. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula IV:~~




~~(IV).~~

~~68. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula V:~~



(V)

wherein:

X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or -O-;

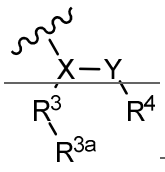
-Y-$R^4$, when present, represents -(($C_1$-$C_6$)alkyl)-$R^4$, -$CH_2$C(O)-$R^4$, -$CH_2$NH-$R^4$, -$CH_2$N(($C_1$-$C_6$)alkyl)-$R^4$, -$CR^aR^b$-$R^4$, -NH-$R^4$, -$NHCH_2$-$R^4$, -NHC(O)-$R^4$, -N(($C_1$-$C_6$)alkyl)-$R^4$, -N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, -N(($CH_2$)$_2$OH)-$R^4$, -N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, -heterocyclyl-$R^4$, -$OR^4$, -$OCH_2$-$R^4$, -OC(O)-$R^4$, -OC(O)$NR^aR^b$, -$SCH_2R^4$, or -$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of -(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;

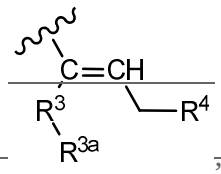
Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, -$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;

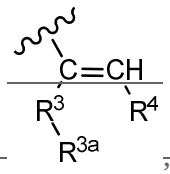
$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, -$SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

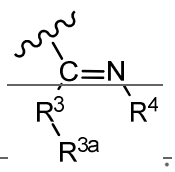
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, and -$SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, -$CH_2OH$, -CH(($C_1$-$C_6$)alkyl)OH, -$CH(NH_2)CH((C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, -$CH_2$S($C_1$-$C_6$)alkyl, amino, or cyano; or -$CH_2$- fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent -NH- fused to the position *ortho* to X on that phenyl; and



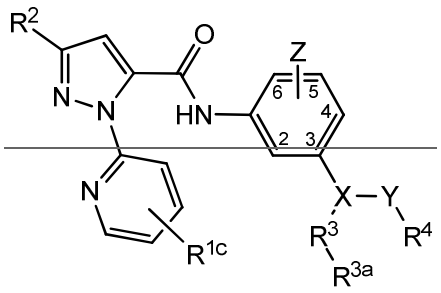
~~can represent~~


~~,~~


~~, or~~


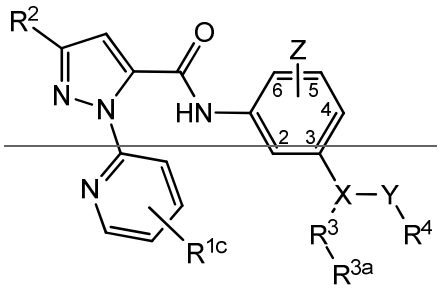
~~.~~

~~69. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula VI:~~




~~(VI).~~

~~70. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula VII:~~




~~(VII)~~

~~wherein:~~

~~X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or –O–;~~

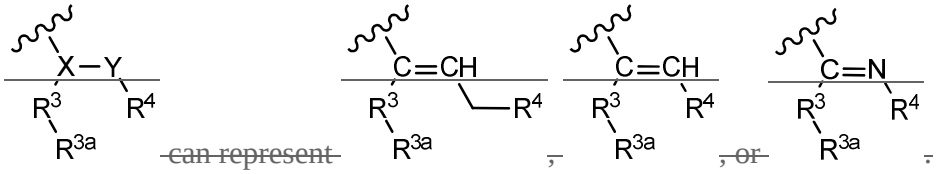
~~–Y–$R^4$, when present, represents –(($C_1$-$C_6$)alkyl)–$R^4$, –$CH_2$C(O)–$R^4$, –$CH_2$NH–$R^4$, –$CH_2$N(($C_1$-$C_6$)alkyl)–$R^4$, –$CR^aR^b$–$R^4$, –NH–$R^4$, –$NHCH_2$–$R^4$, –NHC(O)–$R^4$, –N(($C_1$-$C_6$)alkyl)–$R^4$, –N(($C_1$-$C_6$)alkyl)$CH_2$–$R^4$, –N(($CH_2$)$_2$OH)–$R^4$, –N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, –heterocyclyl–$R^4$, –$OR^4$, –$OCH_2$–$R^4$, –OC(O)–$R^4$, –OC(O)$NR^aR^b$, –$SCH_2R^4$, or –$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of –(($C_1$-$C_6$)alkyl)–$R^4$ is optionally substituted;~~

~~Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, –$CF_3$, –$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, –C(O)$NH_2$, cyano, –NHC(O)($C_1$-$C_6$)alkyl, –$SO_2$($C_1$-$C_6$)alkyl, –$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;~~

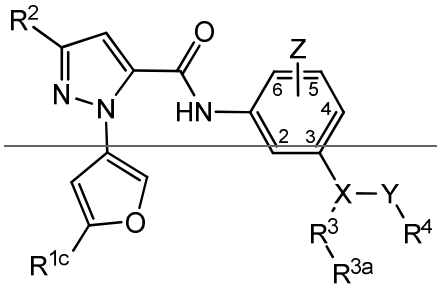
$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, $-SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, $-CF_3$, $-OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, $-C(O)NH_2$, cyano, $-NHC(O)$($C_1$-$C_6$)alkyl, $-SO_2$($C_1$-$C_6$)alkyl, and $-SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, $-CH_2OH$, $-CH$(($C_1$-$C_6$)alkyl)$OH$, $-CH(NH_2)CH$(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, $-CH_2S$($C_1$-$C_6$)alkyl, amino, or cyano; or $-CH_2-$ fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent $-NH-$ fused to the position *ortho* to X on that phenyl; and

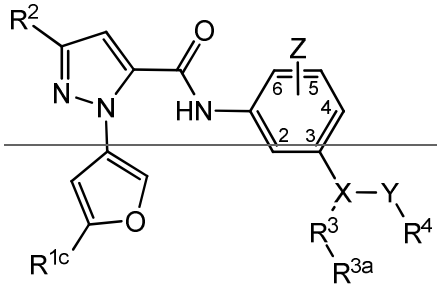



71. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula VIII:




(VIII).

72. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula IX:



(IX)

wherein:

X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or –O–;

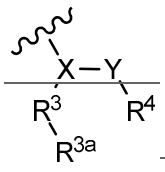
–Y–$R^4$, when present, represents –(($C_1$-$C_6$)alkyl)-$R^4$, –$CH_2$C(O)-$R^4$, –$CH_2$NH-$R^4$, –$CH_2$N(($C_1$-$C_6$)alkyl)-$R^4$, –$CR^aR^b$-$R^4$, –NH-$R^4$, –$NHCH_2$-$R^4$, –NHC(O)-$R^4$, –N(($C_1$-$C_6$)alkyl)-$R^4$, –N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, –N(($CH_2$)$_2$OH)-$R^4$, –N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, –heterocyclyl-$R^4$, –O$R^4$, –$OCH_2$-$R^4$, –OC(O)-$R^4$, –OC(O)$NR^aR^b$, –$SCH_2R^4$, or –S$R^4$, wherein the ($C_1$-$C_6$)alkyl moiety of –(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;

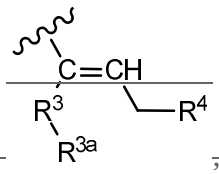
Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, –$CF_3$, –$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, –C(O)$NH_2$, cyano, –NHC(O)($C_1$-$C_6$)alkyl, –$SO_2$($C_1$-$C_6$)alkyl, –$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;

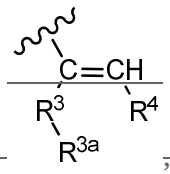
$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, –$SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

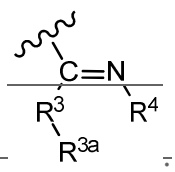
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, –$CF_3$, –$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, –C(O)$NH_2$, cyano, –NHC(O)($C_1$-$C_6$)alkyl, –$SO_2$($C_1$-$C_6$)alkyl, and –$SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, –$CH_2$OH, –CH(($C_1$-$C_6$)alkyl)OH, –CH($NH_2$)CH(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, –$CH_2$S($C_1$-$C_6$)alkyl, amino, or cyano; or –$CH_2$– fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent –NH– fused to the position *ortho* to X on that phenyl; and



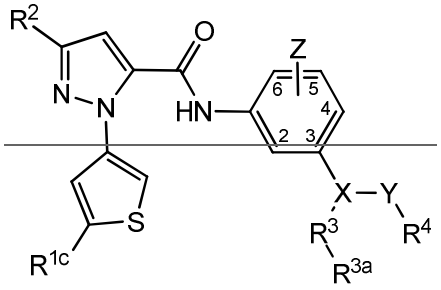
~~can represent~~ 

~~,~~ 

~~, or~~ 

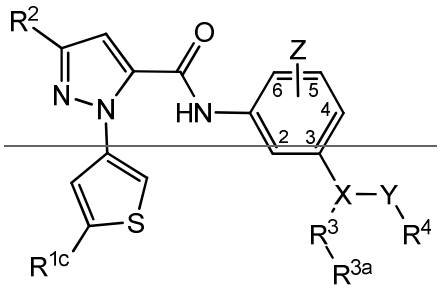
~~.~~

~~73. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula X:~~




~~(X).~~

~~74. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XI:~~




~~(XI)~~

~~wherein:~~

~~X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or O ;~~

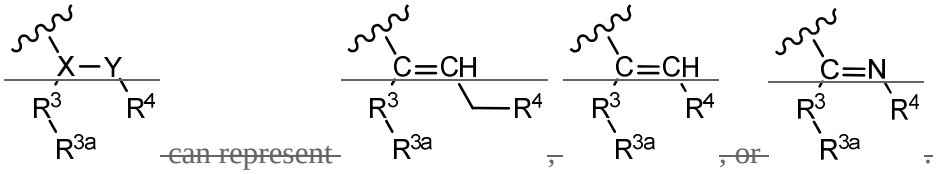
~~-Y-$R^4$, when present, represents -(($C_1$-$C_6$)alkyl)-$R^4$, -$CH_2$C(O)-$R^4$, -$CH_2$NH-$R^4$, -$CH_2$N(($C_1$-$C_6$)alkyl)-$R^4$, -$CR^aR^b$-$R^4$, -NH-$R^4$, -$NHCH_2$-$R^4$, -NHC(O)-$R^4$, -N(($C_1$-$C_6$)alkyl)-$R^4$, -N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, -N(($CH_2$)$_2$OH)-$R^4$, -N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, -heterocyclyl-$R^4$, -O$R^4$, -O$CH_2$-$R^4$, -OC(O)-$R^4$, -OC(O)$NR^aR^b$, -S$CH_2R^4$, or -S$R^4$, wherein the ($C_1$-$C_6$)alkyl moiety of -(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;~~

~~Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -O$CF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -S$O_2$($C_1$-$C_6$)alkyl, -S$O_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;~~

$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, $-SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

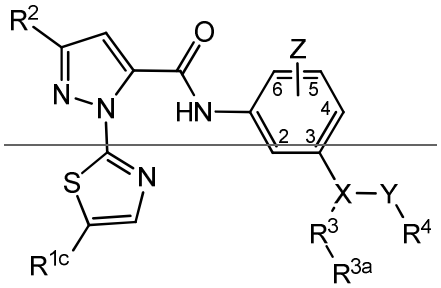
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, $-CF_3$, $-OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, $-C(O)NH_2$, cyano, $-NHC(O)$($C_1$-$C_6$)alkyl, $-SO_2$($C_1$-$C_6$)alkyl, and $-SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, $-CH_2OH$, $-CH$(($C_1$-$C_6$)alkyl)$OH$, $-CH(NH_2)CH$(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, $-CH_2S$($C_1$-$C_6$)alkyl, amino, or cyano; or $-CH_2-$ fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent $-NH-$ fused to the position *ortho* to X on that phenyl; and



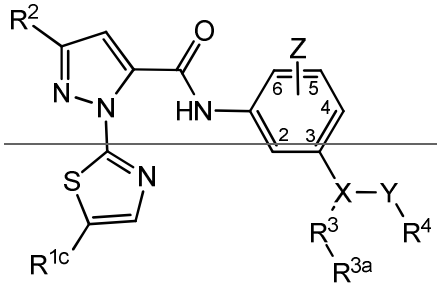
can represent , , or .

75. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XII:



(XII).

76. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XIII:



(XIII)

wherein:

X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or -O-;

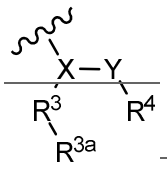
-Y-$R^4$, when present, represents -(($C_1$-$C_6$)alkyl)-$R^4$, -$CH_2$C(O)-$R^4$, -$CH_2$NH-$R^4$, -$CH_2$N(($C_1$-$C_6$)alkyl)-$R^4$, -$CR^aR^b$-$R^4$, -NH-$R^4$, -$NHCH_2$-$R^4$, -NHC(O)-$R^4$, -N(($C_1$-$C_6$)alkyl)-$R^4$, -N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, -N(($CH_2$)$_2$OH)-$R^4$, -N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, -heterocyclyl-$R^4$, -$OR^4$, -$OCH_2$-$R^4$, -OC(O)-$R^4$, -OC(O)$NR^aR^b$, -$SCH_2R^4$, or -$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of -(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;

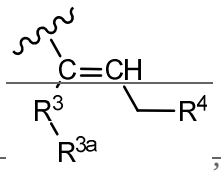
Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, -$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;

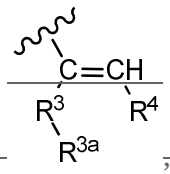
$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, -$SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

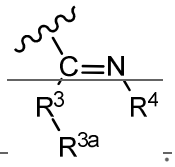
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, and -$SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, -$CH_2$OH, -CH(($C_1$-$C_6$)alkyl)OH, -CH($NH_2$)CH(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, -$CH_2$S($C_1$-$C_6$)alkyl, amino, or cyano; or -$CH_2$- fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent -NH- fused to the position *ortho* to X on that phenyl; and



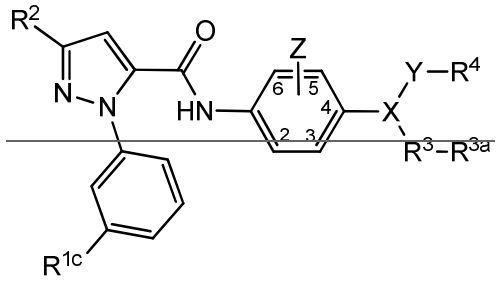
~~can represent~~ 

~~,~~ 

~~, or~~ 

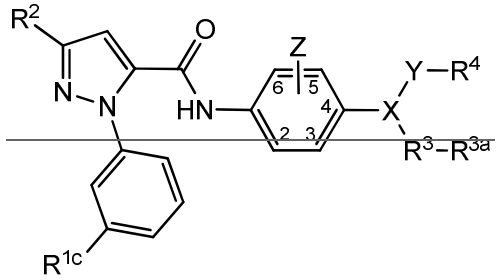
~~.~~

~~77. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XIV:~~




~~(XIV).~~

~~78. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XV:~~




~~(XV)~~

~~wherein:~~

~~X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or -O-;~~

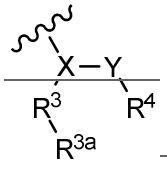
~~-Y-$R^4$, when present, represents -(($C_1$-$C_6$)alkyl)-$R^4$, -$CH_2$C(O)-$R^4$, -$CH_2$NH-$R^4$, -$CH_2$N(($C_1$-$C_6$)alkyl)-$R^4$, -$CR^aR^b$-$R^4$, -NH-$R^4$, -$NHCH_2$-$R^4$, -NHC(O)-$R^4$, -N(($C_1$-$C_6$)alkyl)-$R^4$, -N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, -N(($CH_2$)$_2$OH)-$R^4$, -N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, -heterocyclyl-$R^4$, -$OR^4$, -$OCH_2$-$R^4$, -OC(O)-$R^4$, -OC(O)$NR^aR^b$, -$SCH_2R^4$, or -$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of -(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;~~

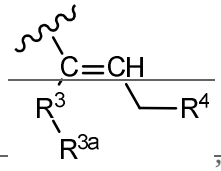
~~Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, -$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;~~

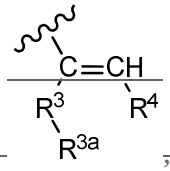
$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, $-SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

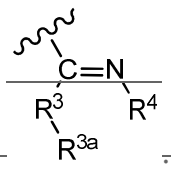
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, $-CF_3$, $-OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, $-C(O)NH_2$, cyano, $-NHC(O)$($C_1$-$C_6$)alkyl, $-SO_2$($C_1$-$C_6$)alkyl, and $-SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, $-CH_2OH$, $-CH$(($C_1$-$C_6$)alkyl)OH, $-CH(NH_2)CH$(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, $-CH_2S$($C_1$-$C_6$)alkyl, amino, or cyano; or $-CH_2-$ fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent $-NH-$ fused to the position *ortho* to X on that phenyl; and



can represent


,


, or


.

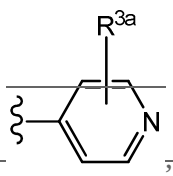
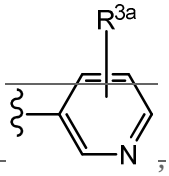
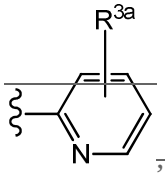
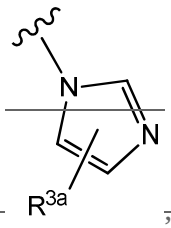
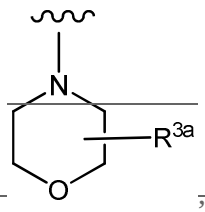
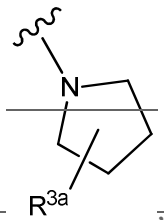
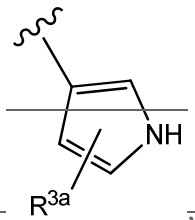
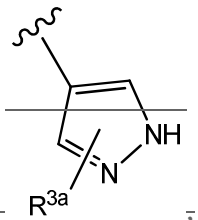
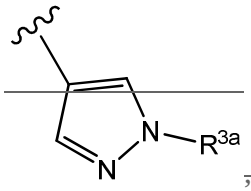
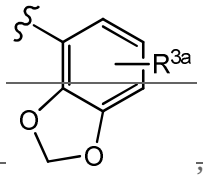
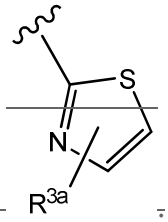
79. The compound of claim 78, wherein X represents CH, and both Y and $R^4$ are present.

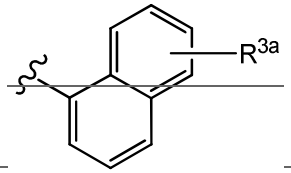
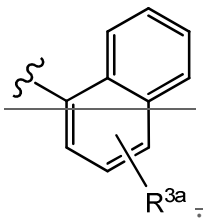
80. The compound of claim 78, wherein $-X-Y-$ represents $-CHNHCH_2-$.

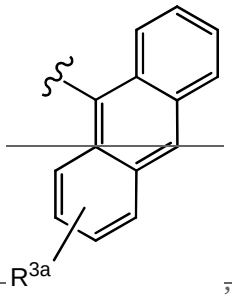
81. The compound of claim 78, wherein $-X-Y-$ represents $-C(OH)CH_2CH_2-$.

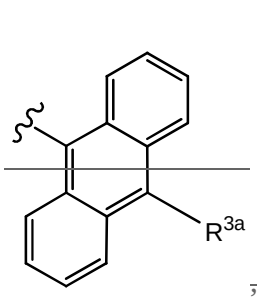
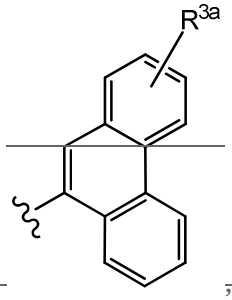
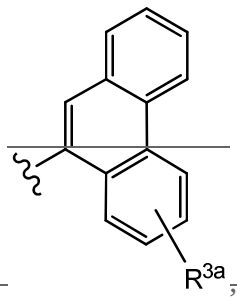
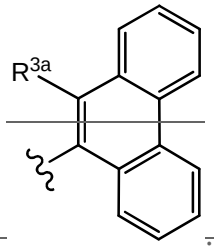
82. The compound of claim 78, wherein $-X-Y-$ represents $-CHOCH_2-$.

83. The compound of claim 78, wherein $R^3$ represents phenylene-$R^{3a}$.

84. The compound of claim 78, wherein $R^3$-$R^{3a}$ represents , , , , , , , , , , , or .

85. The compound of claim 78, wherein $R^3$-$R^{3a}$ represents  or .

86. The compound of claim 78, wherein $R^3$-$R^{3a}$ represents ;

, , , or .

87. The compound of claim 78, wherein $R^{3a}$ is absent.

88. The compound of claim 78, wherein $R^4$ is cyclopropyl.

89. The compound of claim 78, wherein $R^3$ is phenyl, and $R^{3a}$ is *ortho*, *meta*, or *para* -OH.

90. The compound of claim 78, wherein $R^3$ is phenyl, and $R^{3a}$ is *meta* or *para* -$NH_2$.

91. The compound of claim 78, wherein $R^3$ is phenyl, and $R^{3a}$ is *meta* or *para* -CN.

92. The compound of claim 78, wherein Z is absent.

93. The compound of claim 78, wherein Z represents fluoro.

94. The compound of claim 78, wherein Z represents chloro.

95. The compound of claim 78, wherein Z represents 2-F, 3-F, 5-F, 6-F, 6-Cl, or 5-($C_3$-$C_8$)cycloalkyl.

96. The compound of claim 78, wherein Z represents 6-F.

97. The compound of claim 78, wherein $R^{1c}$ represents aminomethyl.

98. The compound of claim 78, wherein $R^{1c}$ represents cyano.

99. The compound of claim 78, wherein $R^{1c}$ represents -$SO_2CH_3$.

100. The compound of any one of claims 78-99, wherein $R^2$ is -$CH_3$ or -$CF_3$.

101. The compound of any one of claims 78-99, wherein $R^2$ is -$CF_3$.

102. The compound of any one of claims 78-99, wherein $R^2$ is *tert*-butyl.

103. The compound of any one of claims 78-99, wherein $R^2$ is cyclopropyl.

104. The compound of any one of claims 78-99, wherein $R^2$ is -$OCH_3$.

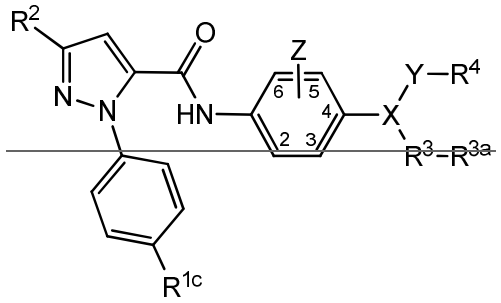
105. The compound of any one of claims 78-99, wherein $R^2$ is $-Si(CH_3)_3$.

106. The compound of any one of claims 78-99, wherein $R^2$ is $-CONH_2$.

107. The compound of any one of claims 78-99, wherein $R^2$ is cyano.

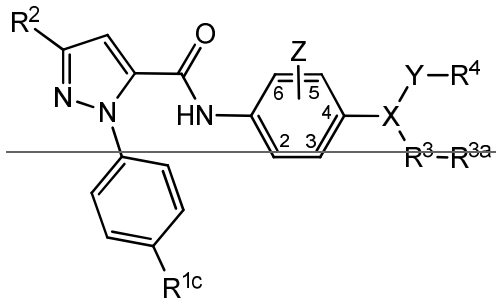
108. The compound of any one of claims 78-99, wherein $R^2$ is phenyl.

109. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XVI:




(XVI).

110. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XVII:




(XVII)

wherein:

X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2N$, N, C(O), or O;

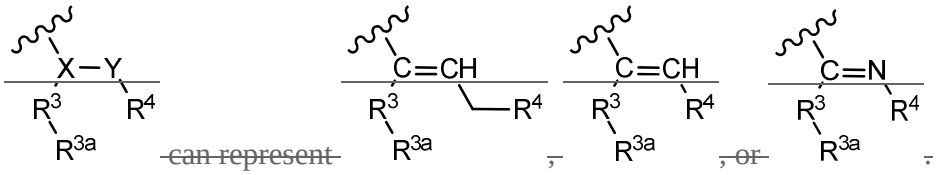
-Y-$R^4$, when present, represents -(($C_1$-$C_6$)alkyl)-$R^4$, -$CH_2C(O)$-$R^4$, -$CH_2NH$-$R^4$, -$CH_2N$(($C_1$-$C_6$)alkyl)-$R^4$, -$CR^aR^b$-$R^4$, -NH-$R^4$, -$NHCH_2$-$R^4$, -NHC(O)-$R^4$, -N(($C_1$-$C_6$)alkyl)-$R^4$, -N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, -N(($CH_2$)$_2$OH)-$R^4$, -N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, -heterocyclyl-$R^4$, -$OR^4$, -$OCH_2$-$R^4$, -OC(O)-$R^4$, -$OC(O)NR^aR^b$, -$SCH_2R^4$, or -$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of -(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;

~~Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, $-CF_3$, $-OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, $-C(O)NH_2$, cyano, $-NHC(O)(C_1$-$C_6$)alkyl, $-SO_2(C_1$-$C_6$)alkyl, $-SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;~~

~~$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, $-SO_2CH_3$, formyl, acyl, or optionally substituted aryl;~~

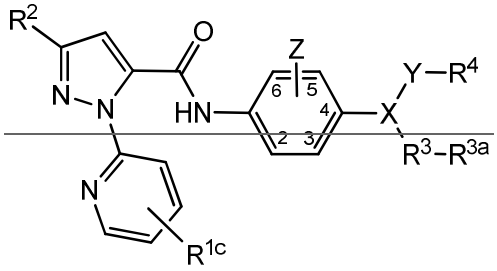
~~$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, $-CF_3$, $-OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, $-C(O)NH_2$, cyano, $-NHC(O)(C_1$-$C_6$)alkyl, $-SO_2(C_1$-$C_6$)alkyl, and $-SO_2NH_2$;~~

~~$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, $-CH_2OH$, $-CH((C_1$-$C_6$)alkyl)OH, $-CH(NH_2)CH((C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, $-CH_2S(C_1$-$C_6$)alkyl, amino, or cyano; or $-CH_2-$ fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent $-NH-$ fused to the position *ortho* to X on that phenyl; and~~



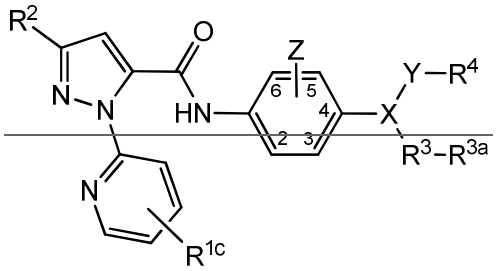
~~can represent~~ , ~~or~~ .

~~111. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XVIII:~~



~~(XVIII).~~

~~112. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XIX:~~



(XIX)

wherein:

X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or -O-;

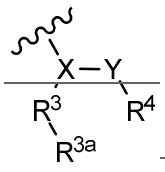
-Y-$R^4$, when present, represents -(($C_1$-$C_6$)alkyl)-$R^4$, -$CH_2$C(O)-$R^4$, -$CH_2$NH-$R^4$, -$CH_2$N(($C_1$-$C_6$)alkyl)-$R^4$, -$CR^aR^b$-$R^4$, -NH-$R^4$, -$NHCH_2$-$R^4$, -NHC(O)-$R^4$, -N(($C_1$-$C_6$)alkyl)-$R^4$, -N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, -N(($CH_2$)$_2$OH)-$R^4$, -N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, -heterocyclyl-$R^4$, -$OR^4$, -$OCH_2$-$R^4$, -OC(O)-$R^4$, -$OC(O)NR^aR^b$, -$SCH_2R^4$, or -$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of -(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;

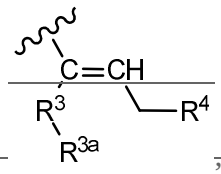
Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, -$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;

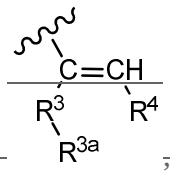
$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, -$SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

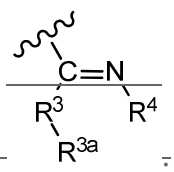
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, and -$SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, -$CH_2OH$, -CH(($C_1$-$C_6$)alkyl)OH, -$CH(NH_2)CH$(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, -$CH_2$S($C_1$-$C_6$)alkyl, amino, or cyano; or -$CH_2$- fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent -NH- fused to the position *ortho* to X on that phenyl; and



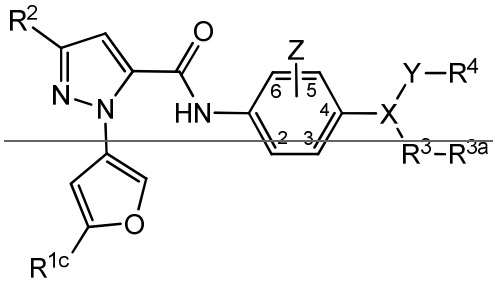
~~can represent~~


~~,~~


~~, or~~


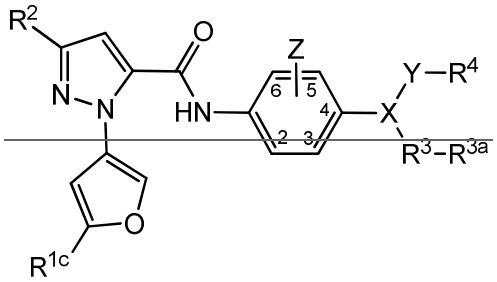
~~.~~

~~113. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XX:~~




~~(XX).~~

~~114. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XXI:~~




~~(XXI)~~

~~wherein:~~

~~X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or –O–;~~

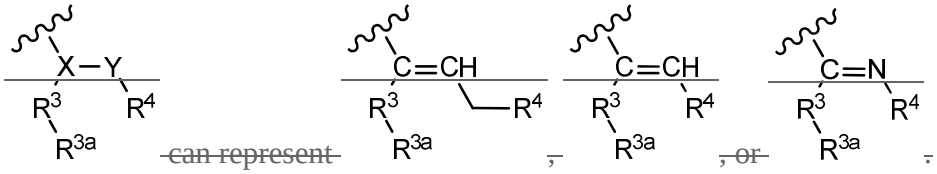
~~–Y–$R^4$, when present, represents –(($C_1$-$C_6$)alkyl)–$R^4$, –$CH_2$C(O)–$R^4$, –$CH_2$NH–$R^4$, –$CH_2$N(($C_1$-$C_6$)alkyl)–$R^4$, –$CR^aR^b$–$R^4$, –NH–$R^4$, –$NHCH_2$–$R^4$, –NHC(O)–$R^4$, –N(($C_1$-$C_6$)alkyl)–$R^4$, –N(($C_1$-$C_6$)alkyl)$CH_2$–$R^4$, –N(($CH_2$)$_2$OH)–$R^4$, –N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, –heterocyclyl–$R^4$, –$OR^4$, –$OCH_2$–$R^4$, –OC(O)–$R^4$, –OC(O)$NR^aR^b$, –$SCH_2R^4$, or –$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of –(($C_1$-$C_6$)alkyl)–$R^4$ is optionally substituted;~~

~~Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, –$CF_3$, –$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, –C(O)$NH_2$, cyano, –NHC(O)($C_1$-$C_6$)alkyl, –$SO_2$($C_1$-$C_6$)alkyl, –$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;~~

$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, $-SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

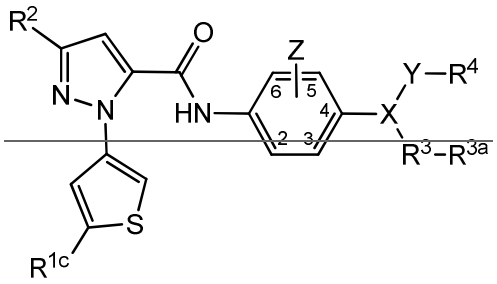
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, $-CF_3$, $-OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, $-C(O)NH_2$, cyano, $-NHC(O)$($C_1$-$C_6$)alkyl, $-SO_2$($C_1$-$C_6$)alkyl, and $-SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, $-CH_2OH$, $-CH$(($C_1$-$C_6$)alkyl)$OH$, $-CH(NH_2)CH$(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, $-CH_2S$($C_1$-$C_6$)alkyl, amino, or cyano; or $-CH_2-$ fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent $-NH-$ fused to the position *ortho* to X on that phenyl; and



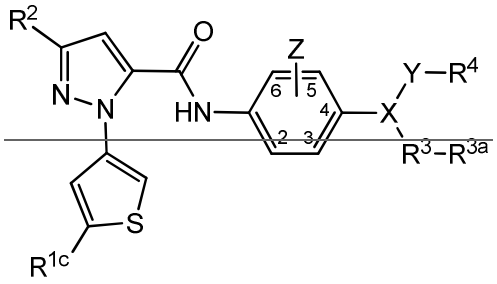
can represent , , or .

115. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XXII:



(XXII).

116. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XXIII:



(XXIII)

wherein:

X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or –O–;

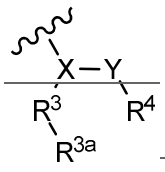
–Y–$R^4$, when present, represents –(($C_1$-$C_6$)alkyl)-$R^4$, –$CH_2$C(O)-$R^4$, –$CH_2$NH-$R^4$, –$CH_2$N(($C_1$-$C_6$)alkyl)-$R^4$, –$CR^aR^b$-$R^4$, –NH-$R^4$, –$NHCH_2$-$R^4$, –NHC(O)-$R^4$, –N(($C_1$-$C_6$)alkyl)-$R^4$, –N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, –N(($CH_2$)$_2$OH)-$R^4$, –N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, –heterocyclyl-$R^4$, –$OR^4$, –$OCH_2$-$R^4$, –OC(O)-$R^4$, –OC(O)$NR^aR^b$, –$SCH_2R^4$, or –$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of –(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;

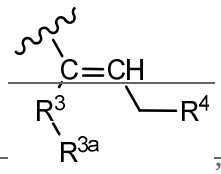
Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, –$CF_3$, –$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, –C(O)$NH_2$, cyano, –NHC(O)($C_1$-$C_6$)alkyl, –$SO_2$($C_1$-$C_6$)alkyl, –$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;

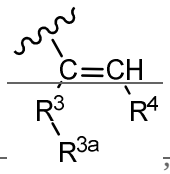
$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, –$SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

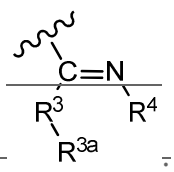
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, –$CF_3$, –$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, –C(O)$NH_2$, cyano, –NHC(O)($C_1$-$C_6$)alkyl, –$SO_2$($C_1$-$C_6$)alkyl, and –$SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, –$CH_2$OH, –CH(($C_1$-$C_6$)alkyl)OH, –$CH(NH_2)CH((C_1$-$C_6)alkyl)_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, –$CH_2$S($C_1$-$C_6$)alkyl, amino, or cyano; or –$CH_2$– fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent –NH– fused to the position *ortho* to X on that phenyl; and



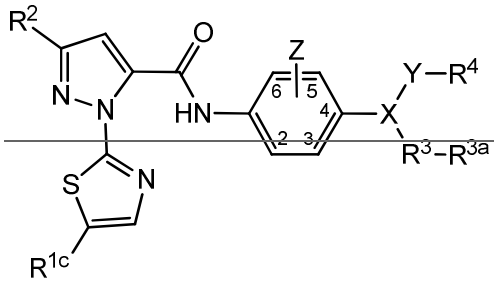
~~can represent~~


~~,~~


~~, or~~


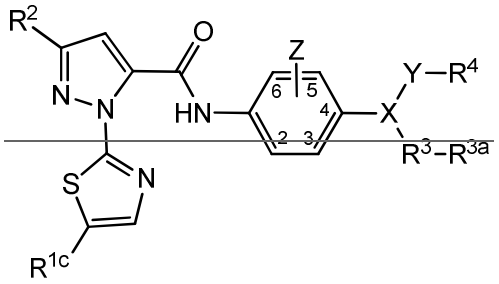
~~.~~

~~117. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XXIV:~~




~~(XXIV).~~

~~118. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XXV:~~




~~(XXV)~~

~~wherein:~~

~~X represents CH, C(OH), C(O($C_1$-$C_6$)alkyl), C(O)N, $CH_2$N, N, C(O), or –O–;~~

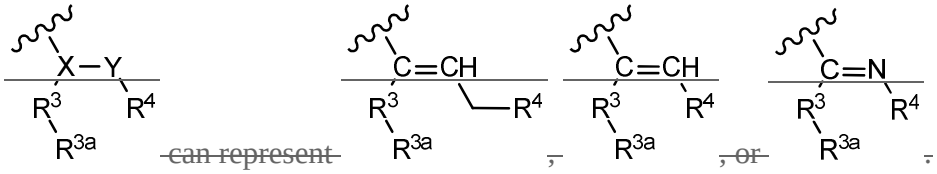
~~–Y–$R^4$, when present, represents –(($C_1$-$C_6$)alkyl)–$R^4$, –$CH_2$C(O)–$R^4$, –$CH_2$NH–$R^4$, –$CH_2$N(($C_1$-$C_6$)alkyl)–$R^4$, –$CR^aR^b$–$R^4$, –NH–$R^4$, –$NHCH_2$–$R^4$, –NHC(O)–$R^4$, –N(($C_1$-$C_6$)alkyl)–$R^4$, –N(($C_1$-$C_6$)alkyl)$CH_2$–$R^4$, –N(($CH_2$)$_2$OH)–$R^4$, –N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, –heterocyclyl–$R^4$, –$OR^4$, –$OCH_2$–$R^4$, –OC(O)–$R^4$, –OC(O)$NR^aR^b$, –$SCH_2R^4$, or –$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of –(($C_1$-$C_6$)alkyl)–$R^4$ is optionally substituted;~~

~~Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, –$CF_3$, –$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, –C(O)$NH_2$, cyano, –NHC(O)($C_1$-$C_6$)alkyl, –$SO_2$($C_1$-$C_6$)alkyl, –$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;~~

$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, $-SO_2CH_3$, formyl, acyl, or optionally substituted aryl;

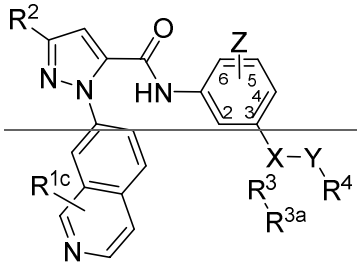
$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, $-CF_3$, $-OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, $-C(O)NH_2$, cyano, $-NHC(O)$($C_1$-$C_6$)alkyl, $-SO_2$($C_1$-$C_6$)alkyl, and $-SO_2NH_2$;

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, $-CH_2OH$, $-CH$(($C_1$-$C_6$)alkyl)OH, $-CH(NH_2)CH$(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, $-CH_2S$($C_1$-$C_6$)alkyl, amino, or cyano; or $-CH_2-$ fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent $-NH-$ fused to the position *ortho* to X on that phenyl; and



can represent , , , or .

119. The compound of claim 1, or a pharmaceutically acceptable salt thereof, represented by formula XXVI:



(XXVI)

wherein:

X represents CH, C(OH), $-C(NH_2)$, or $-C(NR^aR^b)$;

$-Y-R^4$, when present, represents $-$(($C_1$-$C_6$)alkyl)-$R^4$, $-CH_2C(O)-R^4$, $-CH_2NH-R^4$, $-CH_2N$(($C_1$-$C_6$)alkyl)-$R^4$, $-CR^aR^b-R^4$, $-NH-R^4$, $-NHCH_2-R^4$, $-NHC(O)-R^4$, $-N$(($C_1$-$C_6$)alkyl)-$R^4$, $-N$(($C_1$-$C_6$)alkyl)$CH_2-R^4$, $-N$(($CH_2$)$_2$OH)-$R^4$, $-N$[($C_3$-$C_8$)cycloalkyl($C_1$-

~~$C_6$)alkyl]$R^4$, -heterocyclyl-$R^4$, -$OR^4$, -$OCH_2$-$R^4$, -OC(O)-$R^4$, -OC(O)$NR^aR^b$, -$SCH_2R^4$, or -$SR^4$, wherein the ($C_1$-$C_6$)alkyl moiety of -(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;~~

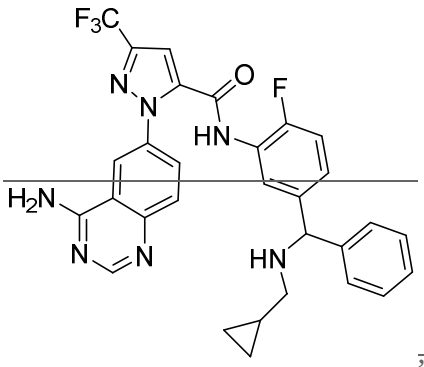
~~Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, -$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;~~

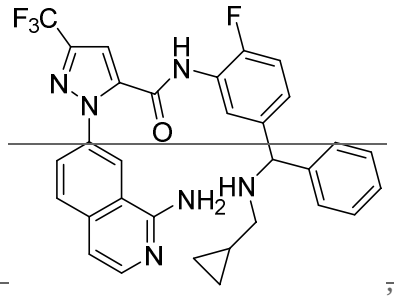
~~$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, -$SO_2CH_3$, formyl, acyl, -$NH_2$, or optionally substituted aryl;~~

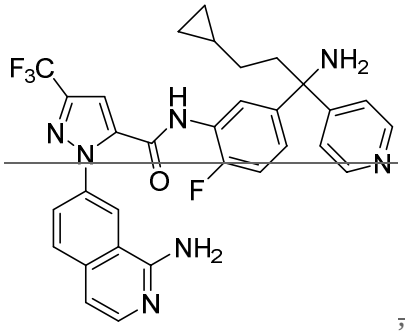
~~$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, and -$SO_2NH_2$; and~~

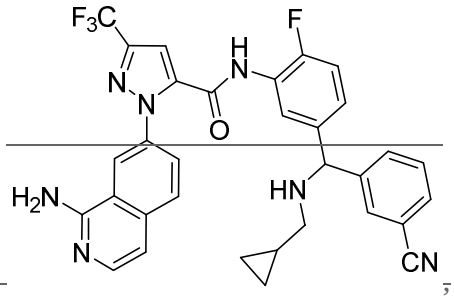
~~$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, -$CH_2OH$, -CH(($C_1$-$C_6$)alkyl)OH, -$CH(NH_2)CH((C_1$-$C_6)alkyl)_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, -$CH_2$S($C_1$-$C_6$)alkyl, amino, or cyano; or -$CH_2$- fused to the 4-position of the ring bearing Z to form a 5- to 7-membered heterocyclic ring with optional substituents; or, when $R^3$ is phenyl, can represent -NH- fused to the position *ortho* to X on that phenyl.~~

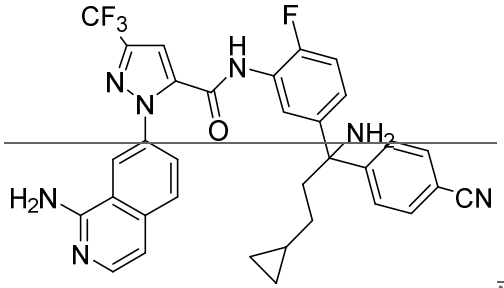
~~120. The compound of claim 119, wherein said compound is selected from the group consisting of:~~

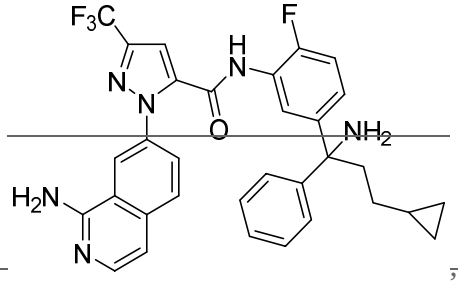


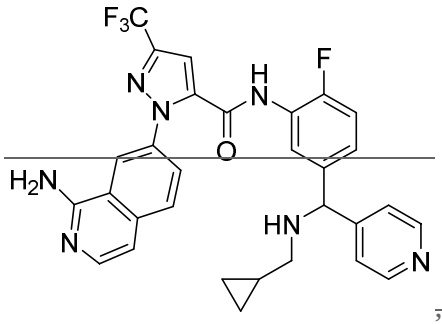


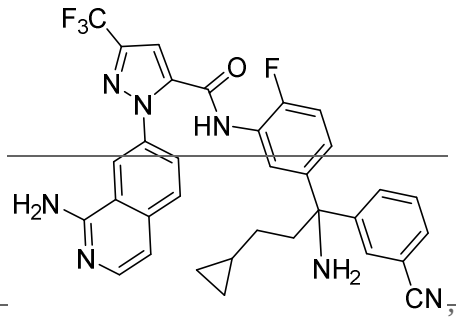


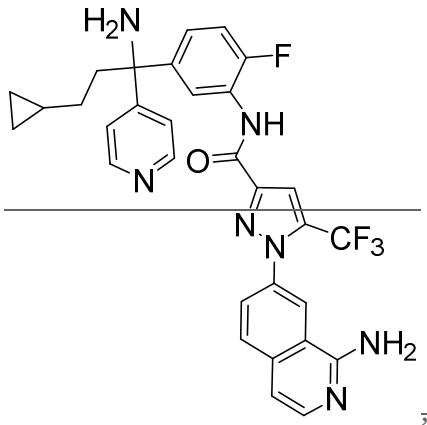




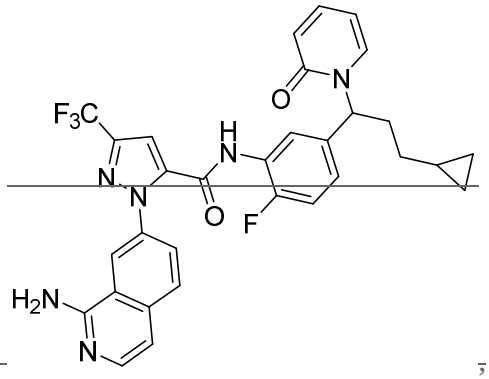




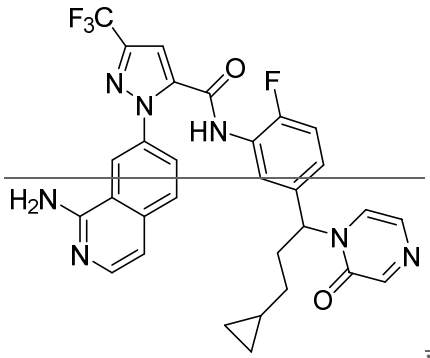




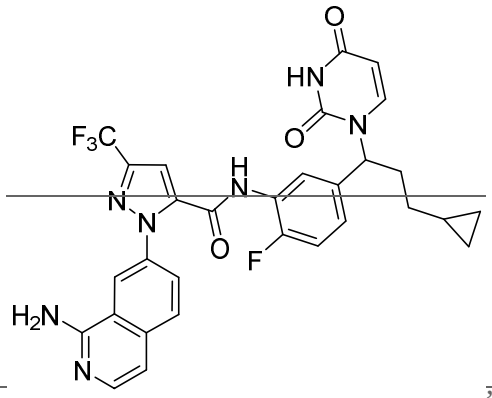
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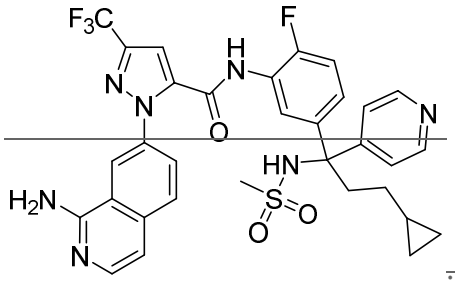
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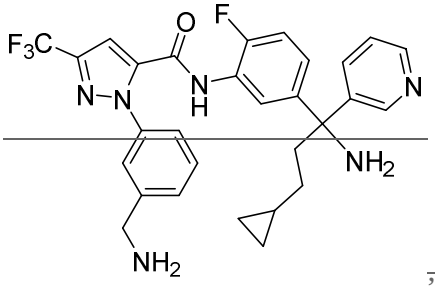


, and

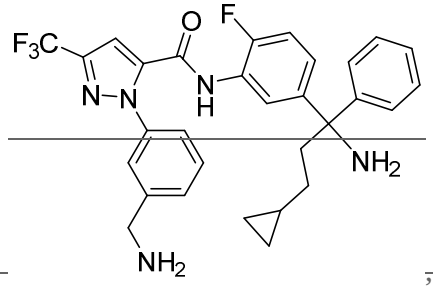


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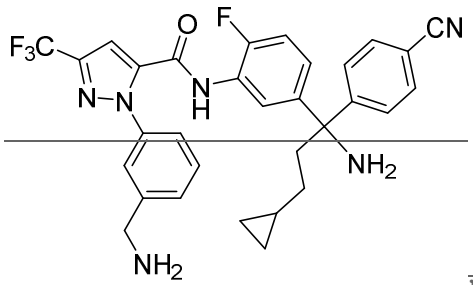
~~121. The compound of claim 1, wherein said compound is selected from the group consisting of:~~



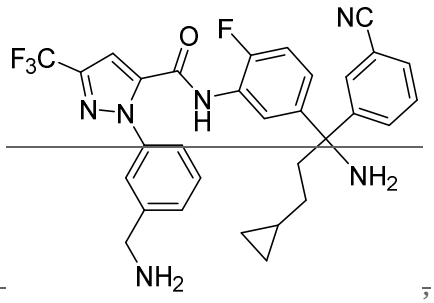
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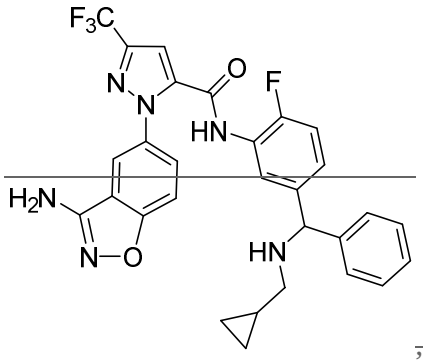
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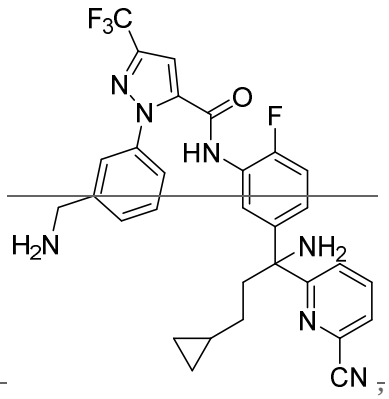
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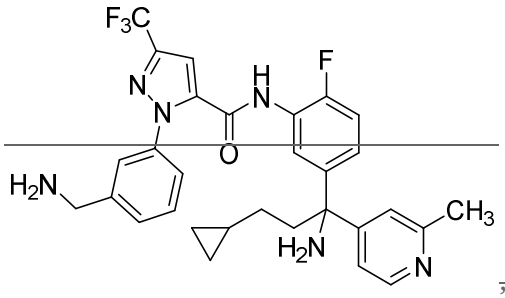
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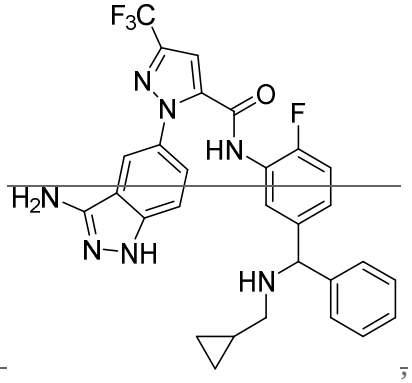
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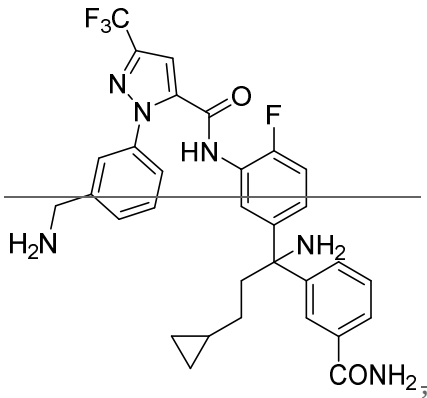
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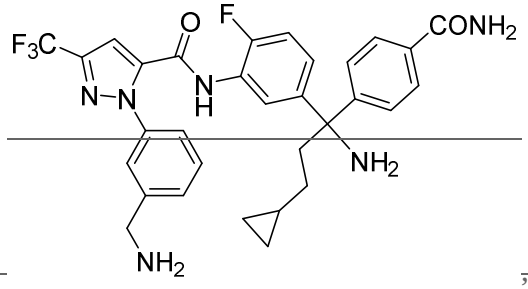
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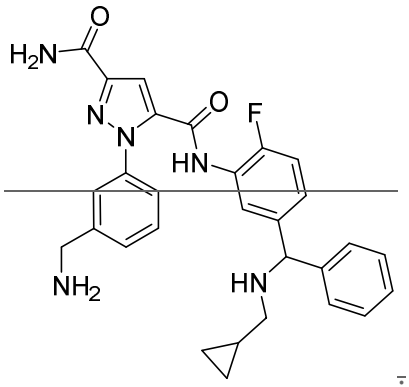
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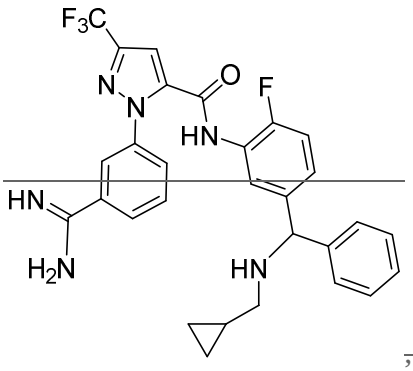


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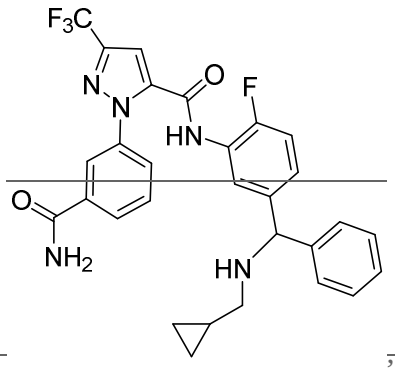


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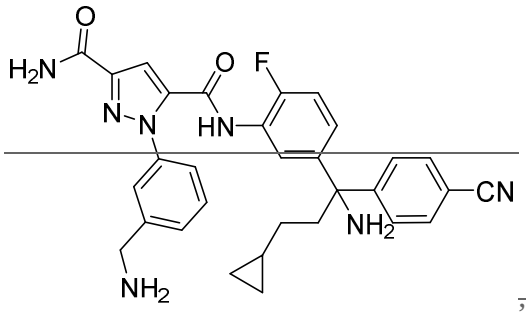
~~122. The compound of claim 1, wherein said compound is selected from the group consisting of:~~



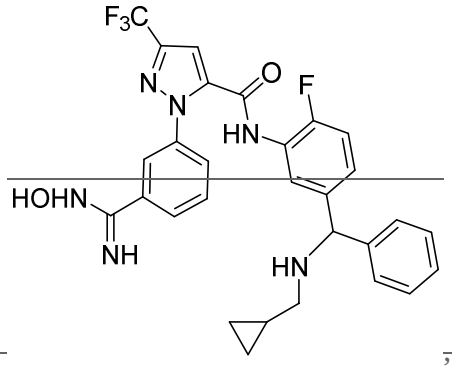
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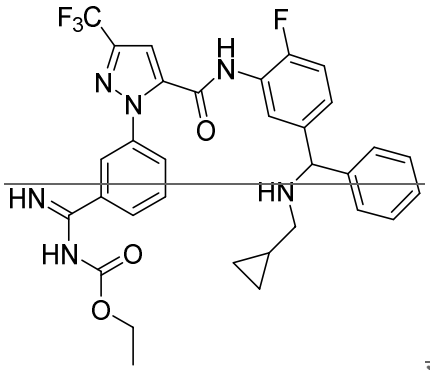
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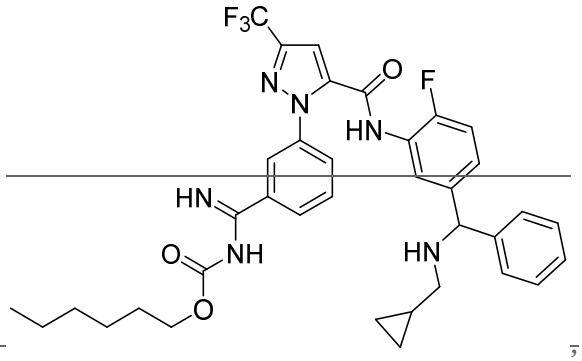
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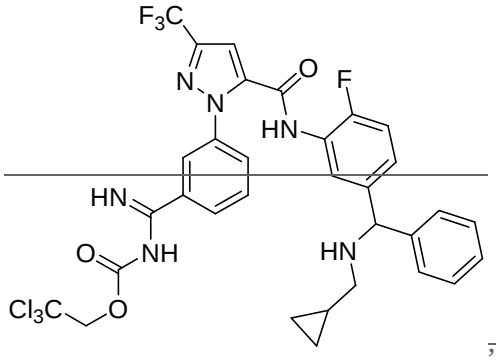
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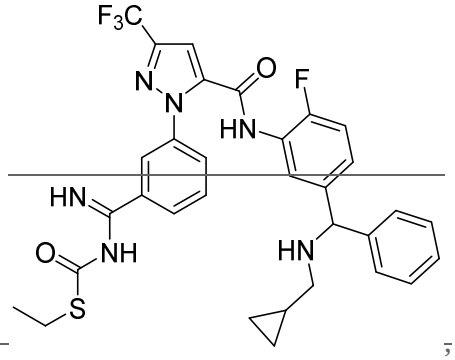
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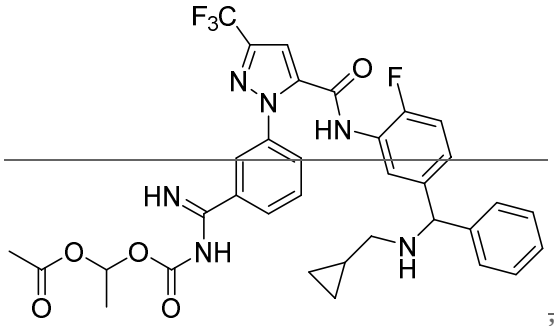
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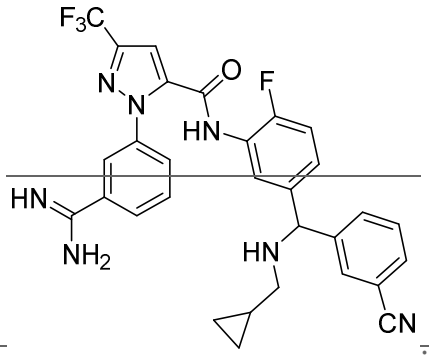


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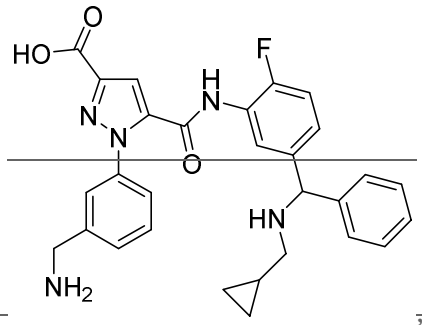
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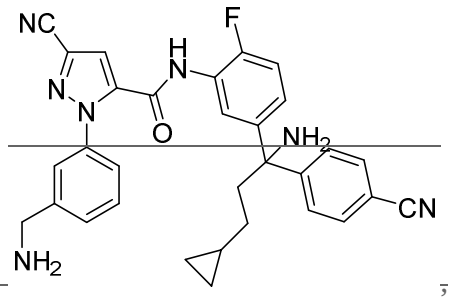



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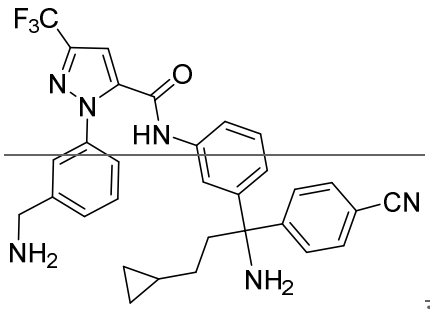
123. The compound of claim 1, wherein said compound is selected from the group consisting of:



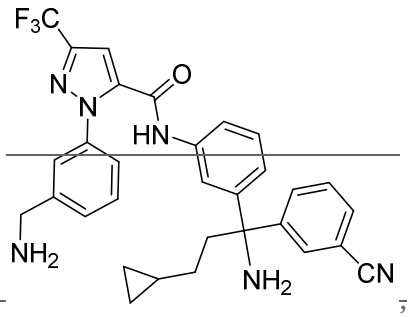
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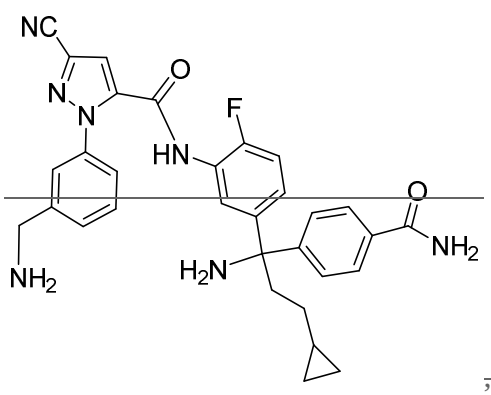
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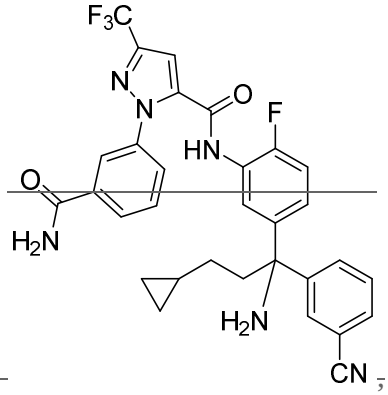


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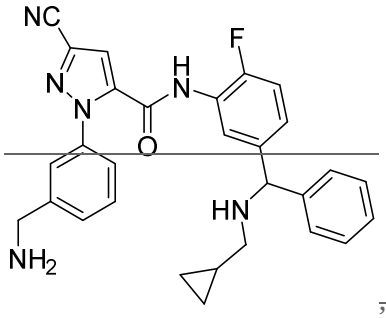


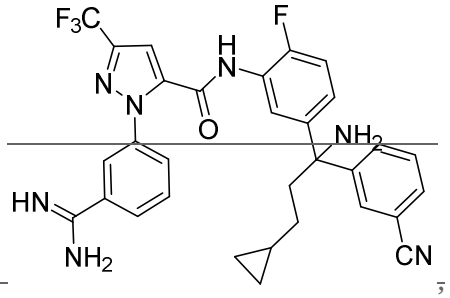
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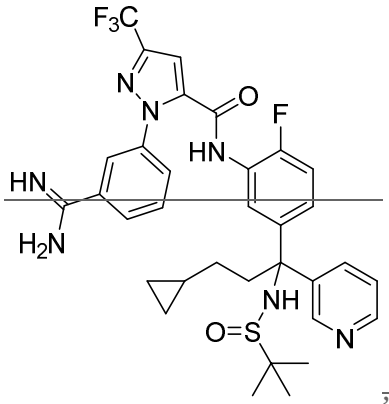
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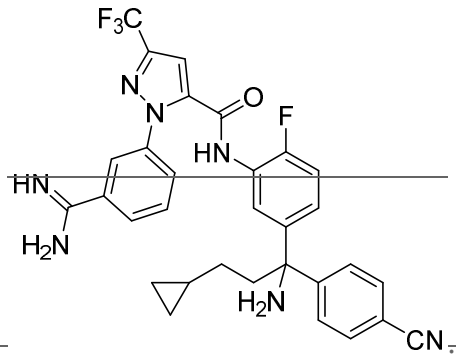




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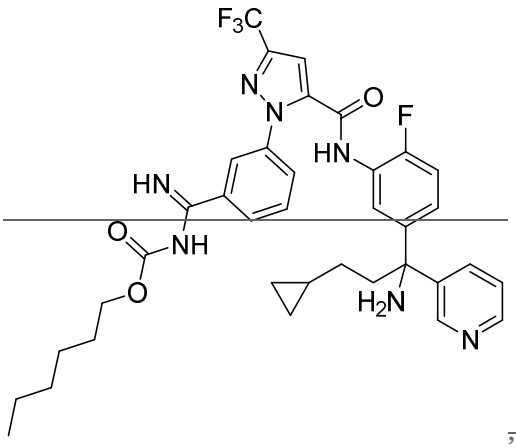
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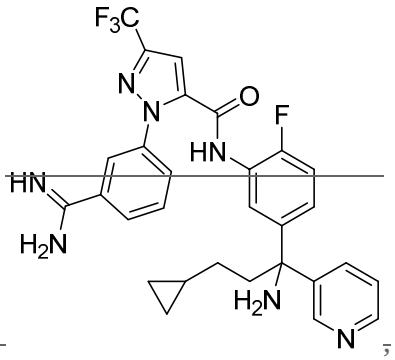


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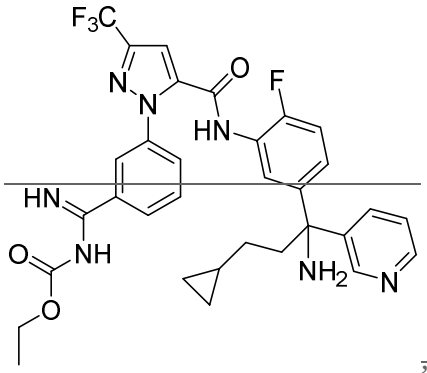
124. The compound of claim 1, wherein said compound is selected from the group consisting of:


F3C
N
N
O
F
HN
HN
O
NH
O
H2N
N

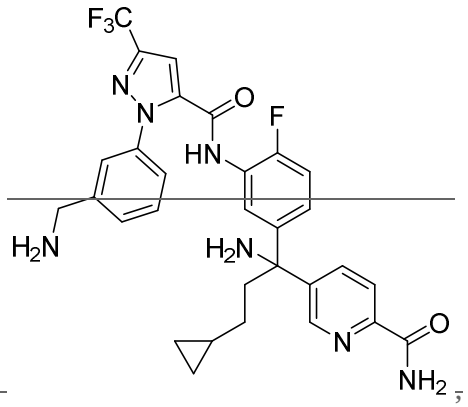
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F3C
N
N
O
F
HN
HN
H2N
H2N
N

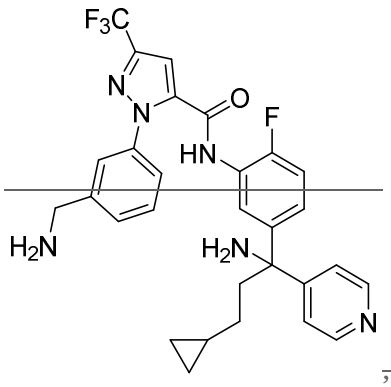
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F3C
N
N
O
F
HN
HN
O
NH
O
NH2
N

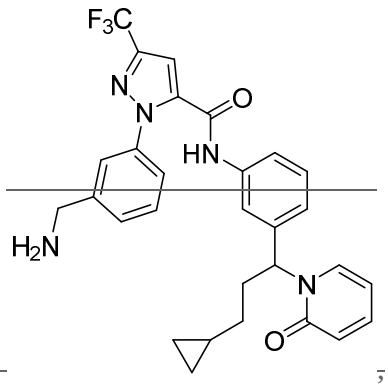
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F3C
N
N
O
F
HN
H2N
H2N
N
O
NH2

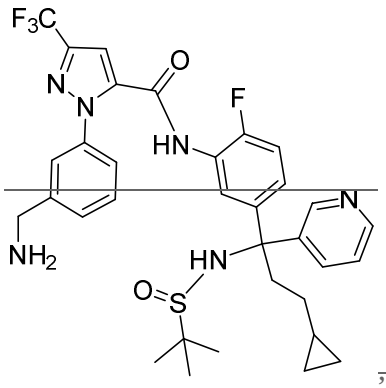
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F3C
N
N
O
F
HN
H2N
H2N
N

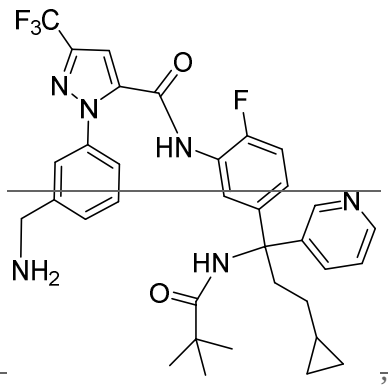
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F3C
N
N
O
HN
H2N
N
O

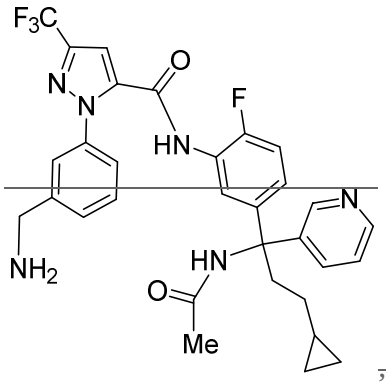
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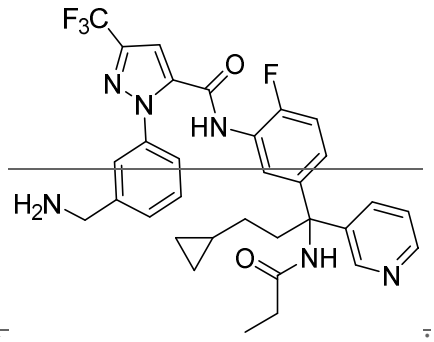
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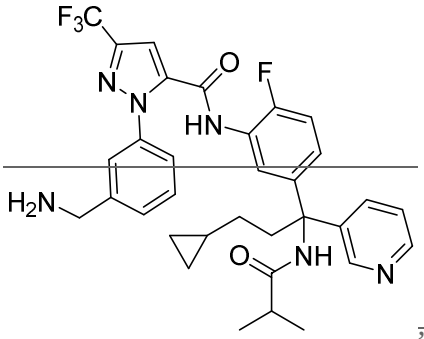


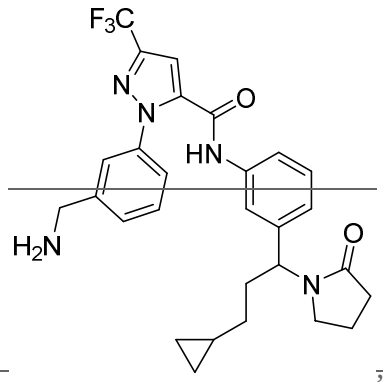
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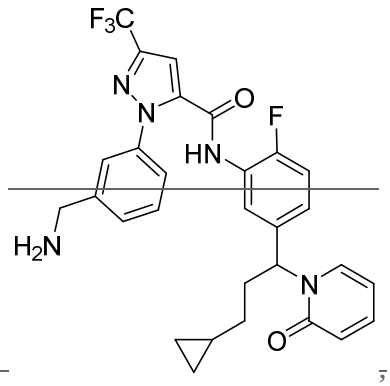


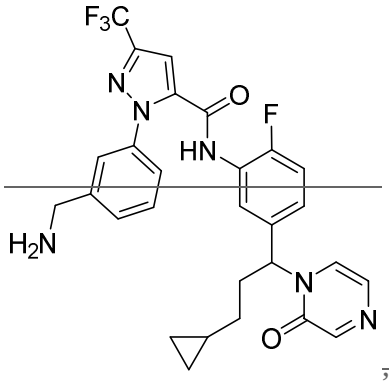
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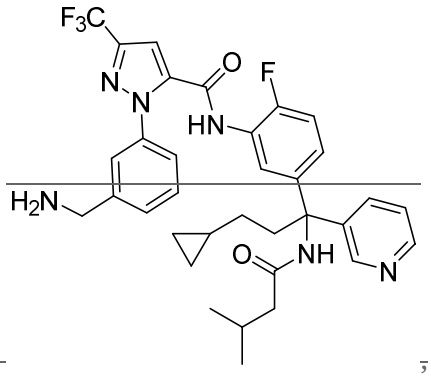
~~125. The compound of claim 1, wherein said compound is selected from the group consisting of:~~

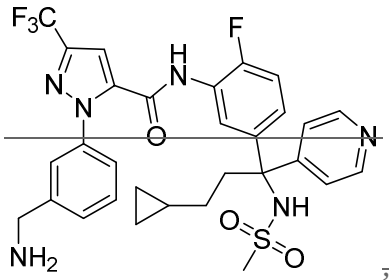


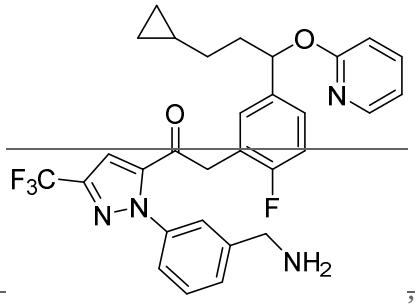


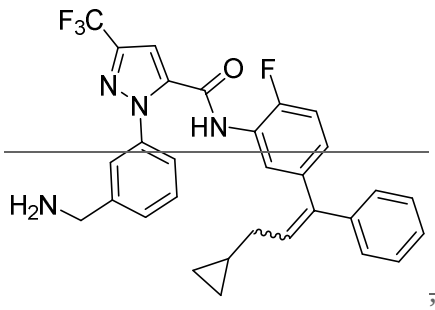


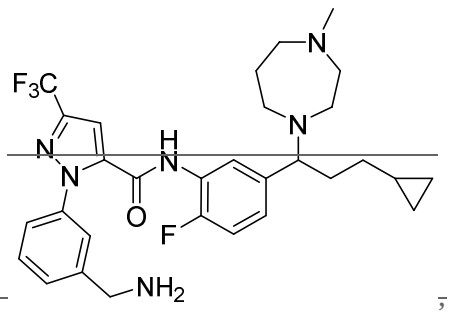


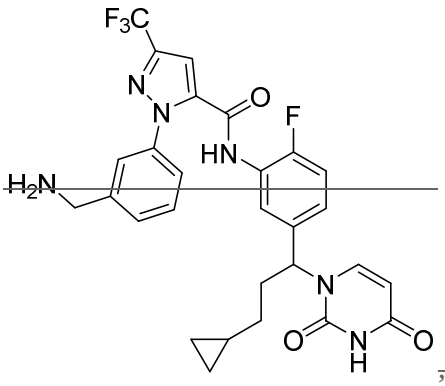




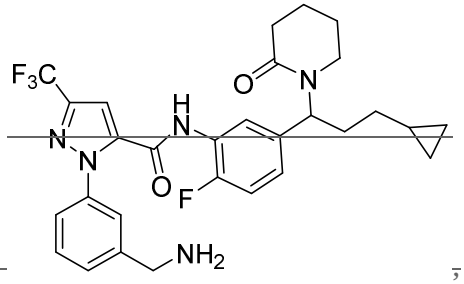




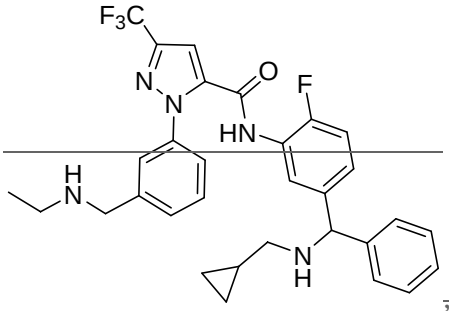




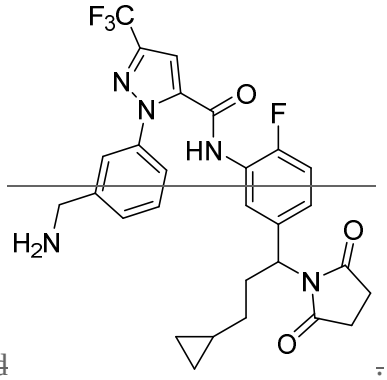
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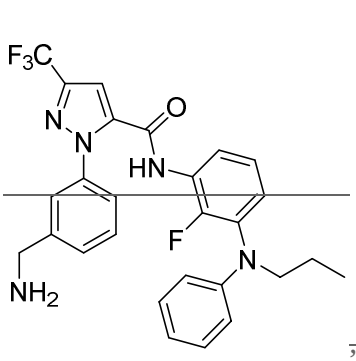


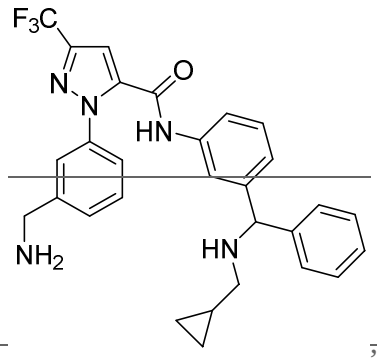
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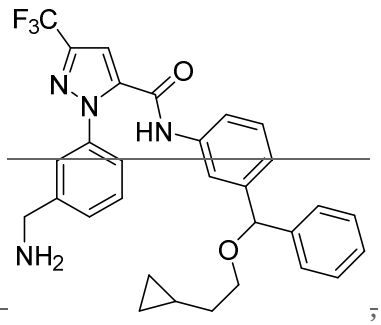


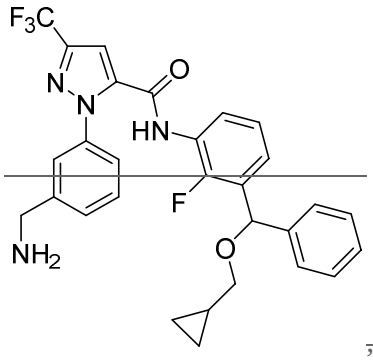
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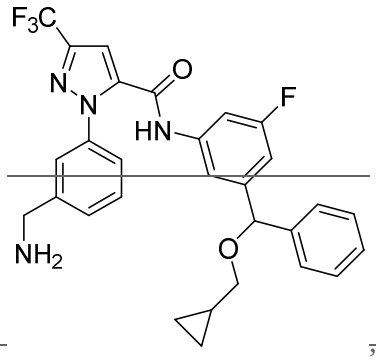
~~126. The compound of claim 1, wherein said compound is selected from the group consisting of:~~

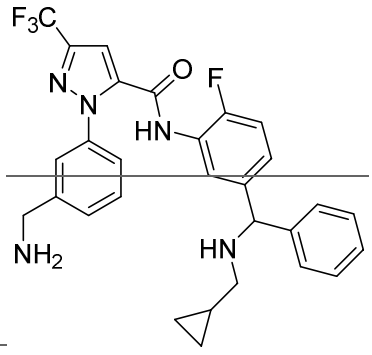

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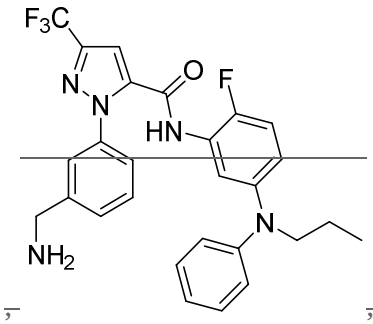

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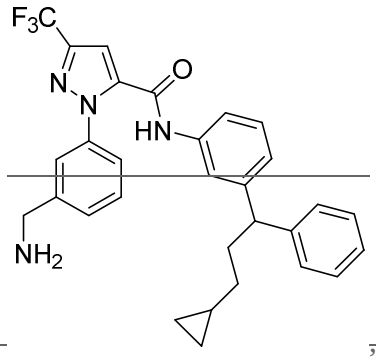

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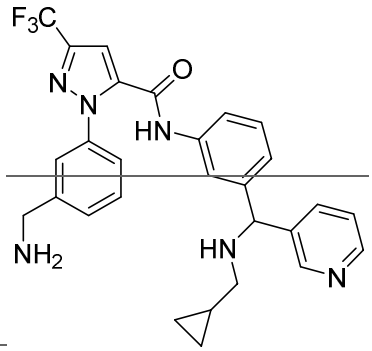

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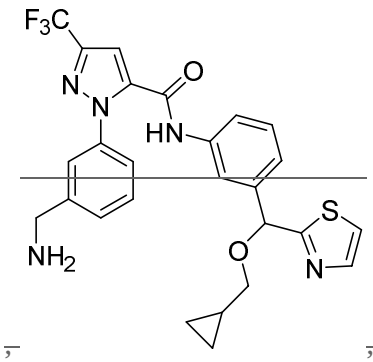

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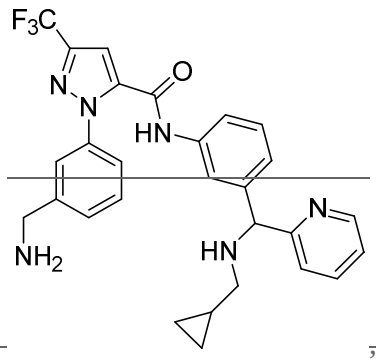

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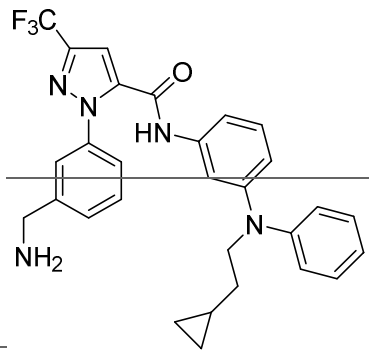

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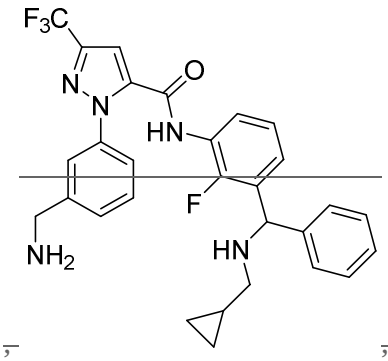
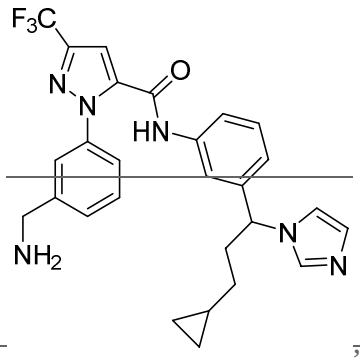
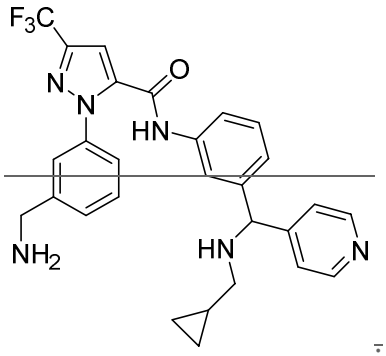

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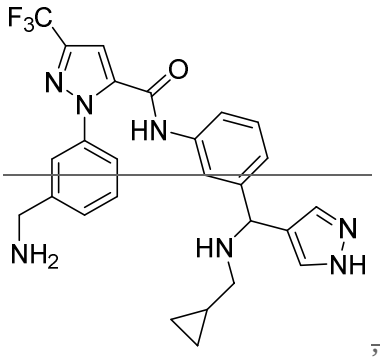
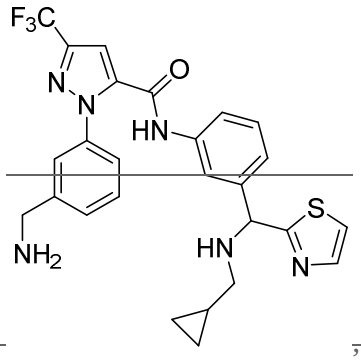
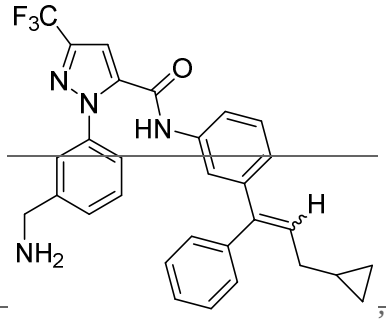
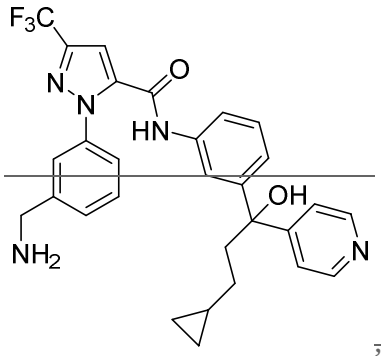
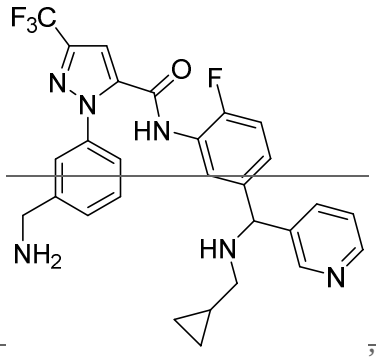

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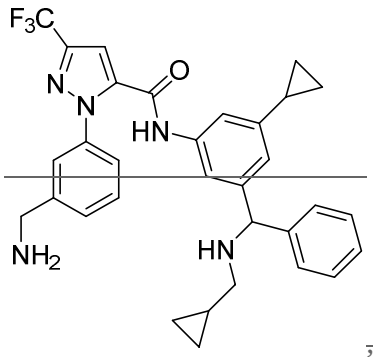
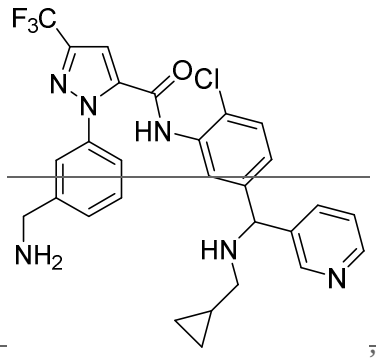
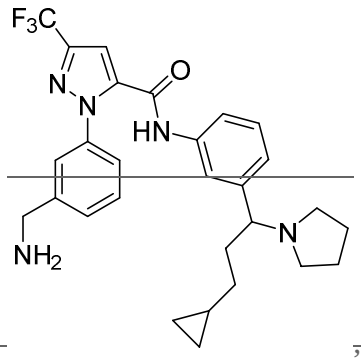

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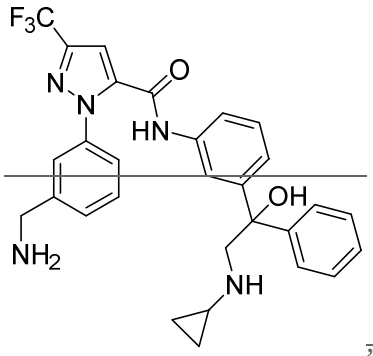
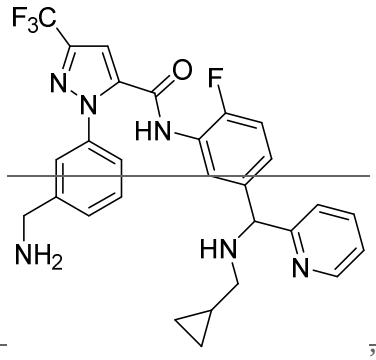
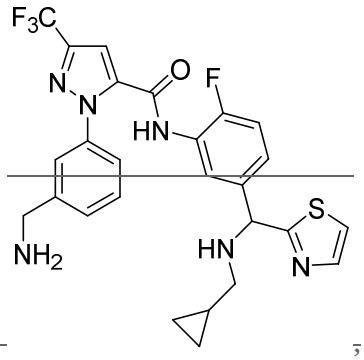

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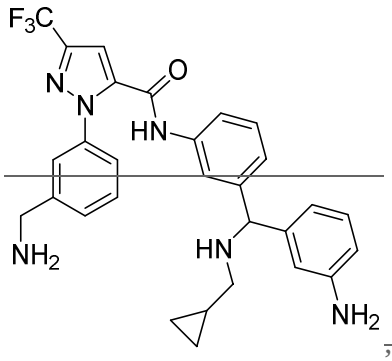
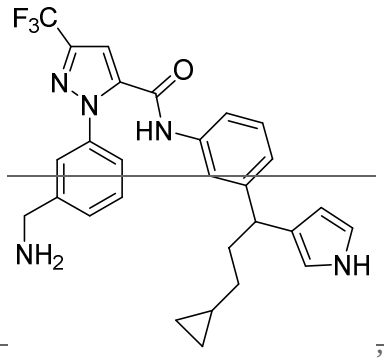




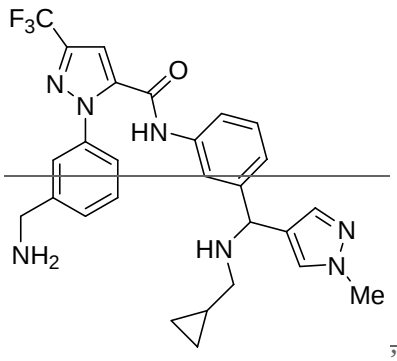
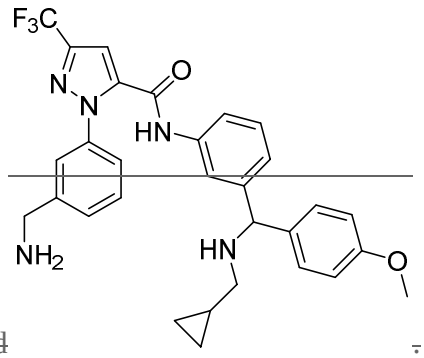
~~127. The compound of claim 1, wherein said compound is selected from the group consisting of:~~

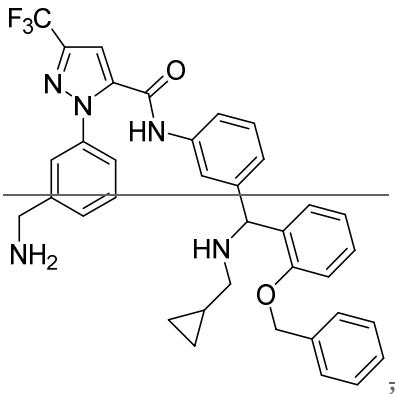
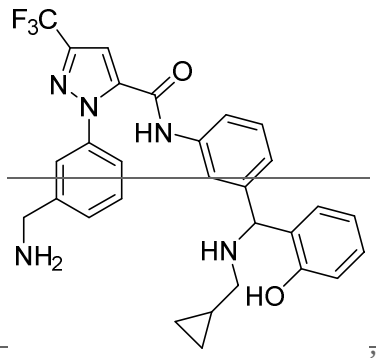
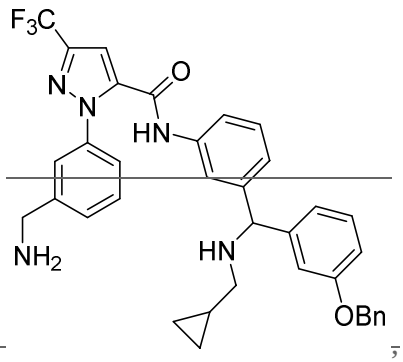
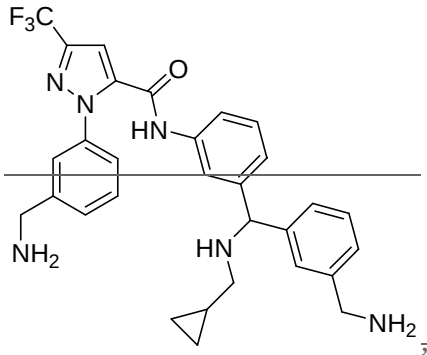
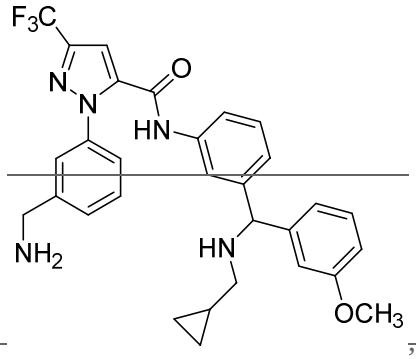
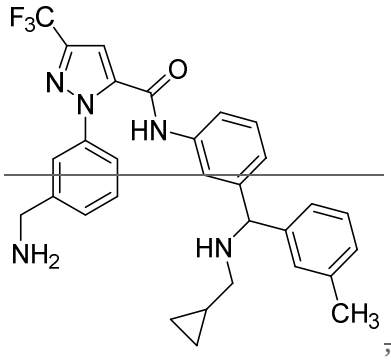
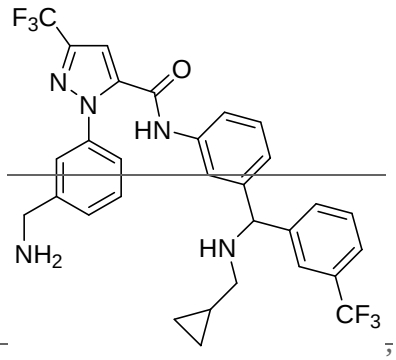
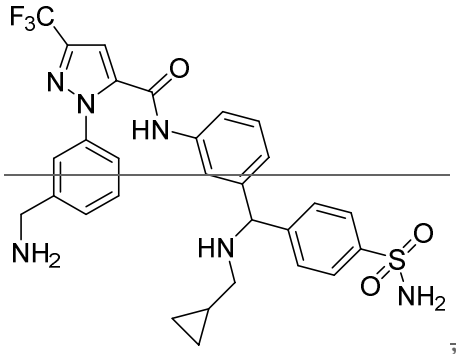
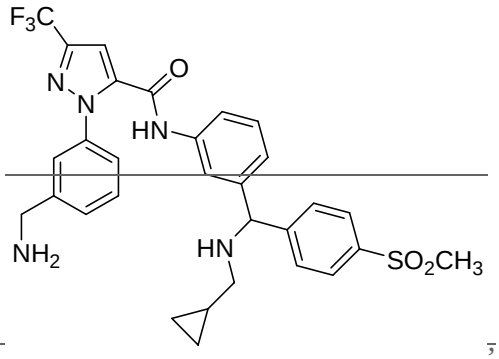




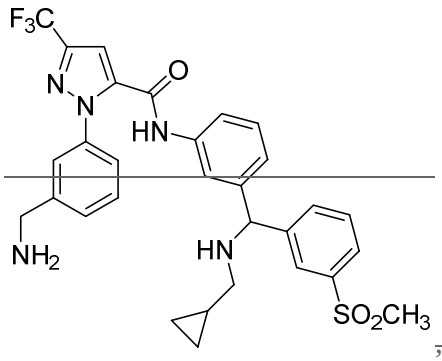



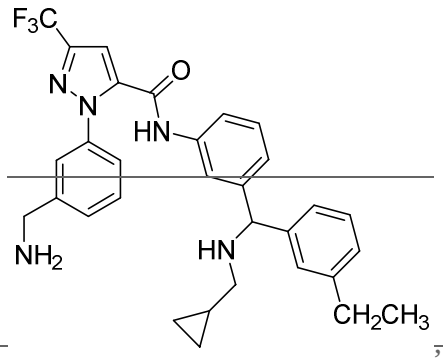
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128. The compound of claim 1, wherein said compound is selected from the group consisting of:

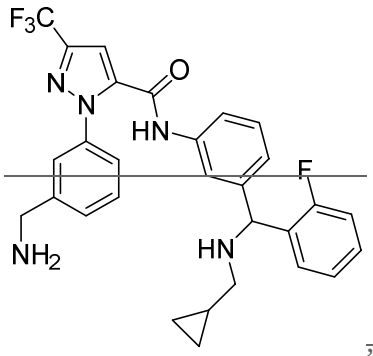












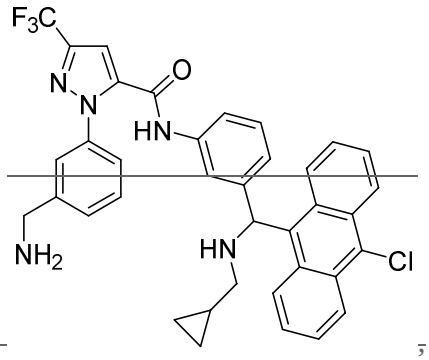
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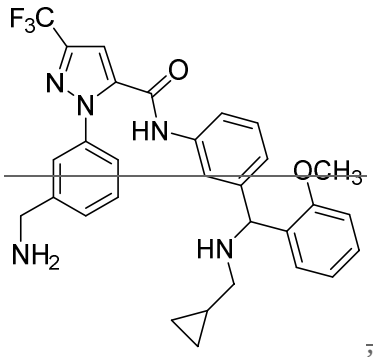
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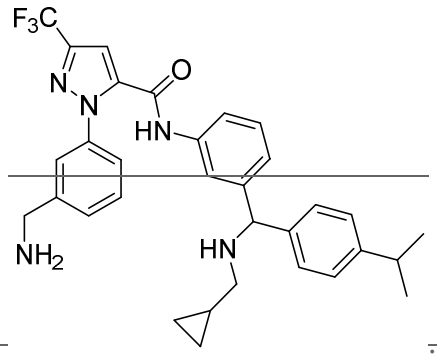
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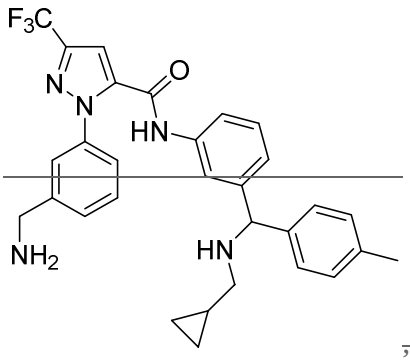


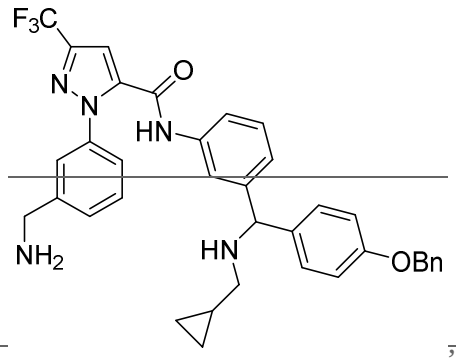
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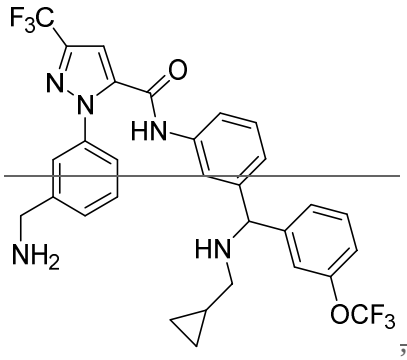


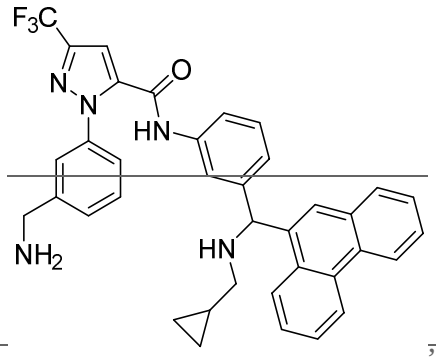
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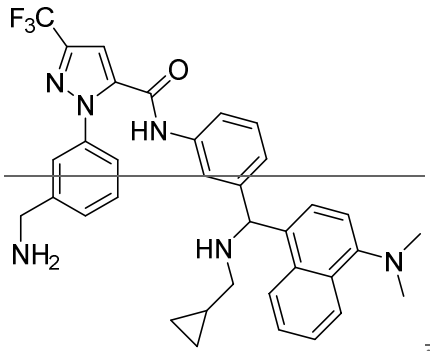
~~129. The compound of claim 1, wherein said compound is selected from the group consisting of:~~

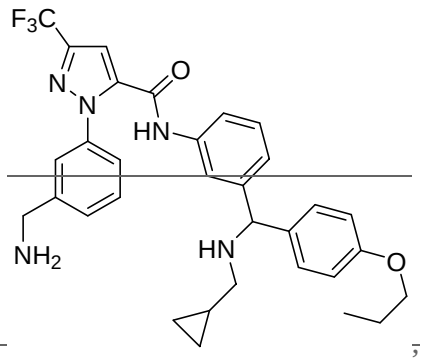


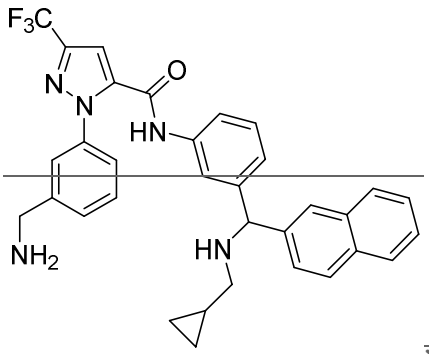


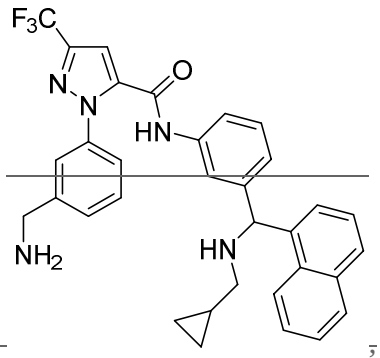


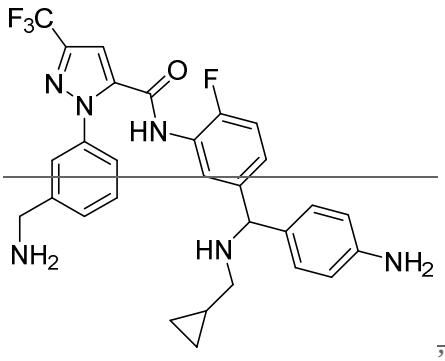




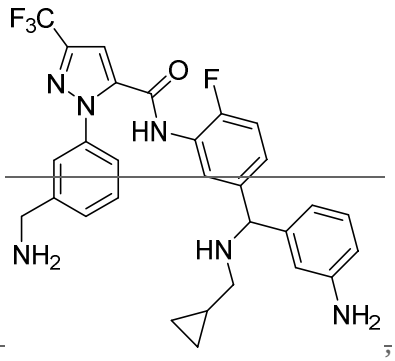




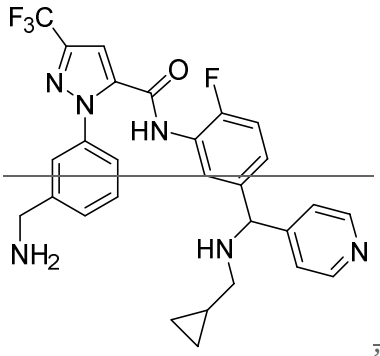




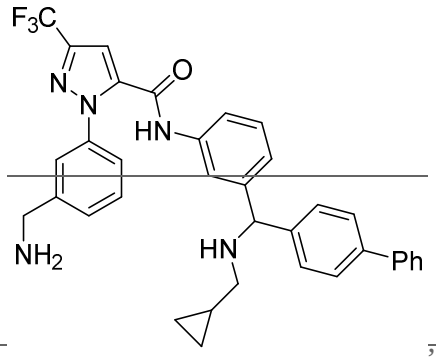
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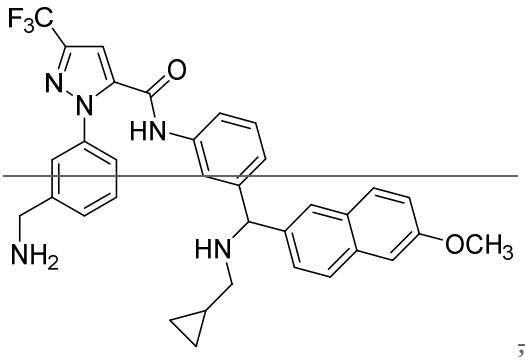
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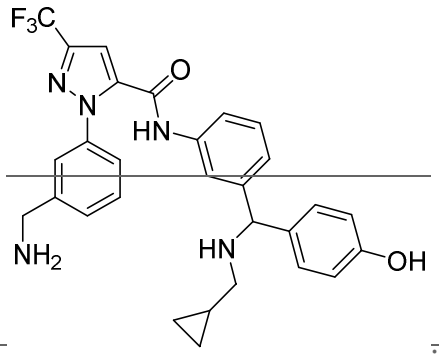
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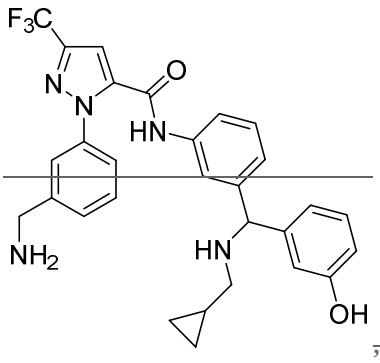
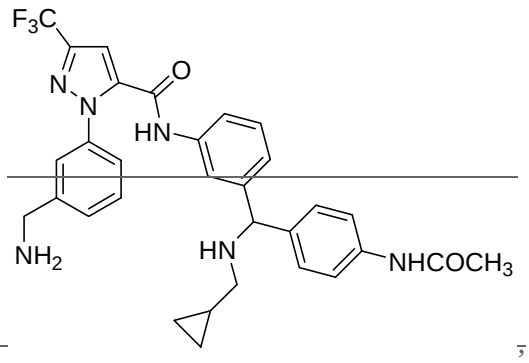
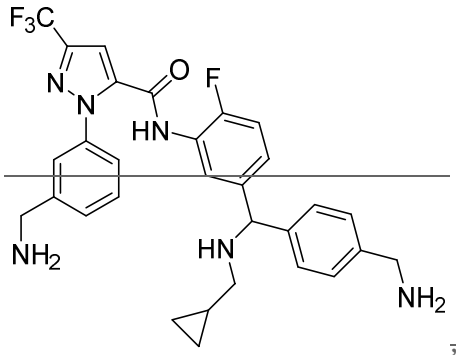
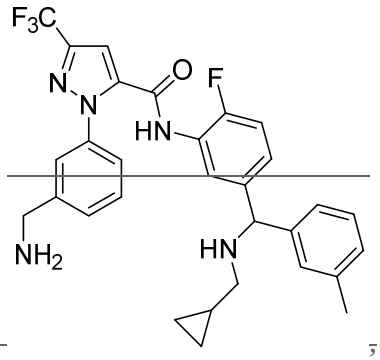
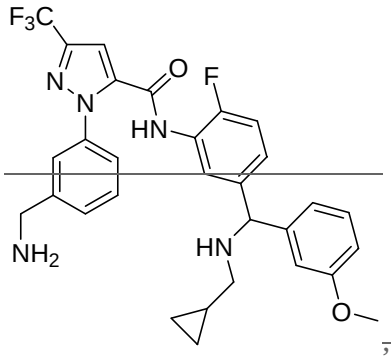
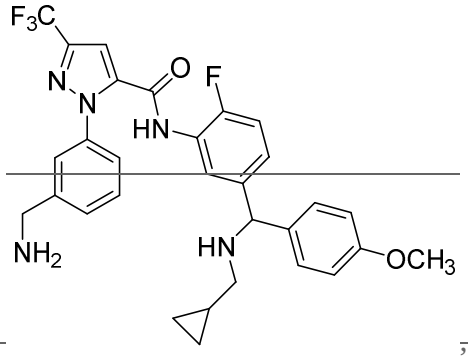
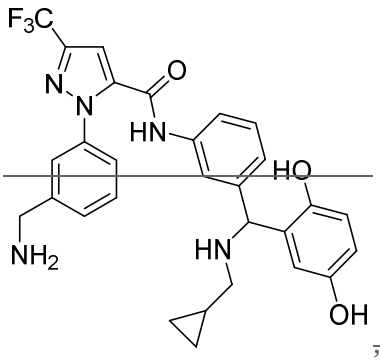
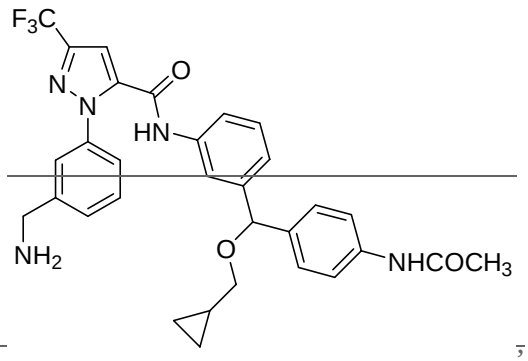


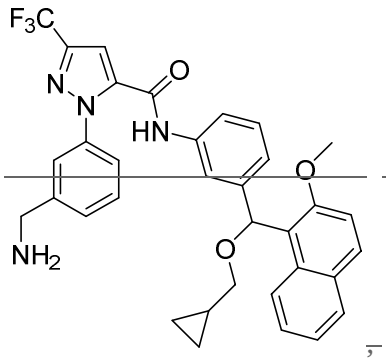
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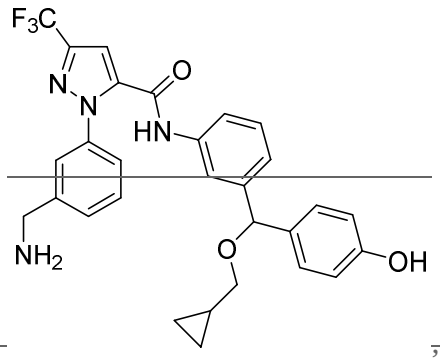
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~~130. The compound of claim 1, wherein said compound is selected from the group consisting of:~~

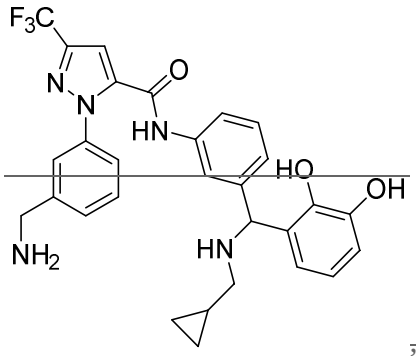











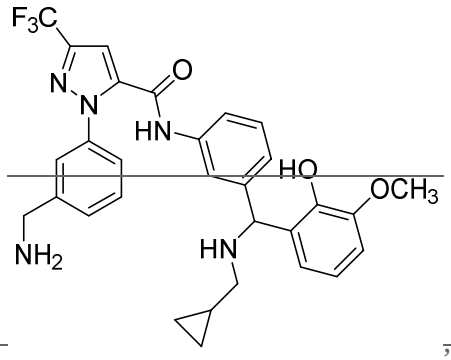
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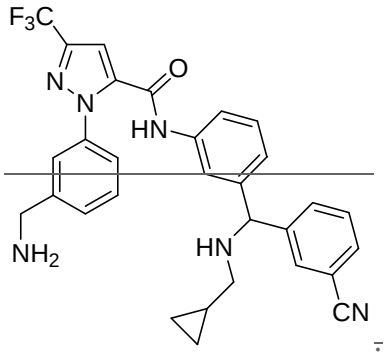
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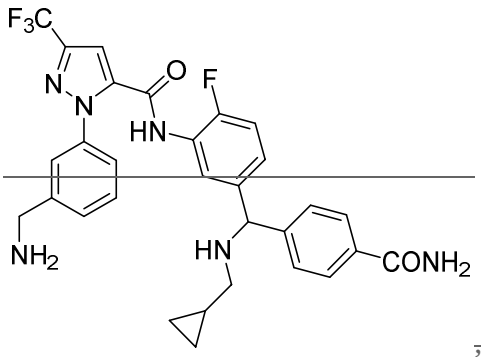
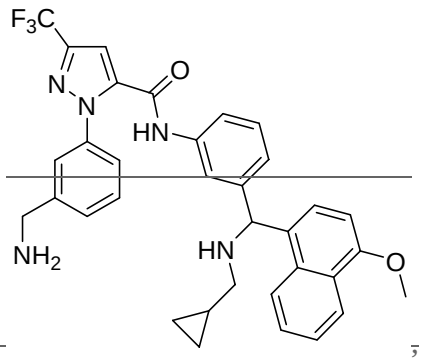
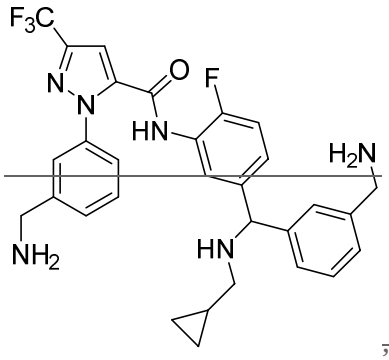
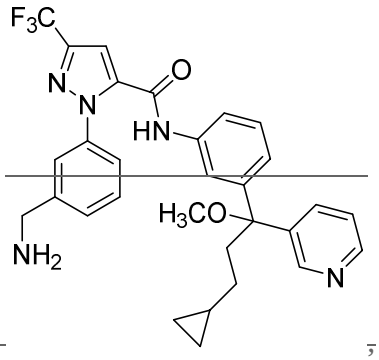
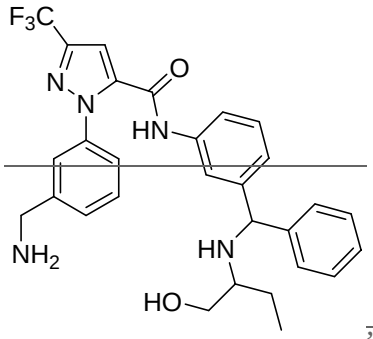
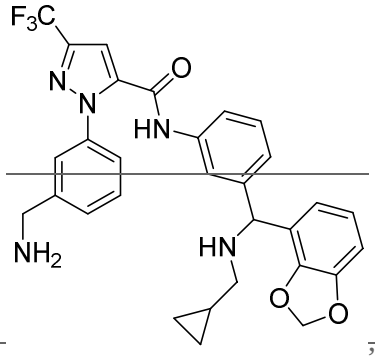
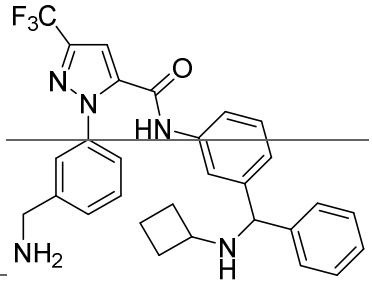
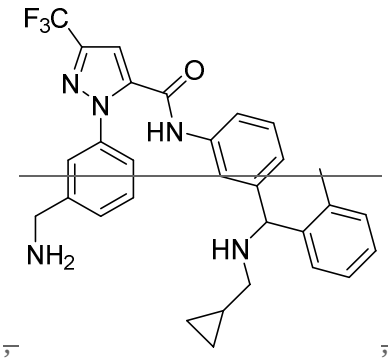
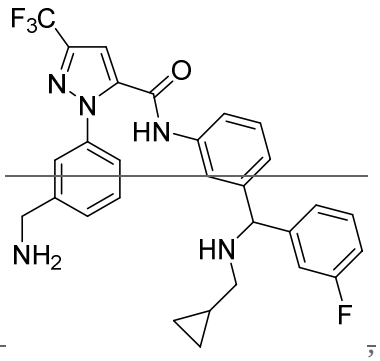


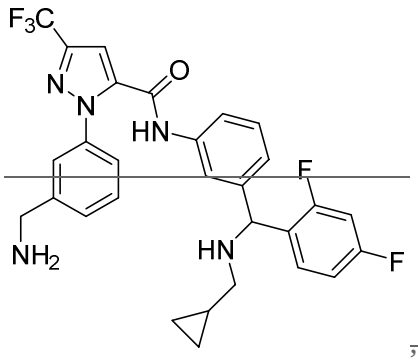
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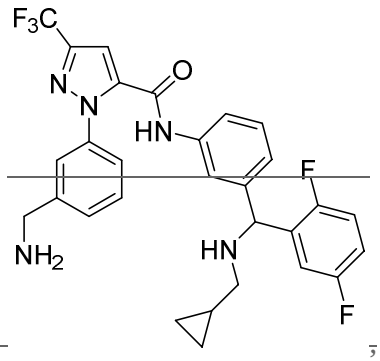
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~~131. The compound of claim 1, wherein said compound is selected from the group consisting of:~~

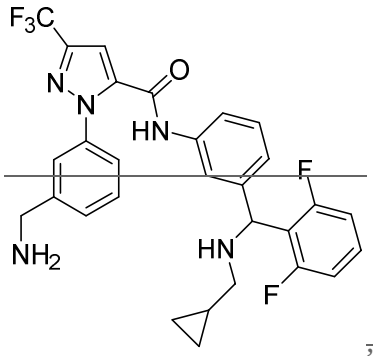












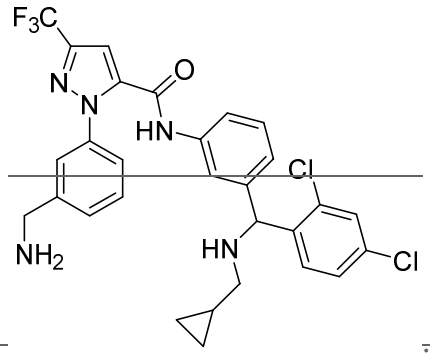
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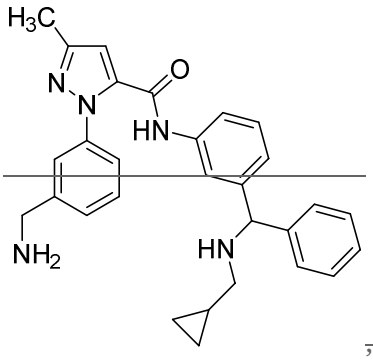


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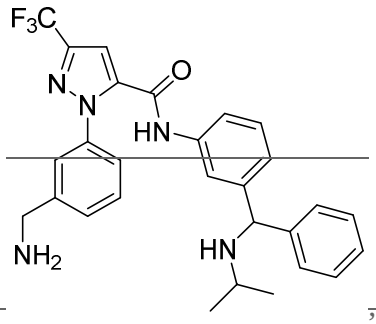


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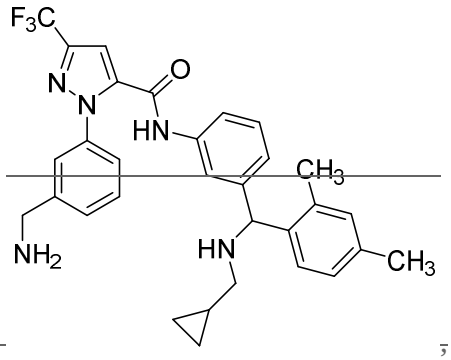
~~132. The compound of claim 1, wherein said compound is selected from the group consisting of:~~



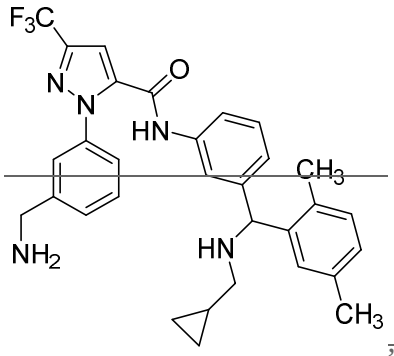
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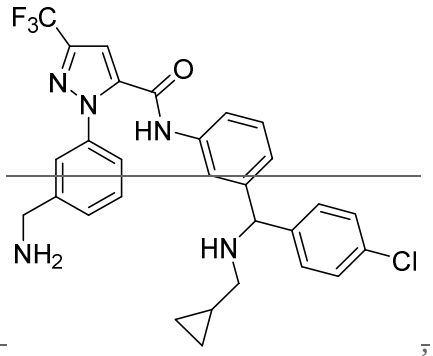
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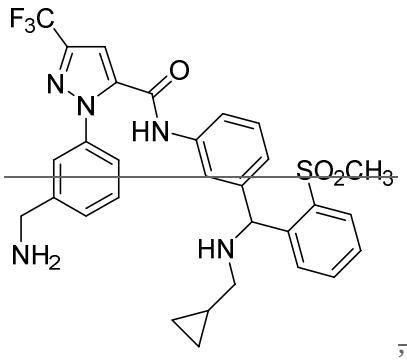
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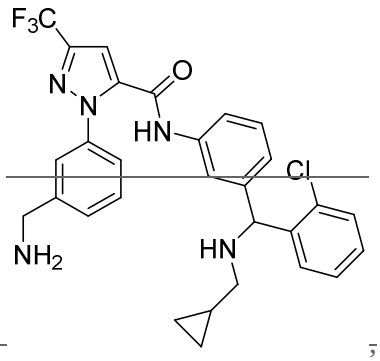
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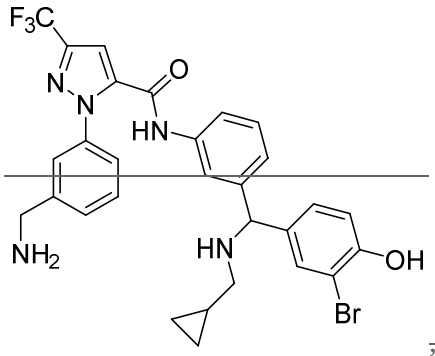
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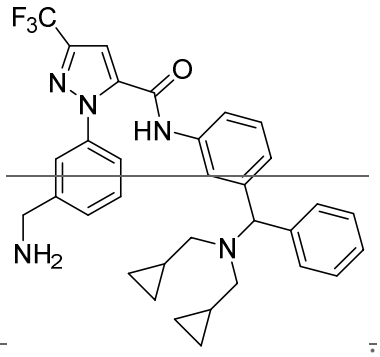

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133. A pharmaceutical composition, comprising a compound of any one of claims 1-132; and a pharmaceutically acceptable carrier.

134. The pharmaceutical composition of claim 133, wherein the pharmaceutical composition is formulated for parenteral administration.

135. The pharmaceutical composition of claim 133, wherein the pharmaceutical composition is formulated for oral administration.

136. The pharmaceutical composition of claim 133, wherein the pharmaceutical composition is formulated for the prophylactic or therapeutic treatment of a disease or condition characterized by unwanted plasma kallikrein activity.

137. A method of treating or preventing a disease or condition characterized by unwanted plasma kallikrein activity, comprising administering to a subject in need thereof a therapeutically effective amount of a compound of any one of claims 1-132.

138. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is selected from the group consisting of stroke, inflammation, reperfusion injury, acute myocardial infarction, deep vein thrombosis, post fibrinolytic treatment condition, angina, edema, angioedema, hereditary angioedema, sepsis, arthritis, hemorrhage, blood loss during cardiopulmonary bypass, inflammatory bowel disease,

~~diabetes mellitus, retinopathy, diabetic retinopathy, diabetic macular edema, diabetic macular degeneration, age-related macular edema, age-related macular degeneration, proliferative retinopathy, neuropathy, hypertension, brain edema, increased albumin excretion, macroalbuminuria, and nephropathy.~~

~~139. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is angioedema.~~

~~140. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is hereditary angioedema.~~

~~141. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is stroke.~~

~~142. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is reperfusion injury.~~

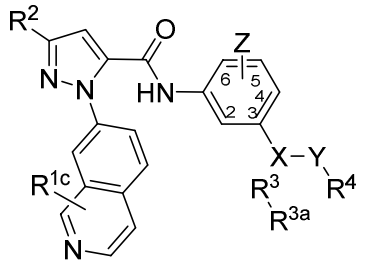
~~143. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is acute myocardial infarction.~~

~~144. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is hemorrhage.~~

~~145. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is blood loss during cardiopulmonary bypass.~~

~~146. The method of claim 137, wherein the disease or condition characterized by unwanted plasma kallikrein activity is selected from the group consisting of retinopathy, diabetic retinopathy, diabetic macular edema, diabetic macular degeneration, age-related macular edema, age-related macular degeneration, and proliferative retinopathy.~~

1. A compound, or a pharmaceutically acceptable salt thereof, represented by formula XXVI:



(XXVI)

wherein:

X represents CH, C(OH), -C($NH_2$), or -C($NR^aR^b$);

-Y-$R^4$ represents -(($C_1$-$C_6$)alkyl)-$R^4$, -$CH_2$C(O)-$R^4$, -$CH_2$NH-$R^4$, -$CH_2$N(($C_1$-$C_6$)alkyl)-$R^4$, -$CR^aR^b$-$R^4$, -NH-$R^4$, -$NHCH_2$-$R^4$, -NHC(O)-$R^4$, -N(($C_1$-$C_6$)alkyl)-$R^4$, -N(($C_1$-$C_6$)alkyl)$CH_2$-$R^4$, -N(($CH_2$)$_2$OH)-$R^4$, -N[($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl]$R^4$, -heterocyclyl-$R^4$, -$OR^4$, -$OCH_2$-$R^4$, -OC(O)-$R^4$, or -OC(O)$NR^aR^b$, wherein the ($C_1$-$C_6$)alkyl moiety of -(($C_1$-$C_6$)alkyl)-$R^4$ is optionally substituted;

Z is absent or represents halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, -$SO_2NH_2$, or ($C_3$-$C_8$)cycloalkyl;

$R^{1c}$ represents halo, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, cyano, -$SO_2CH_3$, formyl, acyl, -$NH_2$, or optionally substituted aryl;

$R^2$ represents halo, ($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl, ($C_1$-$C_6$)fluoroalkyl, -$OCH_3$, -$Si(CH_3)_3$, -$CONH_2$, -C(O)OH, cyano, or phenyl;

$R^3$ represents -NH-, -O-, optionally substituted aryl, heteroaryl, phenyl, carbocyclyl, or heterocyclyl;

$R^{3a}$ is absent or represents one or more substituents independently selected from the group consisting of halo, hydroxy, ($C_1$-$C_6$)alkyl, -$CF_3$, -$OCF_3$, ($C_1$-$C_6$)alkoxy, aryl, aryloxy, amino, amino($C_1$-$C_6$)alkyl, -C(O)$NH_2$, cyano, -NHC(O)($C_1$-$C_6$)alkyl, -$SO_2$($C_1$-$C_6$)alkyl, and -$SO_2NH_2$; and

$R^4$ represents hydrogen, hydroxy, optionally substituted ($C_1$-$C_6$)alkyl, optionally substituted ($C_3$-$C_8$)cycloalkyl, heterocyclyl($C_1$-$C_6$)alkyl, ($C_3$-$C_8$)cycloalkyl($C_1$-$C_6$)alkyl, -$CH_2OH$, -CH(($C_1$-$C_6$)alkyl)OH, -$CH(NH_2)CH(($C_1$-$C_6$)alkyl)$_2$, optionally substituted aryl, optionally substituted aryl($C_1$-$C_6$)alkyl, heteroaryl, optionally substituted heteroaryl($C_1$-$C_6$)alkyl, -$CH_2$S($C_1$-$C_6$)alkyl, amino, or cyano;

each $R^a$ and $R^b$ is independently H, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, aryl($C_1$-$C_8$)alkyl, ($C_3$-$C_8$)carbocyclyl, -C(=O)$R^c$, -C(=O)$OR^c$, -C(=O)$NR^cR^d$, -C(=O)$SR^c$, -S(O)$R^c$, -S(O)$_2R^c$, -S(O)($OR^c$), or –$SO_2NR^cR^d$;

each $R^c$ and $R^d$ is independently H, ($C_1$-$C_8$)alkyl, ($C_2$-$C_8$)alkenyl, ($C_2$-$C_8$)alkynyl, ($C_4$-$C_8$) carbocyclyl, optionally substituted aryl, optionally substituted heteroaryl, -C(=O)($C_1$-$C_8$)alkyl, -S(O)$_n$($C_1$-$C_8$)alkyl, or aryl($C_1$-$C_8$)alkyl; or when $R^c$ and $R^d$ are bonded to a common nitrogen atom, then they may form a 3- to 7-membered heterocyclic ring;

n is 2 or 3; and

the stereochemical configuration at any chiral center is *R*, *S*, or a mixture of *R* and *S*.

2. The compound of claim 1, wherein X represents CH or -C($NH_2$).

3. The compound of claim 1 or 2, wherein X represents CH.

4. The compound of any one of claims 1-3, wherein Z represents halo.

5. The compound of any one of claims 1-4, wherein Z represents F.

6. The compound of any one of claims 1-5, wherein $R^{1c}$ represents -$NH_2$.

7. The compound of any one of claims 1-6, wherein $R^2$ represents ($C_1$-$C_6$)fluoroalkyl.

8. The compound of any one of claims 1-7, wherein $R^2$ represents $CF_3$.

9. The compound of any one of claims 1-8, wherein $R^3$ represents optionally substituted aryl, heteroaryl, phenyl, or heterocyclyl.

10. The compound of any one of claims 1-8, wherein $R^3$ represents optionally substituted phenyl.

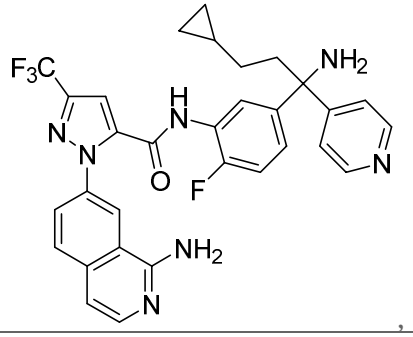
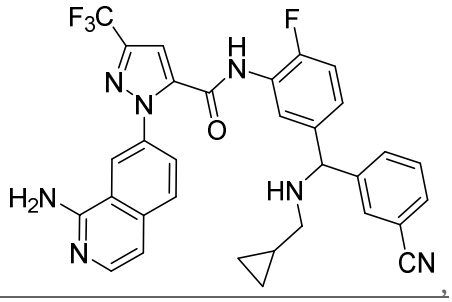
11. The compound of any one of claims 1-10, wherein $R^{3a}$ is absent or represents cyano.

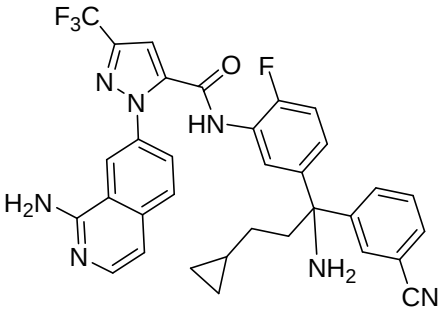
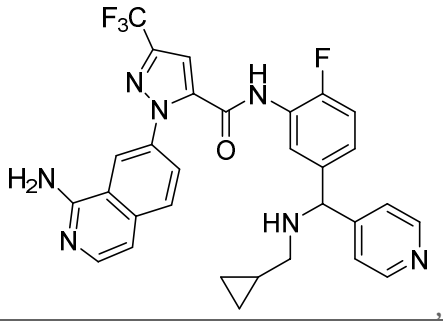
12. The compound of any one of claims 1-11, wherein -Y-$R^4$ represents -(($C_1$-$C_6$)alkyl)-$R^4$, -NH-$R^4$, or -$NHCH_2$-$R^4$.

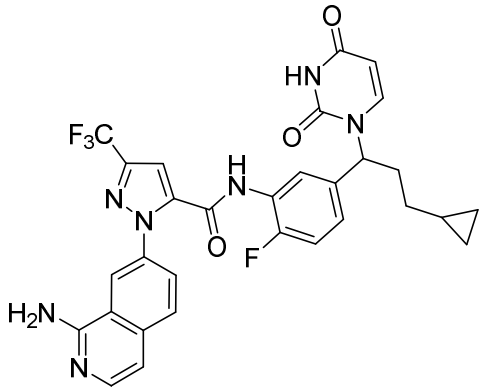
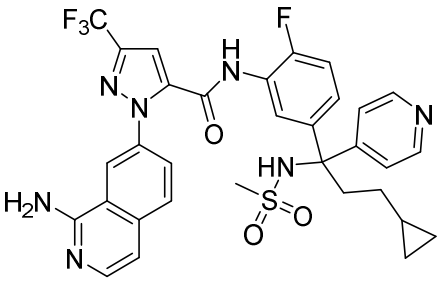
13. The compound of any one of claims 1-12, wherein $R^4$ represents optionally substituted ($C_3$-$C_8$)cycloalkyl.

14. The compound of any one of claims 1-11, wherein -Y-$R^4$ represents -$NHCH_2$-$R^4$ and $R^4$ represents $C_3$-cycloalkyl.

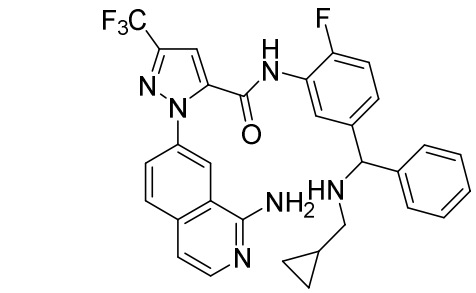
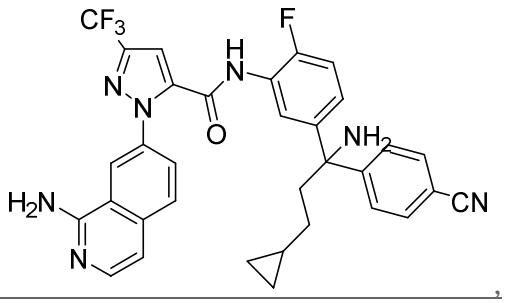
15. The compound of claim 1, wherein said compound is selected from the group consisting of:



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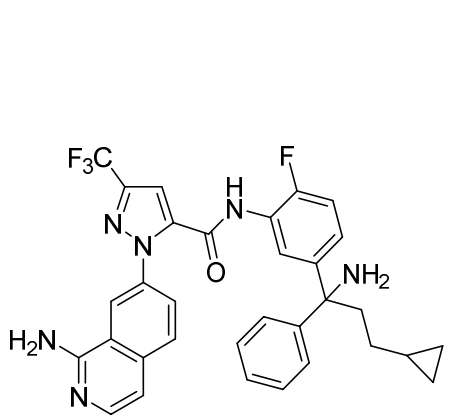
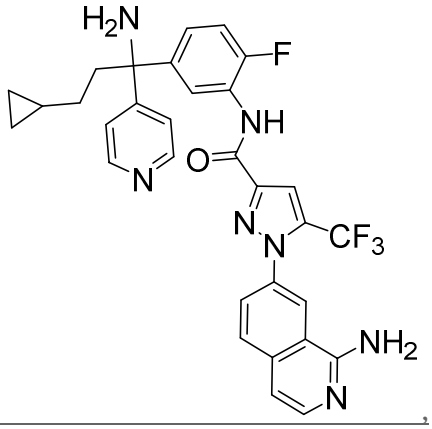

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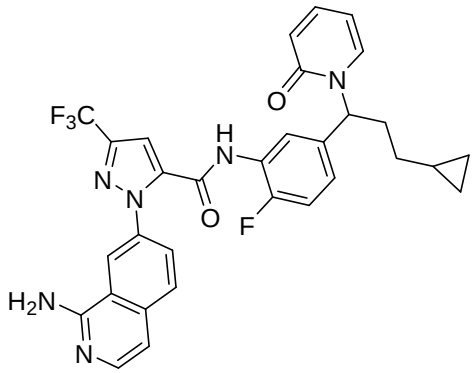
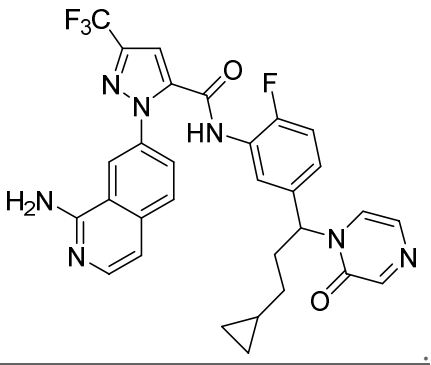
16. The compound of claim 1, wherein said compound is selected from the group consisting of:

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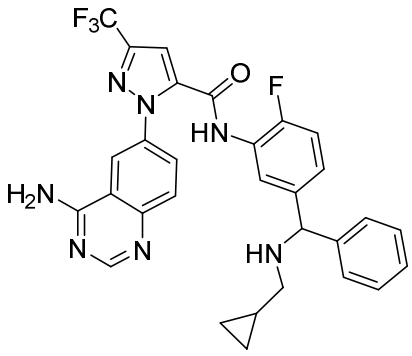
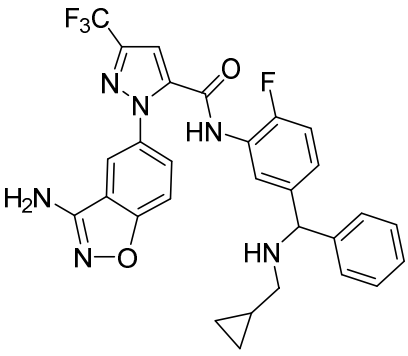



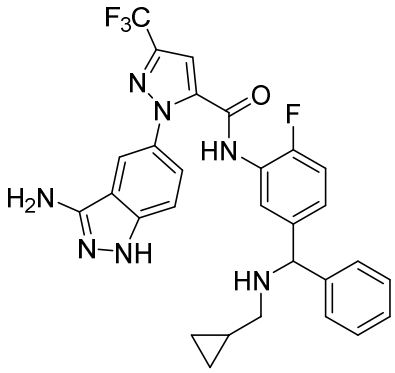
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, and .

17. A compound, or a pharmaceutically acceptable salt thereof, wherein said compound is selected from the group consisting of:



and


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18. The compound of any one of claims 1-17, wherein the pharmaceutically acceptable salt thereof is a hydrochloride salt.

19. The compound of any one of claims 1-18, wherein the pharmaceutically acceptable salt thereof is a bis(hydrochloride) salt.

20. A pharmaceutical composition, comprising a compound of any one of claims 1-19, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

21. The pharmaceutical composition of claim 20, wherein the pharmaceutical composition is formulated for parenteral administration.

22. The pharmaceutical composition of claim 20, wherein the pharmaceutical composition is formulated for oral administration.

23. Use of the compound of any one of claims 1-19, in the manufacture of a medicament for treating or preventing a disease or condition characterized by unwanted plasma kallikrein activity;

wherein the disease or condition characterized by unwanted plasma kallikrein activity is selected from the group consisting of stroke, inflammation, reperfusion injury, acute myocardial infarction, deep vein thrombosis, post fibrinolytic treatment condition, angina, edema, angioedema, hereditary angioedema, sepsis, arthritis, hemorrhage, blood loss during cardiopulmonary bypass, inflammatory bowel disease, diabetes mellitus, retinopathy, diabetic retinopathy, diabetic macular edema, diabetic macular degeneration, age-related macular edema, age-related macular degeneration, proliferative retinopathy, neuropathy, hypertension, brain edema, increased albumin excretion, macroalbuminuria, and nephropathy.

24. The use of claim 23, wherein the disease or condition characterized by unwanted plasma kallikrein activity is angioedema.

25. The use of claim 23, wherein the disease or condition characterized by unwanted plasma kallikrein activity is hereditary angioedema.

26. The use of claim 23, wherein the disease or condition characterized by unwanted plasma kallikrein activity is stroke.

27. The use of claim 23, wherein the disease or condition characterized by unwanted plasma kallikrein activity is reperfusion injury.

28. The use of claim 23, wherein the disease or condition characterized by unwanted plasma kallikrein activity is acute myocardial infarction.

29. The use of claim 23, wherein the disease or condition characterized by unwanted plasma kallikrein activity is hemorrhage.

30. The use of claim 23, wherein the disease or condition characterized by unwanted plasma kallikrein activity is blood loss during cardiopulmonary bypass.

31. The use of claim 23, wherein the disease or condition characterized by unwanted plasma kallikrein activity is selected from the group consisting of retinopathy, diabetic retinopathy, diabetic macular edema, diabetic macular degeneration, age-related macular edema, age-related macular degeneration, and proliferative retinopathy.

32. The compound of any one of claims 1-19, for use in therapy.