C_1-C_4 alkyloxycarbonyl, C_1-C_6 alkylsulfonyl, and hydroxyl; or, alternatively, two adjacent R^a or R^b, together with the atoms in groups A or B to which they are attached, form an additional fused aryl, heteroaryl, cycloalkyl, or heterocyclyl ring with from 0 to 5 R^z substituents;

each R^c is a member independently selected from the group consisting of C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_6 cycloalkyl, (C_3-C_6 cycloalkyl)C_1-C_3alkyl, and C_1-C_7 acyl;

each u is an integer independently selected from 0 to 4;

v is an integer from 0 to 5;

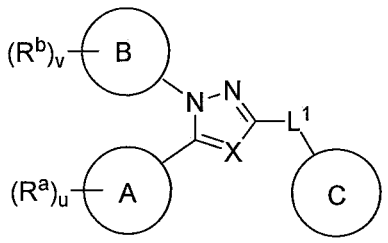
X is N or CR^d; or, alternatively, X is CR^d, wherein X and the member Z^1, together with atoms in the rings in which they are included, form the additional fused, five- to eight-membered cycloalkyl or heterocyclyl ring with from 0 to 5 R^z substituents;

each R^d is a member independently selected from the group consisting of halo, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, and C_3-C_6 cycloalkoxy;

L^1 is a member selected from the group consisting of C=O, C=S, C=NH, and $C=NR^c$;

Y^6, Y^7, Y^8, Y^9, and Y^{10}, if present, are each a member independently selected from the group consisting of N, CH, and CR^b; or, alternatively for Y^8 and Y^9, the members $-Y^6=Y^7-$ or $-Y^8=Y^9-$ are combined into a single member selected from the group consisting of NR^c, O, and S.

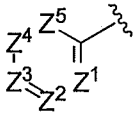
[0008a] In another aspect, the invention provides a compound of Formula I:



or a pharmaceutically acceptable salt thereof;

wherein:

A is a cyclic group of Formula Ia:



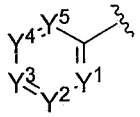
Ia

wherein Z^1, Z^2, Z^3, Z^4, and Z^5 are each a member selected from the group consisting of N, CH, and CR^a; or, alternatively for Z^1, the member Z^1 and X, together with atoms in the rings to which they are attached, form an additional fused, five- to eight-membered cycloalkyl or heterocyclyl ring with from 0 to 4 R^z substituents;

with the proviso that at least one member selected from the group consisting of Z^2, Z^3, and Z^4 is N;

each R^z is a member independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 haloalkyl, and C_1-C_3 alkoxy; or, alternatively, two R^z substituents, together with the carbon atom to which they are attached, join to form an oxo, spirocycloalkyl, or spiroheterocyclyl group;

B is a cyclic group of Formula Ib:



Ib

wherein Y^1, Y^2, Y^3, Y^4, and Y^5 are each a member independently selected from the group consisting of N, CH, and CR^b; or, alternatively, the members

$-Y^2=Y^3-$ or $-Y^4=Y^5-$ are combined into a single member selected from the group consisting of NH, NR^c, O, and S;

each R^a and R^b is a member independently selected from the group consisting of cyano, carboxyl, C_1-C_4 alkyl, C_1-C_4 hydroxyalkyl, C_3-C_8 cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, halo, C_0-C_6 amino, C_1-C_6 amido, C_1-C_4 alkyloxycarbonyl, C_1-C_6 alkylsulfonyl, and hydroxyl; or, alternatively, two adjacent R^a or R^b, together with the atoms in groups A or B to which they are attached, form an additional fused aryl, heteroaryl, cycloalkyl, or heterocyclyl ring with from 0 to 4 R^z substituents;

each R^c is a member independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_6 cycloalkyl, (C_3-C_6 cycloalkyl)C_1-C_3alkyl, and C_1-C_7 acyl;

each u is an integer independently selected from 0 to 4;

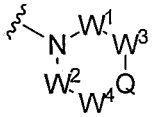
v is an integer from 0 to 5;

X is N or CR^d; or, alternatively, X is CR^d, wherein X and the member Z^1, together with atoms in the rings in which they are included, form the additional fused, five- to eight-membered cycloalkyl or heterocyclyl ring with from 0 to 4 R^z substituents;

each R^d is a member independently selected from the group consisting of hydrogen, halo, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, and C_3-C_6 cycloalkoxy;

each L^1, L^2, and L^3, if present, is a member independently selected from the group consisting of C=O, C=S, C=NH, and $C=NR^c$;

C is a cyclic group of Formula Ic:



Ic

wherein Q is a member selected from the group consisting of $C(R^e)(D)$, N(E), F, and G; or, alternatively, the members $-W^3-Q-$ or $-W^4-Q-$ join to form a member H; and

wherein W^1, W^2, W^3, and W^4 are each an independently selected $C(R^f)_2$; or, alternatively, the members $-W^3-Q-$ or $-W^4-Q-$ join to form a member H;

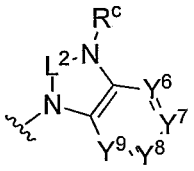
R^e is a member selected from the group consisting of hydrogen, C_1-C_3 alkyl, and C_1-C_3 fluoroalkyl; or, alternatively, R^e and an R^f substituent of W^1, W^2, W^3, or W^4 join to form a $-(C(R^z)_2)_t-$ bridge or a $-(CH_2)_t-$ bridge, wherein t is an integer selected from 2 or 3;

each R^f is a member independently selected from the group consisting of hydrogen, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, and halo; or, alternatively, two adjacent R^f, together with the atoms in group C to which they are attached, form an additional aryl, heteroaryl, cycloalkyl, or heterocyclyl fused ring with from 0 to 4 R^z substituents; or, alternatively, two geminal R^f, together with the atom in group C to which they are attached, form a spirocycloalkyl or spiroheterocyclyl ring with from 0 to 4 R^z substituents; or, alternatively, two axial R^f substituents of a pair of W^n selected from the group consisting of (W^1 and W^2), (W^2 and W^3), and (W^3 and W^4) join to form a $-(C(R^z)_2)_t-$ bridge or a

-$(CH_2)_t$-; or, alternatively, R^e and an R^f substituent of W^1, W^2, W^3, or W^4 join to form a -$(C(R^z)_2)_t$- bridge or a -$(CH_2)_t$- bridge;

each t is an integer selected from 2 or 3;

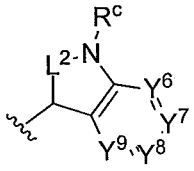
D is a bicyclic group of Formula Id:



;

Id

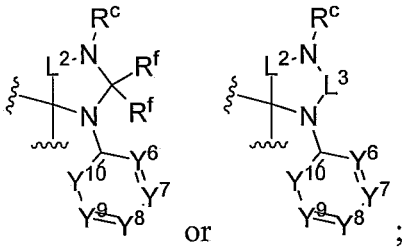
E is a bicyclic group of Formula Ie:



;

Ie

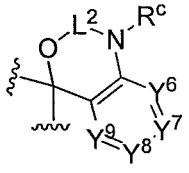
F is a spirocyclic group of Formula If:



or ;

If

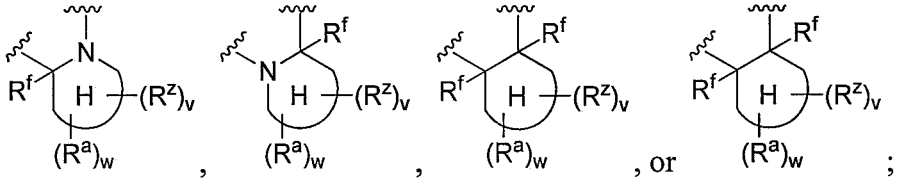
G is a bicyclic spirocyclic group of Formula Ig:



;

Ig

H is a fused group of Formula Ih:



, , , or ;

Ih

wherein the H ring is a fused, five- to eight-membered cycloalkyl or heterocyclyl ring;

wherein v is an integer from 0 to 4; and

wherein w is an integer from 0 to 2; and

Y^6, Y^7, Y^8, Y^9, and Y^{10}, if present, are each a member independently selected from the group consisting of N, CH, and CR^b; or, alternatively for Y^8 and Y^9, the members $-Y^6=Y^7-$ or $-Y^8=Y^9-$ are combined into a single member selected from the group consisting of NR^c, O, and S.

[0009] In another aspect, the invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound of Formula I or II and at least one pharmaceutically acceptable carrier, excipient, or diluent.

[0010] In another aspect, the invention provides a method of treating or preventing pain comprising administering to a patient in need thereof a therapeutically effective amount, or a prophylactically effective amount, of a compound of of Formula I or II.

[0010a] In another aspect, there is provided the use of a therapeutically effective amount, or a prophylactically effective amount, of a compound as described herein, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating or preventing pain.

[0010b] In another aspect, there is provided the use of a therapeutically effective amount, or a prophylactically effective amount, of a compound as described herein, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prevention of pain before, during or after surgical procedure.

[0010c] In another aspect, there is provided the use of a therapeutically effective amount, or a prophylactically effective amount, of a compound as described herein, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prevention of pain associated with an interventional procedure, wherein the medicament is to be periprocedurally administered.

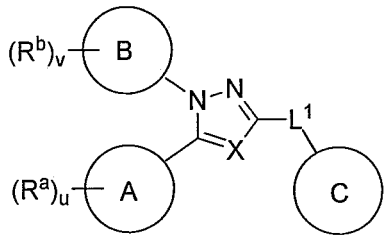
[0011] Certain other aspects and embodiments of the present invention are set forth herein and will be apparent to those of skill in the art.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] Figure 1 shows the paw withdrawal threshold (PWT in g) observed in rats treated with a compound of the invention after spinal nerve ligation.

WHAT IS CLAIMED IS:

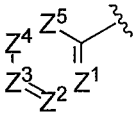
1. A compound of Formula I:



or a pharmaceutically acceptable salt thereof;

wherein:

A is a cyclic group of Formula Ia:



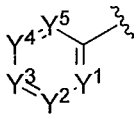
Ia

wherein Z^1, Z^2, Z^3, Z^4, and Z^5 are each a member selected from the group consisting of N, CH, and CR^a; or, alternatively for Z^1, the member Z^1 and X, together with atoms in the rings to which they are attached, form an additional fused, five- to eight-membered cycloalkyl or heterocyclyl ring with from 0 to 4 R^z substituents;

with the proviso that at least one member selected from the group consisting of Z^2, Z^3, and Z^4 is N;

each R^z is a member independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 haloalkyl, and C_1-C_3 alkoxy; or, alternatively, two R^z substituents, together with the carbon atom to which they are attached, join to form an oxo, spirocycloalkyl, or spiroheterocyclyl group;

B is a cyclic group of Formula Ib:



Ib

wherein Y^1, Y^2, Y^3, Y^4, and Y^5 are each a member independently selected from the group consisting of N, CH, and CR^b; or, alternatively, the members

$-Y^2=Y^3-$ or $-Y^4=Y^5-$ are combined into a single member selected from the group consisting of NH, NR^c, O, and S;

each R^a and R^b is a member independently selected from the group consisting of cyano, carboxyl, C_1-C_4 alkyl, C_1-C_4 hydroxyalkyl, C_3-C_8 cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, halo, C_0-C_6 amino, C_1-C_6 amido, C_1-C_4 alkyloxycarbonyl, C_1-C_6 alkylsulfonyl, and hydroxyl; or, alternatively, two adjacent R^a or R^b, together with the atoms in groups A or B to which they are attached, form an additional fused aryl, heteroaryl, cycloalkyl, or heterocyclyl ring with from 0 to 4 R^z substituents;

each R^c is a member independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_6 cycloalkyl, (C_3-C_6 cycloalkyl)C_1-C_3alkyl, and C_1-C_7 acyl;

each u is an integer independently selected from 0 to 4;

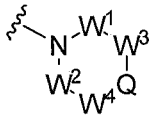
v is an integer from 0 to 5;

X is N or CR^d; or, alternatively, X is CR^d, wherein X and the member Z^1, together with atoms in the rings in which they are included, form the additional fused, five- to eight-membered cycloalkyl or heterocyclyl ring with from 0 to 4 R^z substituents;

each R^d is a member independently selected from the group consisting of hydrogen, halo, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, and C_3-C_6 cycloalkoxy;

each L^1, L^2, and L^3, if present, is a member independently selected from the group consisting of C=O, C=S, C=NH, and $C=NR^c$;

C is a cyclic group of Formula Ic:



Ic

wherein Q is a member selected from the group consisting of $C(R^e)(D)$, N(E), F, and G; or, alternatively, the members $-W^3-Q-$ or $-W^4-Q-$ join to form a member H; and

wherein W^1, W^2, W^3, and W^4 are each an independently selected $C(R^f)_2$; or, alternatively, the members $-W^3-Q-$ or $-W^4-Q-$ join to form a member H;

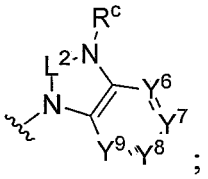
R^e is a member selected from the group consisting of hydrogen, C_1-C_3 alkyl, and C_1-C_3 fluoroalkyl; or, alternatively, R^e and an R^f substituent of W^1, W^2, W^3, or

W^4 join to form a $-(C(R^z)_2)_t-$ bridge or a $-(CH_2)_t-$ bridge, wherein t is an integer selected from 2 or 3;

each R^f is a member independently selected from the group consisting of hydrogen, C_1-C_3 alkyl, C_1-C_3 fluoroalkyl, and halo; or, alternatively, two adjacent R^f, together with the atoms in group C to which they are attached, form an additional aryl, heteroaryl, cycloalkyl, or heterocyclyl fused ring with from 0 to 4 R^z substituents; or, alternatively, two geminal R^f, together with the atom in group C to which they are attached, form a spirocycloalkyl or spiroheterocyclyl ring with from 0 to 4 R^z substituents; or, alternatively, two axial R^f substituents of a pair of W^n selected from the group consisting of (W^1 and W^2), (W^2 and W^3), and (W^3 and W^4) join to form a $-(C(R^z)_2)_t-$ bridge or a $-(CH_2)_t-$; or, alternatively, R^e and an R^f substituent of W^1, W^2, W^3, or W^4 join to form a $-(C(R^z)_2)_t-$ bridge or a $-(CH_2)_t-$ bridge;

each t is an integer selected from 2 or 3;

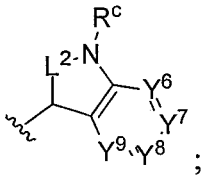
D is a bicyclic group of Formula Id:



;

Id

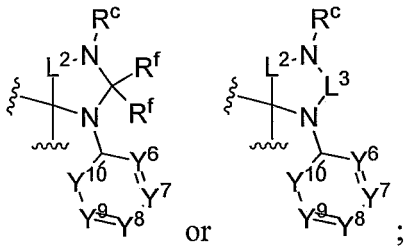
E is a bicyclic group of Formula Ie:



;

Ie

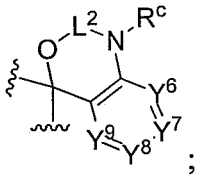
F is a spirocyclic group of Formula If:



;

If

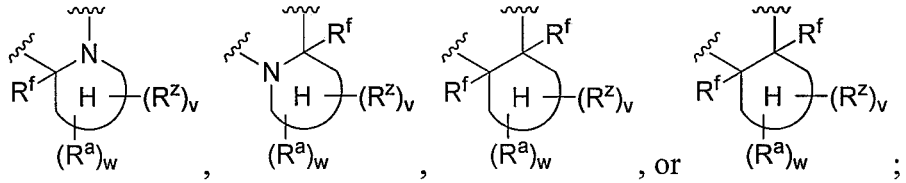
G is a bicyclic spirocyclic group of Formula Ig:



;

Ig

H is a fused group of Formula Ih:



;

Ih

wherein the H ring is a fused, five- to eight-membered cycloalkyl or heterocyclyl ring;

wherein v is an integer from 0 to 4; and

wherein w is an integer from 0 to 2; and

Y^6, Y^7, Y^8, Y^9, and Y^{10}, if present, are each a member independently selected from the group consisting of N, CH, and CR^b; or, alternatively for Y^8 and Y^9, the members $-Y^6=Y^7-$ or $-Y^8=Y^9-$ are combined into a single member selected from the group consisting of NR^c, O, and S.

2. The compound or salt of claim 2, wherein Q is $C(R^e)(D)$.

3. The compound or salt of claim 2, wherein Q is N(E).

4. The compound or salt of claim 2, wherein Q is F.

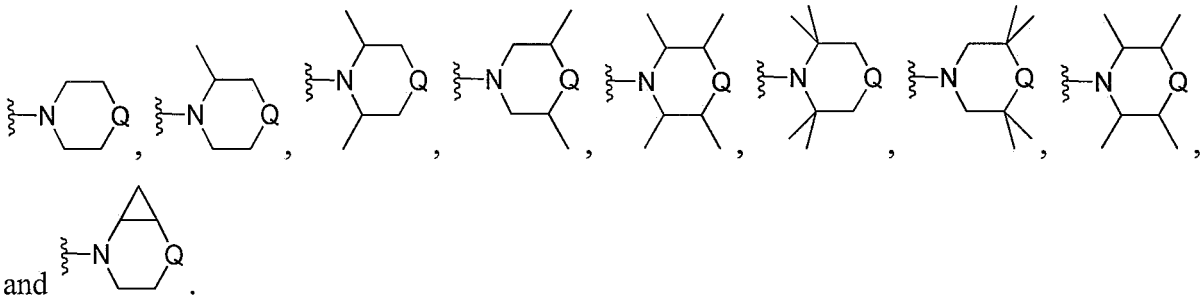
5. The compound or salt of claim 2, wherein Q is G.

6. The compound or salt of claim 2, wherein the members $-W^3-Q-$ or $-W^4-Q-$ join to form a member H.

7. The compound or salt of any one of the preceding claims, wherein W^1, W^2, W^3, and W^4 comprise from 1 to 4 independently selected R^f groups other than hydrogen.

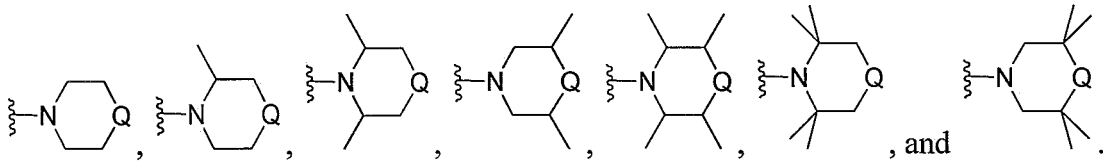
8. The compound or salt of any one of the preceding claims, wherein W^1, W^2, W^3, and W^4 comprise from 1 to 4 independently selected R^f alkyl groups.

9. The compound or salt of any one of the preceding claims, wherein C is a member selected from the group consisting of:



and .

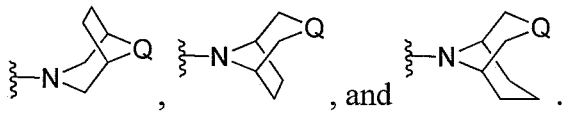
10. The compound or salt of any one of the preceding claims, wherein C is a member selected from the group consisting of:



, and .

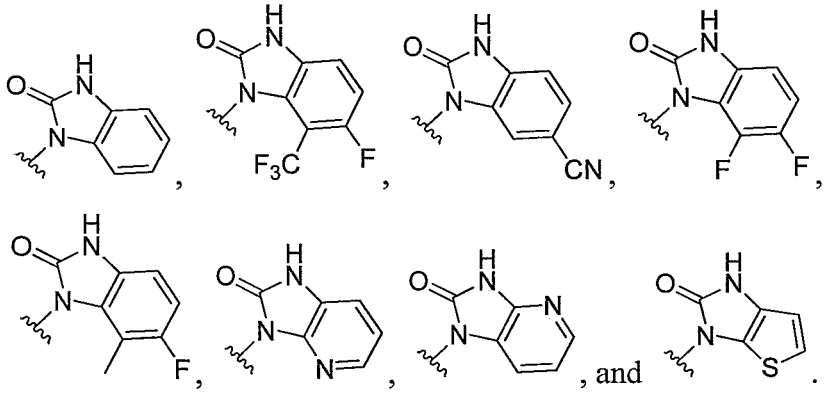
11. The compound or salt of any one of the preceding claims, wherein the pair of W^n is selected from the group consisting of (W^1 and W^2) and (W^3 and W^4).

12. The compound or salt of claim 11, wherein C is a member selected from the group consisting of:



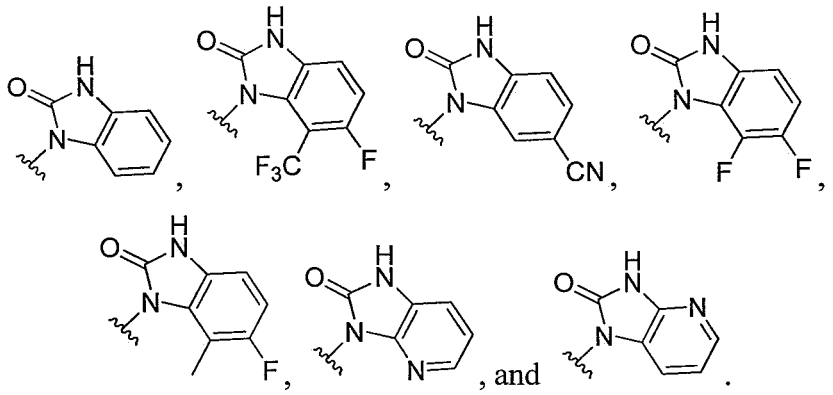
, and .

13. The compound or salt of any one of the preceding claims, wherein D is a member selected from the group consisting of:

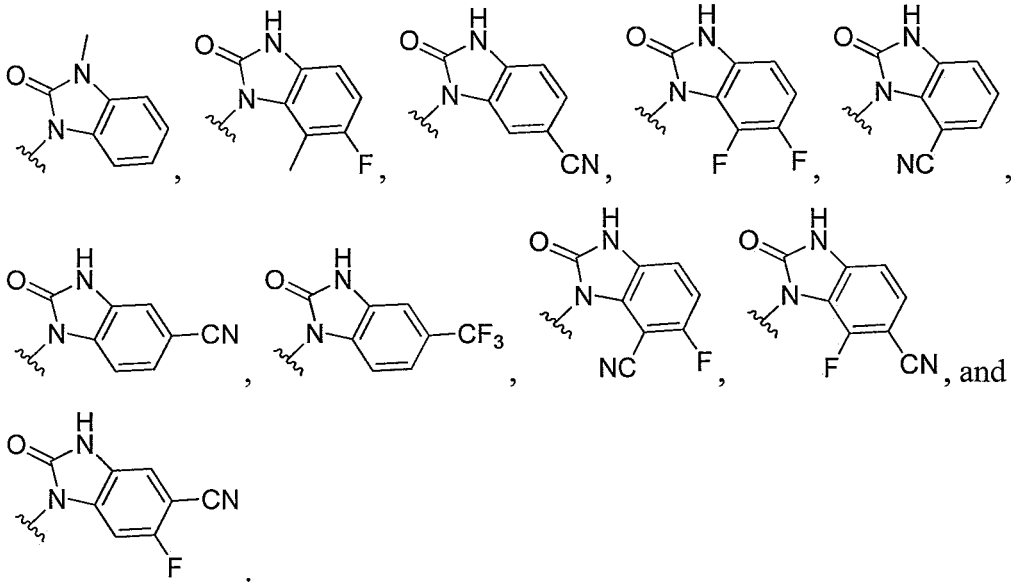


, and .

14. The compound or salt of any one of the preceding claims, wherein D is a member selected from the group consisting of:



15. The compound or salt of any one of the preceding claims, wherein D is a member selected from the group consisting of:



16. The compound or salt of any one of the preceding claims, wherein L^2 is C=O.

17. The compound or salt of any one of the preceding claims, wherein L^3 is C=O.

18. The compound or salt of any one of the preceding claims, wherein Z^1, Z^2, Z^3, Z^4, and Z^5 are each a member selected from the group consisting of N, CH, and CR^a.

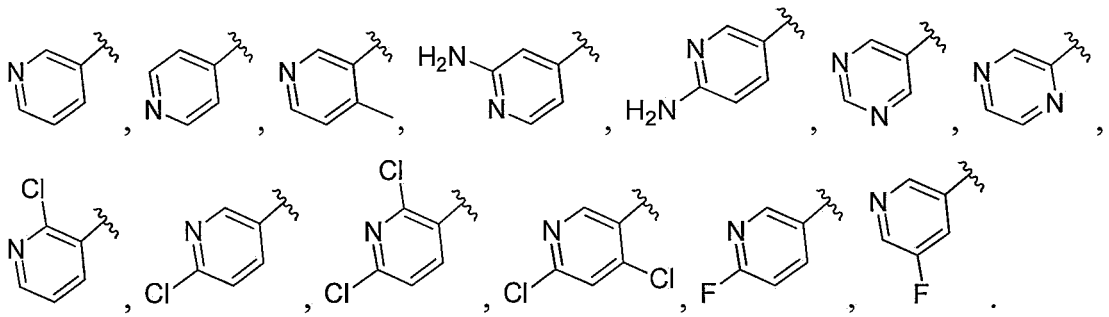
19. The compound or salt of any one of the preceding claims, wherein Z^1 and X, together with atoms in the rings to which they are attached, form an additional fused, five- to eight-membered cycloalkyl or heterocyclyl ring with from 0 to 4 R^z substituents.

20. The compound or salt of any one of the preceding claims, wherein Z^2 is N.

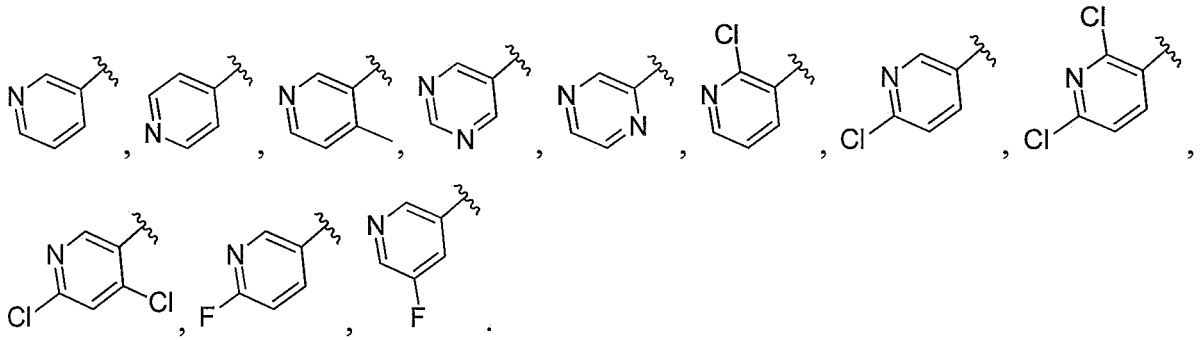
21. The compound or salt of any one of the preceding claims, wherein Z^3 is N.

22. The compound or salt of any one of the preceding claims, wherein Z^4 is N.

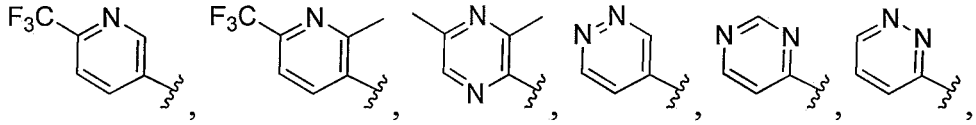
23. The compound or salt of any one of the preceding claims, wherein A is a member selected from the group consisting of:



24. The compound or salt of any one of the preceding claims, wherein A is a member selected from the group consisting of:



25. The compound or salt of any one of the preceding claims, wherein A is a member selected from the group consisting of:


, and salts thereof.

26. The compound or salt of any one of the preceding claims, wherein Y^1, Y^2, Y^3, Y^4, and Y^5 are each a member independently selected from the group consisting of N, CH, and CR^b.

27. The compound or salt of any one of the preceding claims, wherein Y^1 is CR^b, and wherein the Y^1 R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, and trifluoromethoxy.

28. The compound or salt of any one of claims 1-26, wherein Y^1 is N.

29. The compound or salt of any one of the preceding claims, wherein Y^2 is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, and trifluoromethoxy.

30. The compound or salt of any one of claims 1-28, wherein Y^2 is N.

31. The compound or salt of any one of the preceding claims, wherein Y^3 is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, and trifluoromethoxy.

32. The compound or salt of any one of claims 1-30, wherein Y^3 is N.

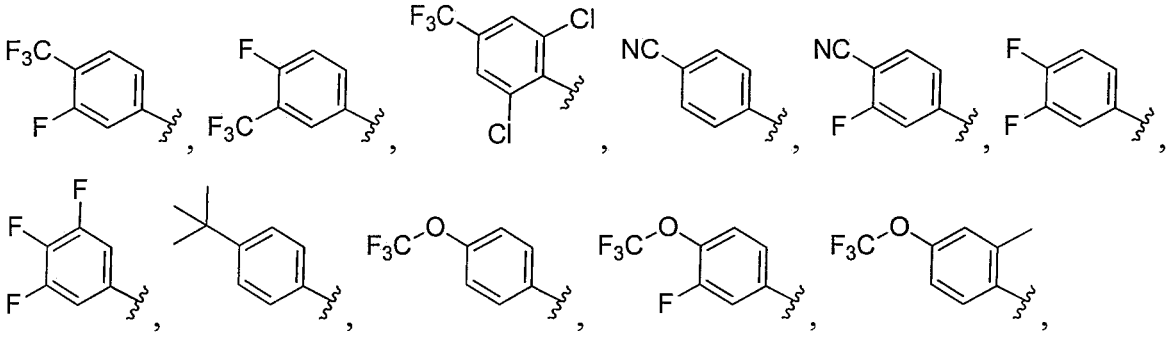
33. The compound or salt of any one of the preceding claims, wherein Y^4 is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, and trifluoromethoxy.

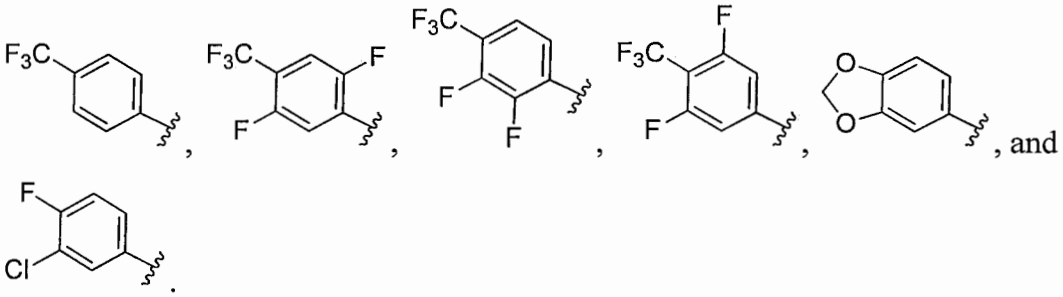
34. The compound or salt of any one of claims 1-32, wherein Y^4 is N.

35. The compound or salt of any one of the preceding claims, wherein Y^5 is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, and trifluoromethoxy.

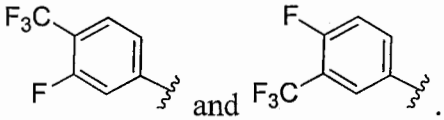
36. The compound or salt of any one of claims 1-34, wherein Y^5 is N.

37. The compound or salt of any one of the preceding claims, wherein B is a member selected from the group consisting of:

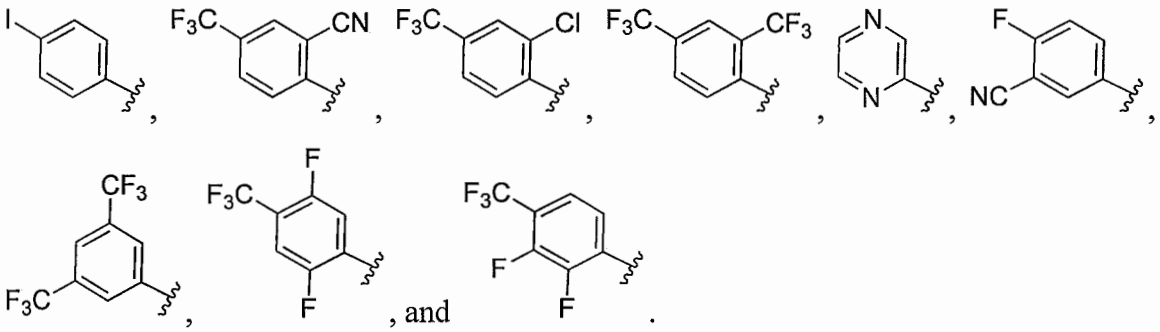




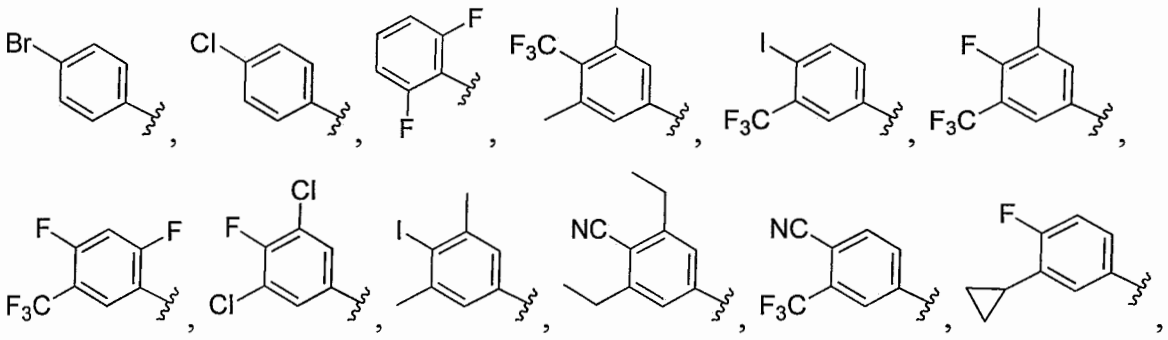
38. The compound or salt of any one of the preceding claims, wherein B is a member selected from the group consisting of:

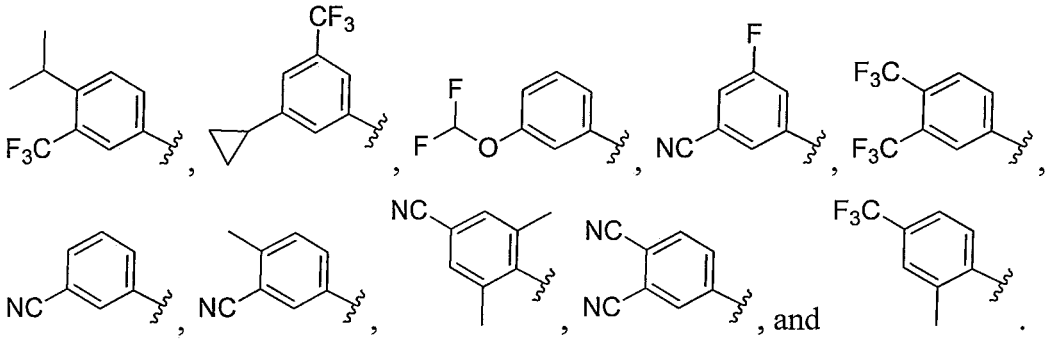


39. The compound or salt of any one of claims 1-35, wherein B is a member selected from the group consisting of:



40. The compound or salt of any one of claims 1-35, wherein B is a member selected from the group consisting of:





41. The compound or salt of any one of the preceding claims, wherein each R^a and R^b is a member independently selected from the group consisting of cyano, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, halo, C_0-C_6 amino, C_1-C_6 amido, and hydroxyl.

42. The compound or salt of any one of the preceding claims, wherein each R^a and R^b is a member independently selected from the group consisting of cyano, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and halo.

43. The compound or salt of any one of the preceding claims, wherein u is an integer independently selected from 0 to 3.

44. The compound or salt of any one of the preceding claims, wherein v is an integer independently selected from 0 to 3.

45. The compound or salt of any one of the preceding claims, wherein X is N.

46. The compound or salt of any one of the preceding claims, wherein each R^c is independently selected from the group consisting of hydrogen, cyano, C_1-C_3 alkyl, trifluoromethyl, cycloalkyl, trifluoromethoxy, and C_1-C_3 alkoxy.

47. The compound or salt of any one of the preceding claims, wherein each R^c is independently selected from the group consisting of hydrogen, cyano, C_1-C_3 alkyl, trifluoromethyl, cyclopropyl, trifluoromethoxy, and C_1-C_3 alkoxy.

48. The compound or salt of any one of the preceding claims, wherein each R^c is independently selected from the group consisting of hydrogen, methyl, bromo, chloro, trifluoromethyl, ethyl, isopropyl, isobutyl, cyclopropyl, cyclobutyl, and cyclopropylmethyl.

49. The compound or salt of any one of the preceding claims, wherein L^1 is C=O.

50. The compound or salt of any one of the preceding claims, wherein Y^6, Y^7, Y^8, Y^9, and Y^{10}, if present, are each a member selected from the group consisting of N, CH, and CR^b.

51. The compound or salt of any one of the preceding claims, wherein Y^6 is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, trifluoromethoxy, -C(O)N(H)Me, $-NMe_2$, and $-SO_2Me$.

52. The compound or salt of any one of claims 1-50, wherein Y^6 is N.

53. The compound or salt of any one of the preceding claims, wherein Y^7 is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, and trifluoromethoxy.

54. The compound or salt of any one of claims 1-52, wherein Y^7 is N.

55. The compound or salt of any one of the preceding claims, wherein Y^8 is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, trifluoromethoxy, -C(O)N(H)Me, $-NMe_2$, and $-SO_2Me$.

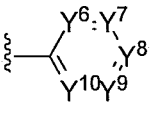
56. The compound or salt of any one of claims 1-54, wherein Y^8 is N.

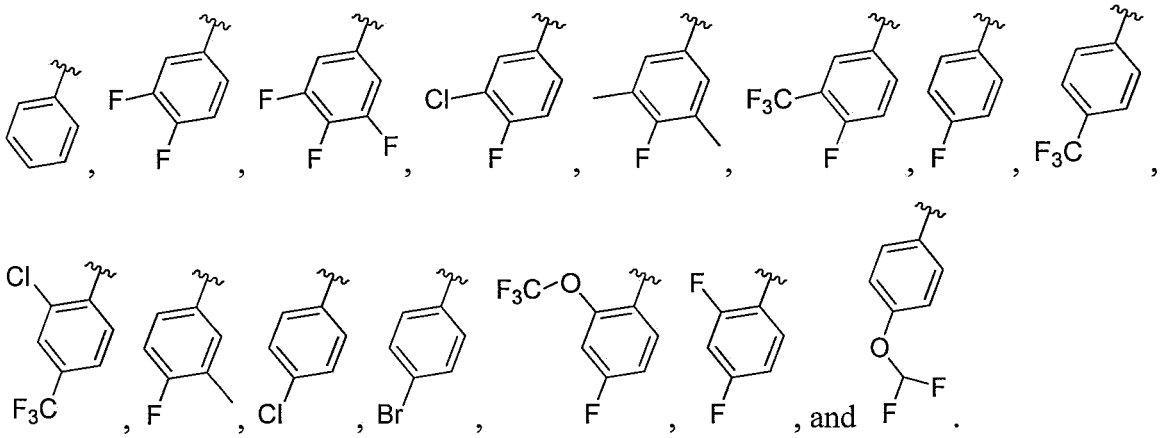
57. The compound or salt of any one of the preceding claims, wherein Y^9 is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, and trifluoromethoxy.

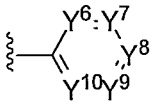
58. The compound or salt of any one of claims 1-56, wherein Y^9 is N.

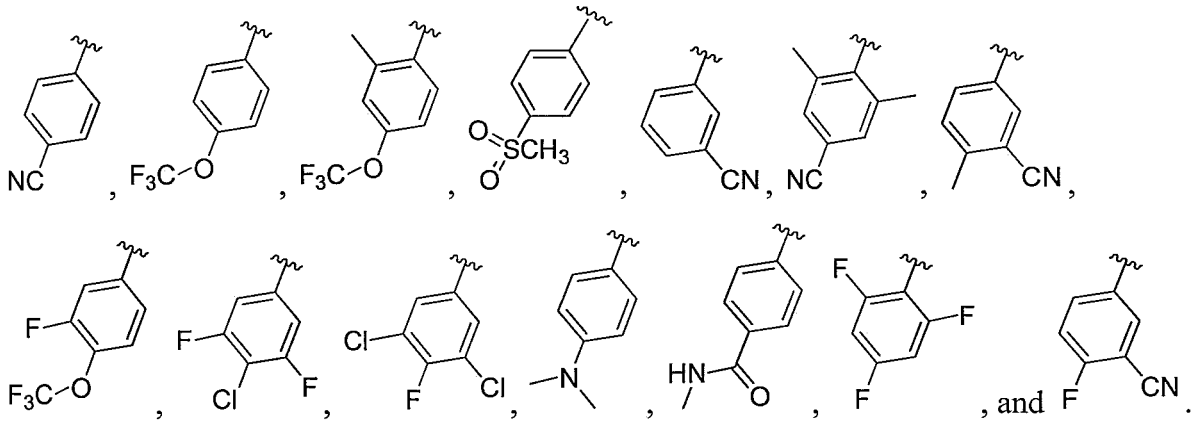
59. The compound or salt of any one of the preceding claims, wherein Y^{10} is CR^b, and R^b is a member selected from the group consisting of chloro, cyano, fluoro, methyl, trifluoromethyl, trifluoromethoxy, -C(O)N(H)Me, $-NMe_2$, and $-SO_2Me$.

60. The compound or salt of any one of claims 1-59, wherein Y^{10} is N.

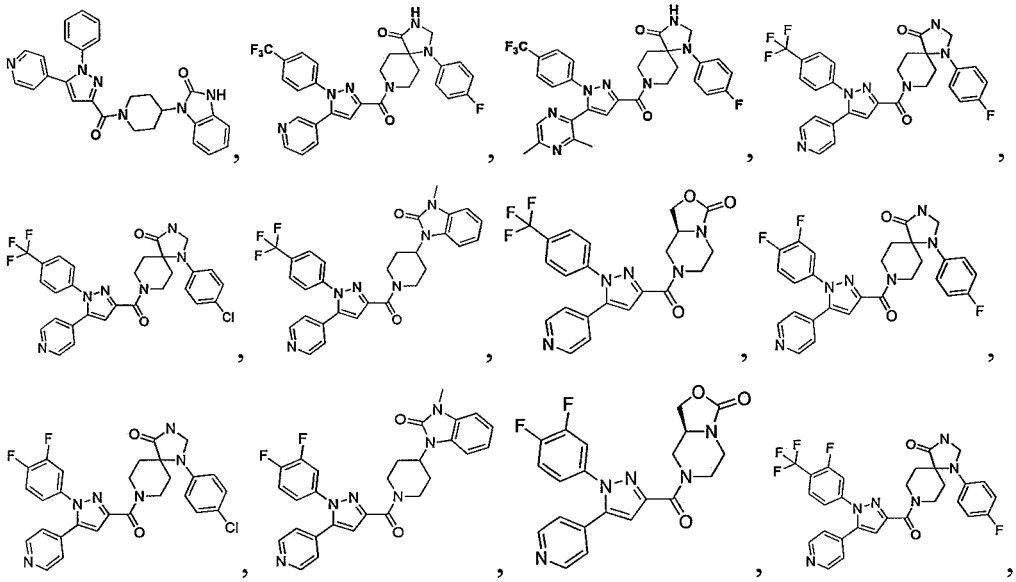
61. The compound or salt of any one of claims 1-50, wherein  is a member selected from the group consisting of:

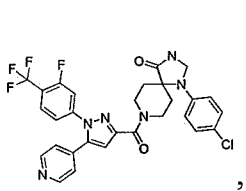


62. The compound or salt of any one of claims 1-50, wherein  is a member selected from the group consisting of:



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

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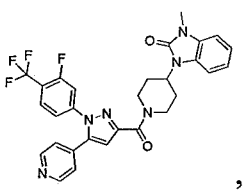
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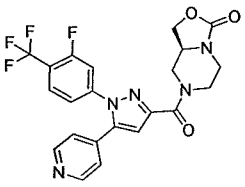
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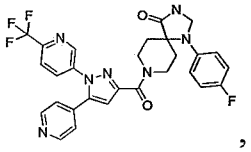
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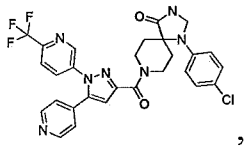
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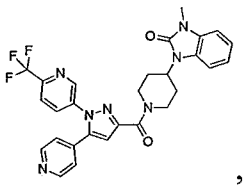
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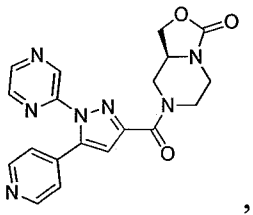
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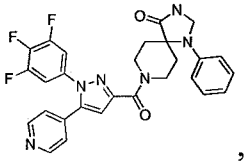
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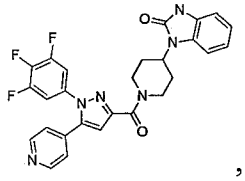
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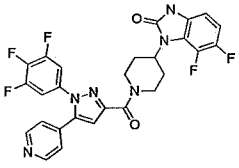
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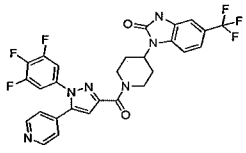
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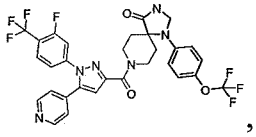
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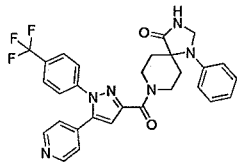
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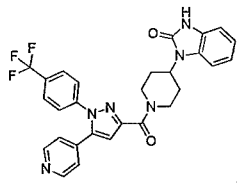
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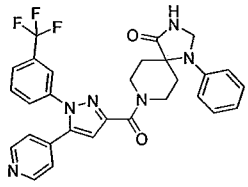
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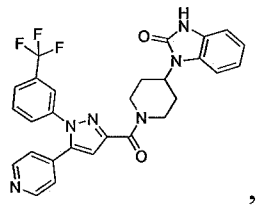
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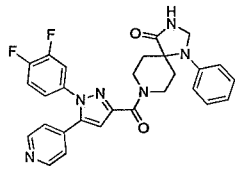
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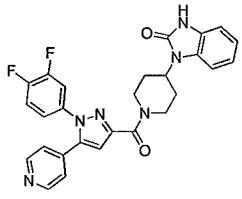
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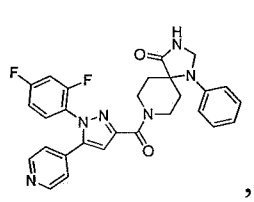
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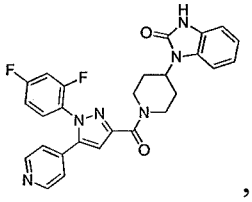
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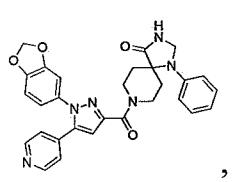
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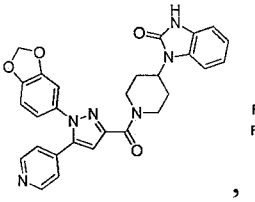
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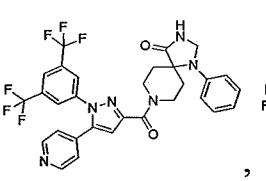
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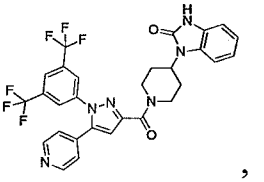
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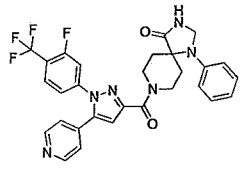
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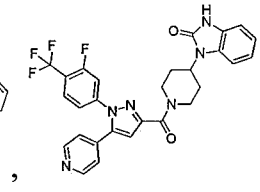
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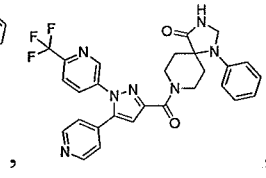
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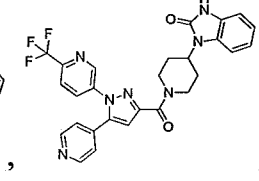
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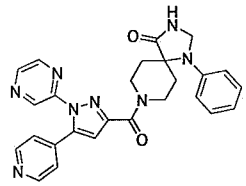
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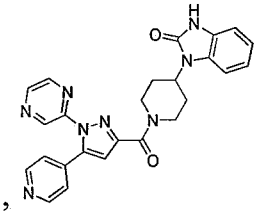
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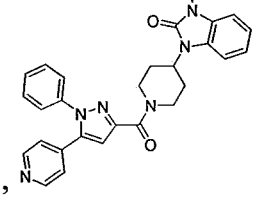
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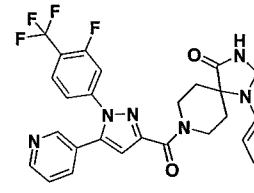
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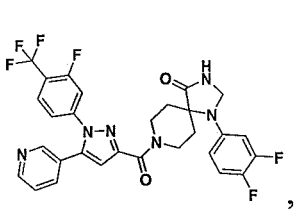
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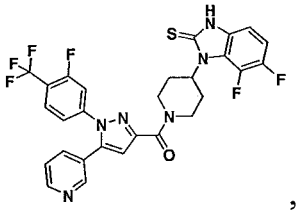
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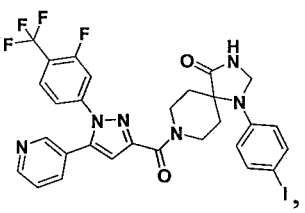
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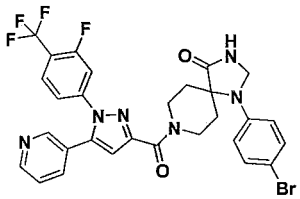
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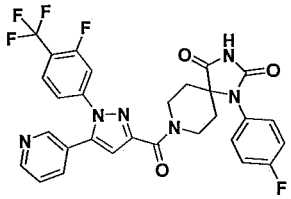
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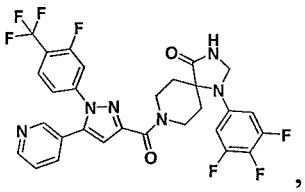
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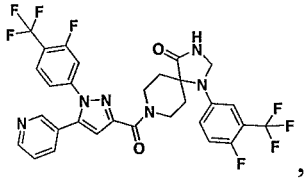
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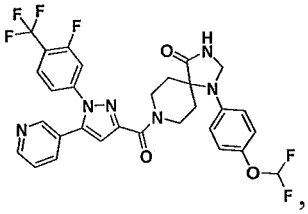
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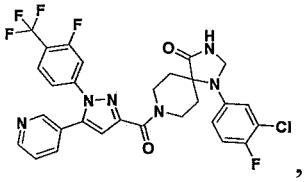
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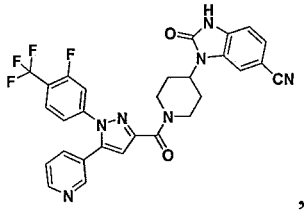
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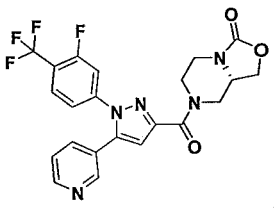
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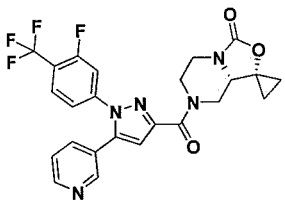
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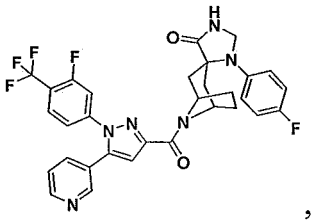
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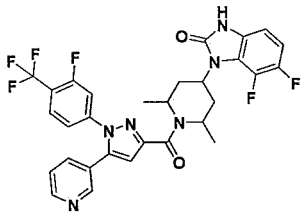
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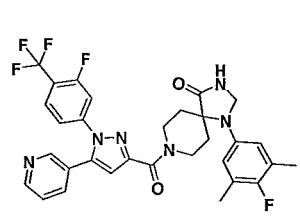
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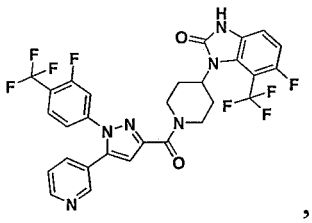
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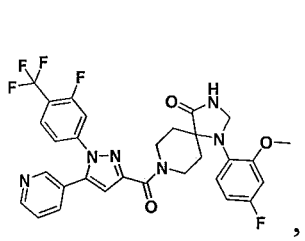
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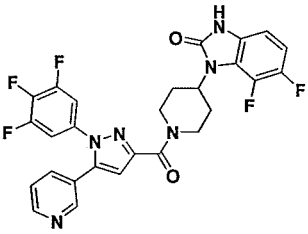
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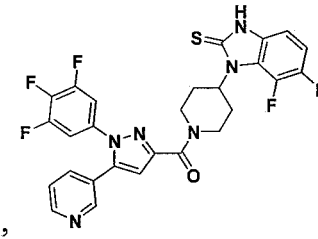
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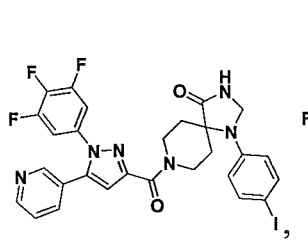
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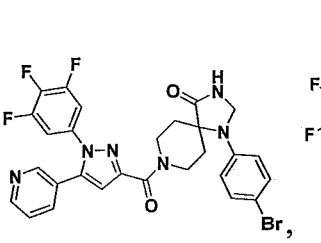
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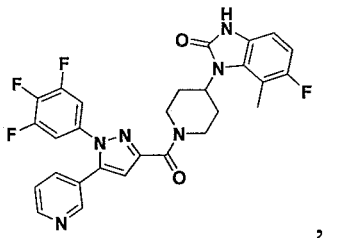
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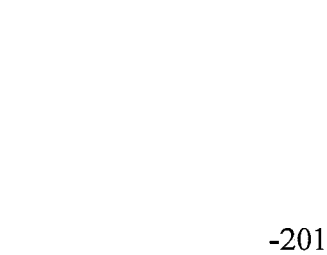
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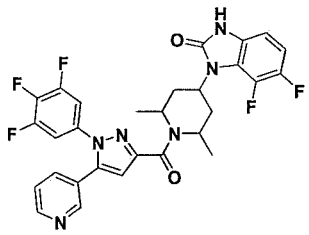
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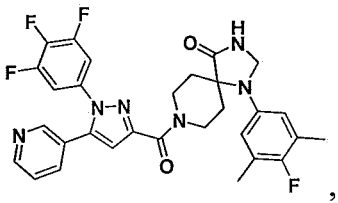
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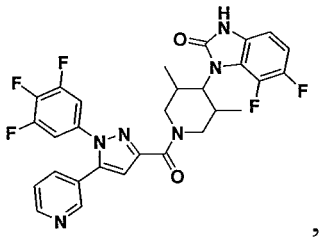
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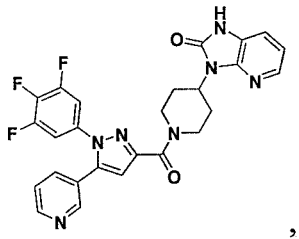
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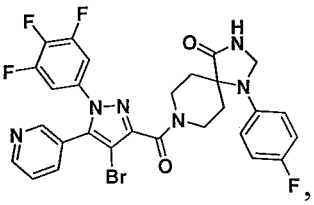
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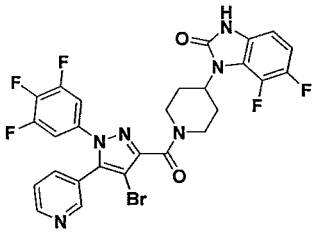
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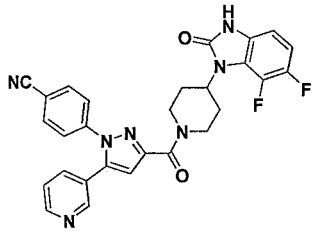
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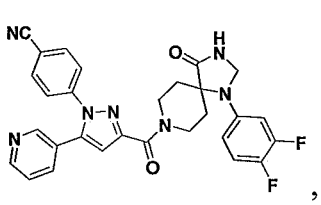
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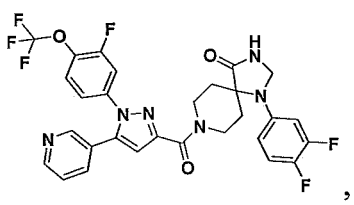
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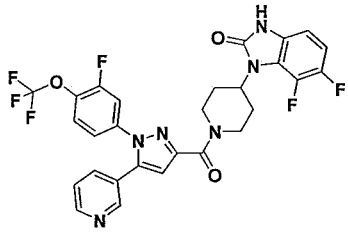
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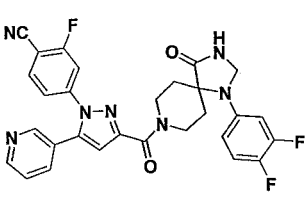
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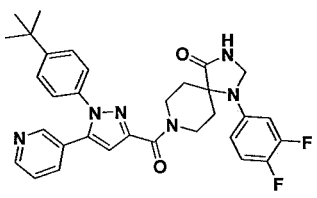
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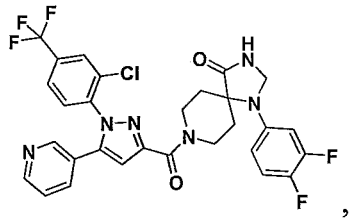
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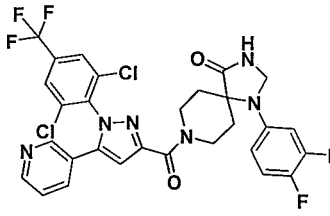
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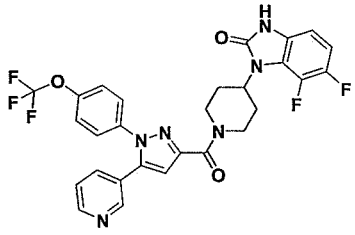
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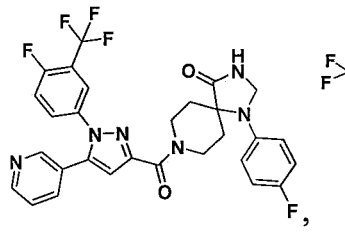
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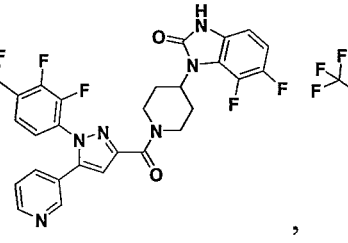
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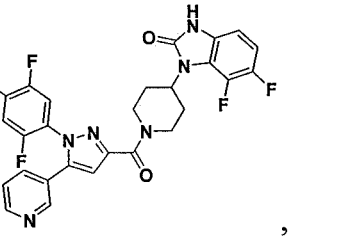
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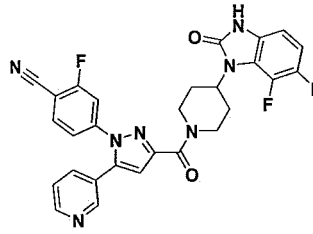
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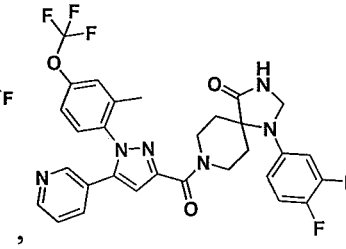
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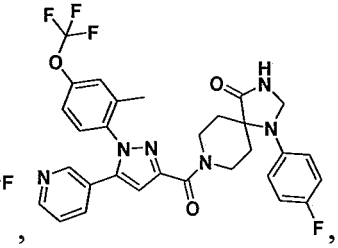
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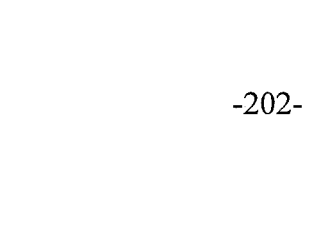
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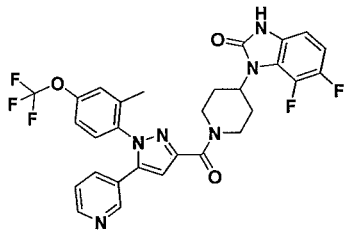
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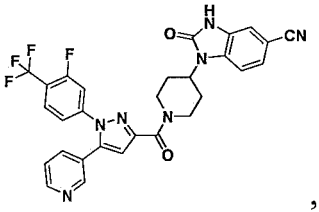
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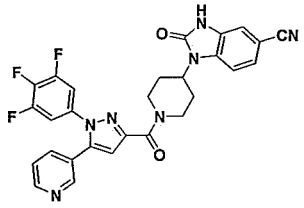
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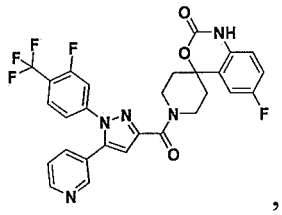
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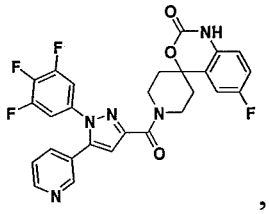
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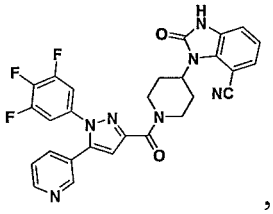
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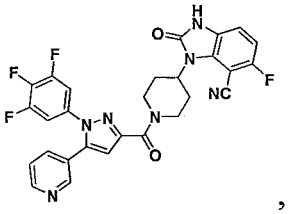
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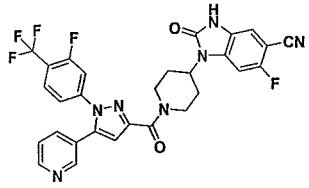
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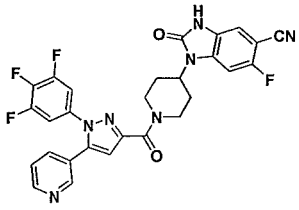
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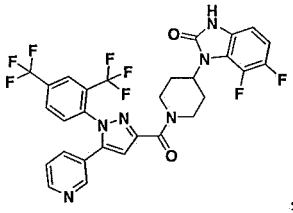
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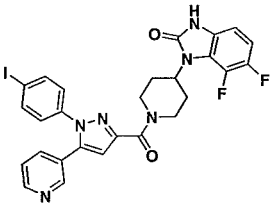
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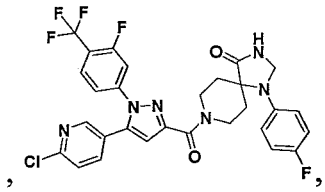
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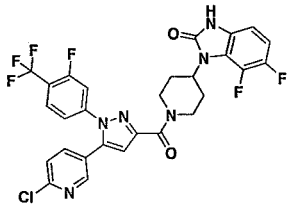
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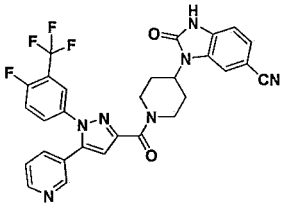
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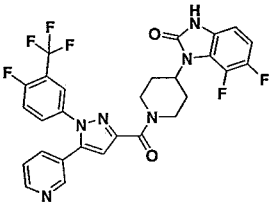
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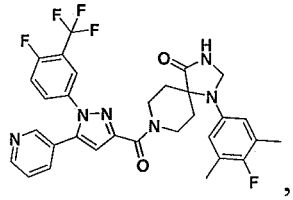
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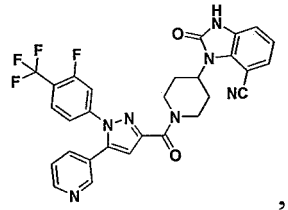
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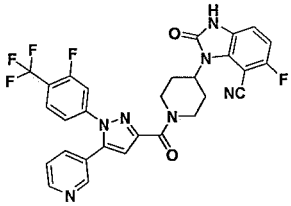
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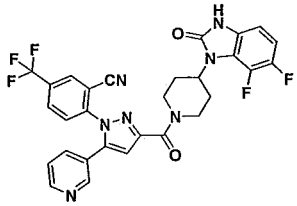
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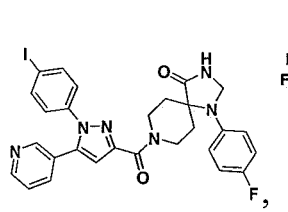
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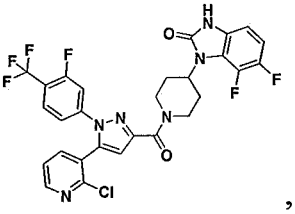
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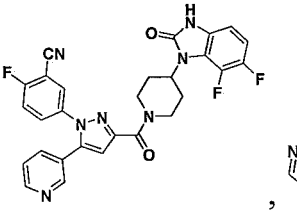
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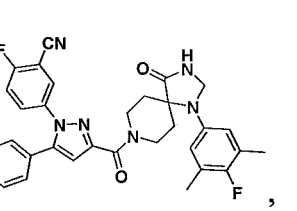
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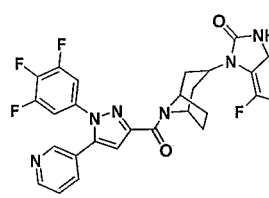
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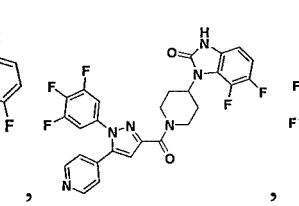
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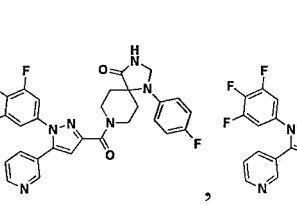
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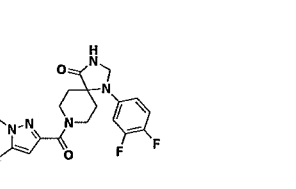
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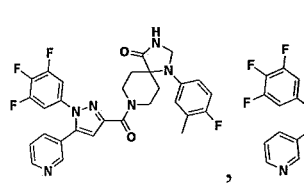
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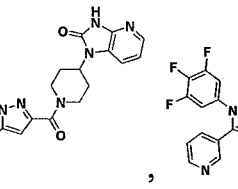
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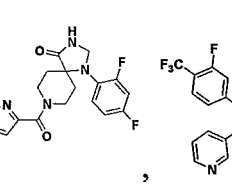
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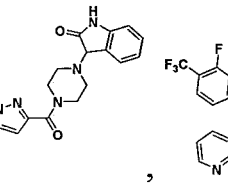
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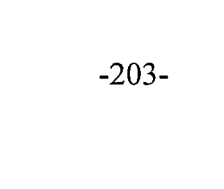
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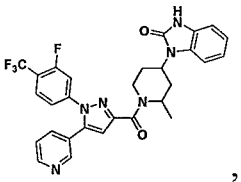
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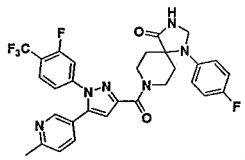
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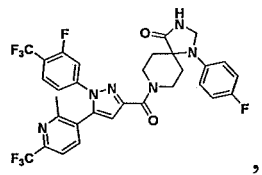
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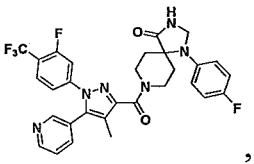
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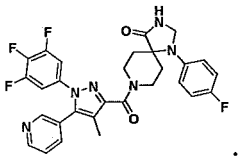
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64. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-63, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier, excipient, or diluent.

65. The pharmaceutical composition according to claim 64 further comprising a second therapeutic agent selected from the group consisting of: i) opioid receptor agonists, ii) opioid receptor antagonists, iii) calcium channel antagonists, iv) 5-HT receptor agonists, v) 5-HT receptor antagonists vi) sodium channel antagonists, vii) NMDA receptor agonists, viii) NMDA receptor antagonists, ix) COX-2 selective inhibitors, x) neurokinin receptor antagonists, including NK1 antagonists, xi) non-steroidal anti-inflammatory drugs, xii) selective serotonin reuptake inhibitors , xiii) selective serotonin and norepinephrine reuptake inhibitors, xiv) tricyclic antidepressant drugs, xv) norepinephrine modulators, xvi) 5-lipoxygenase inhibitors, xvii) cannabinoid receptor agonists, xviii) inhibitors of fatty acid amide hydrolase, ixx) beta-adrenergic receptor agonists, x) prostanoid receptor antagonists, xxi) leukotriene receptor antagonists, xxii) histamine receptor antagonists, xxiii) steroids, xxiv) CGRP antagonists, xxv) peroxisome proliferator-activated receptor (PPAR) agonists, and xxvi) acetaminophen.

66. The pharmaceutical composition of claim 64 or 65, wherein the composition is formulated as a solution or a suspension.

67. The pharmaceutical composition of any one of claims 64-66, wherein the composition is formulated for intraarticular, intravesical, intramuscular, intradermal, intraperitoneal, intraocular, intravitreal, intrathecal, subcutaneous, intravenous, or intravenous infusion administration.

68. Use of a therapeutically effective amount, or a prophylactically effective amount, of a compound of any one of claims 1-63, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating or preventing pain.

69. The use of claim 68, wherein pain comprises acute pain, chronic pain, inflammatory pain, neuropathic pain, nociceptive pain, or periprocedural pain.

70. The use of claim 68 or 69, wherein said medicament is to be administered with a second therapeutic agent selected from the group consisting of: i) opioid receptor agonists, ii) opioid receptor antagonists, iii) calcium channel antagonists, iv) 5-HT receptor agonists, v) 5-HT receptor antagonists, vi) sodium channel antagonists, vii) NMDA receptor agonists, viii) NMDA receptor antagonists, ix) COX-2 selective inhibitors, x) neurokinin receptor antagonists, including NK1 antagonists, xi) non-steroidal anti-inflammatory drugs, xii) selective serotonin reuptake inhibitors, xiii) selective serotonin and norepinephrine reuptake inhibitors, xiv) tricyclic antidepressant drugs, xv) antiepileptic drugs, xvi) 5-lipoxygenase inhibitors, xvii) cannabinoid receptor agonists, xviii) inhibitors of fatty acid amide hydrolase (FAAH), ixx) beta-adrenergic receptor agonists, xx) prostanoid receptor antagonists, xxi) leukotriene receptor antagonists, xxii) histamine receptor antagonists, xxiii) steroids, xxiv) CGRP antagonists, xxv) peroxisome proliferator-activated receptor (PPAR) agonists, and xxvi) acetaminophen.

71. The use of claim 70, wherein the 5-HT receptor agonist is a 5-HT_{1B} receptor agonist or a $5HT_{1D}$ receptor agonist.

72. The use of claim 70, wherein the 5-HT receptor agonist is a triptan.

73. The use of claim 72, wherein the triptan is sumatriptan, rizatriptan, naratriptan, zolmitriptan, eletriptan, almotriptan, or frovatriptan.

74. The use of claim 70, wherein the opioid receptor agonist is morphine, codeine, hydrocodone, oxymorphone, pentazocine, nalbuphine, fentanyl, sufentanil, tramadol, meperidine, methadone, or etorphine.

75. The use of claim 70, wherein the non-steroid anti-inflammatory drug is aspirin, ibuprofen, naproxen, ketoprofen, flurbiprofen, loxoprofen, indomethacin, etodolac, diflunisal, ketorolac, nabumetone, oxaprozin, piroxicam, meloxicam, or diclofenac.

76. The use of claim 70, wherein the COX-2 inhibitor is celecoxib, etoricoxib, lumiracoxib, parecoxib, rofecoxib, or valdecoxib.

77. The use of claim 70, wherein the second therapeutic agent is acetaminophen.

78. Use of a therapeutically effective amount, or a prophylactically effective amount, of a compound of any one of claims 1-63, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prevention of pain before, during or after surgical procedure.

79. Use of a therapeutically effective amount, or a prophylactically effective amount, of a compound of any one of claims 1-63, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prevention of pain associated with an interventional procedure, wherein the medicament is to be periprocedurally administered.

80. The use of any one of claims 68-79, wherein the therapeutically effective amount, or the prophylactically effect amount, of the compound is to be administered by intraarticular, intravesical, intramuscular, intradermal, intraperitoneal, intraocular, intravitreal, intrathecal, subcutaneous, intravenous, or intravenous infusion administration.